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Grado en Odontología

BUILDING BETTER ORAL HEALTH COMMUNITIES: ORAL HEALTH IN RARE DISEASE PATIENTS

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Resumen

Introducción: Las enfermedades raras, debido a su baja incidencia, a menudo son poco conocidas por los odontólogos. Estas enfermedades se presentan de diversas formas: desde alteraciones de la mucosa oral (por ejemplo, fibromatosis gingival) o alteraciones periodontales (como el síndrome de Papillon-Lefèvre), hasta alteraciones embriológicas que tienen manifestaciones craneofaciales y ortodóncicas (por ejemplo, craneosinostosis).

Es importante que los profesionales de la salud bucal comprendan el impacto de una afección para brindar consejos relevantes, ayudar a los pacientes a aliviar la sintomatología y educar acerca de los factores de riesgo.

Objetivos: Este estudio tiene como objetivo analizar la salud bucal en pacientes con enfermedades raras y sus necesidades. Una mayor comprensión debería dar pie a un diagnóstico más temprano por parte de los profesionales de la salud bucal.

Al educar sobre los factores de riesgo con estrategias a medida, esperamos reducir la incidencia de daño irreversible de la cavidad oral (como la caries y la enfermedad periodontal en la fibrosis quística y el síndrome de Prader-Willi) y mejorar la calidad de vida.

Materiales y métodos: Los artículos científicos se han seleccionado utilizando criterios de inclusión y exclusión, tales como el idioma (inglés o español) y el tiempo (dentro de los diez años). Entre las palabras clave, cabe destacar: enfermedades raras, salud bucal, ortodoncia y periodoncia.

Asimismo, se han empleado bases de datos como PubMed, MedLine, Cochrane y UEM Biblioteca-CRAI.

Resultados: En esta investigación, se han seleccionado veintiséis tipos de enfermedades raras. Se describen las manifestaciones orales y las opciones de tratamiento. Doce son periodontales y gingivales, ocho craneofaciales y nueve de ortodoncia. En seis de ellas se observaron patologías de las mucosas y en otras nueve un aumento de la caries.

Discusión de los resultados: Las encuestas de calidad de vida demuestran infelicidad e insatisfacción, especialmente con las alteraciones estéticas. Se han encontrado inequidades en el tratamiento de ciertos tipos de enfermedades raras en contraste a otras. Se han incluido recomendaciones para enfoques de tratamiento en enfermedades categorizadas según su manifestación.

Conclusiones: Los odontólogos, como proveedores de atención primaria, tienen el deber de cuidar a sus pacientes, incluidos aquellos con afecciones menos conocidas. Este estudio tiene como objetivo proporcionar una idea de estas condiciones y resaltar los problemas que enfrentan quienes las padecen. Un enfoque multidisciplinario integrado es fundamental para aumentar la confianza y la satisfacción del paciente.

Abstract

Introduction: Rare diseases, due to their low incidence, are often poorly understood by dental practitioners. These diseases have many presentations, including alterations to oral mucosae (for example Gingival Fibromatosis), periodontium (including Papillon–Lefèvre syndrome) and diseases with embryological alterations have craniofacial and orthodontic manifestations (for instance craniosynostosis).

It is important that oral health professionals understand a condition's impact to provide relevant advice, assist patients to alleviate symptomatology, and educate on risk factors.

Objectives: This study aims to review oral health in rare diseases and patient needs. Greater understanding should assist earlier diagnosis by oral care professionals.

In educating on risk factors with bespoke strategies, we hope to reduce incidence of irreversible oral cavity damage (such as tooth decay and periodontal disease in Cystic Fibrosis, and Prader-Willi syndrome), and improve quality of life.

Materials and Methods: Scientific articles were selected using inclusion and exclusion criteria, including language (English or Spanish) and time (within ten years). Key words included rare diseases, oral health, orthodontics, and periodontics. We utilised databases including PubMed, MedLine, Cochrane, and UEM Biblioteca-CRAI.

Results: From this research, we selected twenty-six distinct rare diseases. We described oral manifestations and treatment options. Twelve were periodontal and gingival, eight craniofacial, and nine orthodontic. Six included mucosal pathologies and nine increased carious decay.

Discussion of Results: Quality of life surveys demonstrated unhappiness, and dissatisfaction, especially with aesthetic alterations. Inequities were found regarding treatment of certain types of rare diseases received over others. We made recommendations for treatment approaches in diseases categorised by manifestation type.

Conclusions: Dentists, as primary care providers, have a duty of care to their patients, including those with less well-known conditions. This study aims to provide an insight into these conditions and highlight issues facing those with them. An integrated multi-disciplinary approach is crucial to increase patient trust and satisfaction.

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Introduction

Rare diseases are defined in Europe as those with fewer than five cases per ten thousand, and those with approximately one case per one thousand five hundred in the United States. Understandably, this acutely low incidence rate has resulted in poor public awareness, as well as reduced understanding by dental practitioners. These diseases have a wide range of etiopathological origins and presentations. (1,2)

These manifestations include oral mucosa abnormalities (in conditions including Gingival Fibromatosis and Prader-Willi Syndrome), periodontal alterations (such as in Cystic Fibrosis and Von Willebrand Disease), as well as a number of rare diseases with manifestations of craniofacial and orthodontic significance related to alterations in embryological development (including Craniosynostosis and Marfan syndrome). Syndromes may also manifest in various ways, including sensory deficiency. Those with facial anomalies may cause complications with normal oral function. Many rare diseases can cause psychological and emotional distress, which may also result in reduced awareness of the importance of good oral hygiene routines. Furthermore, some of these diseases can be life-threatening. (3)

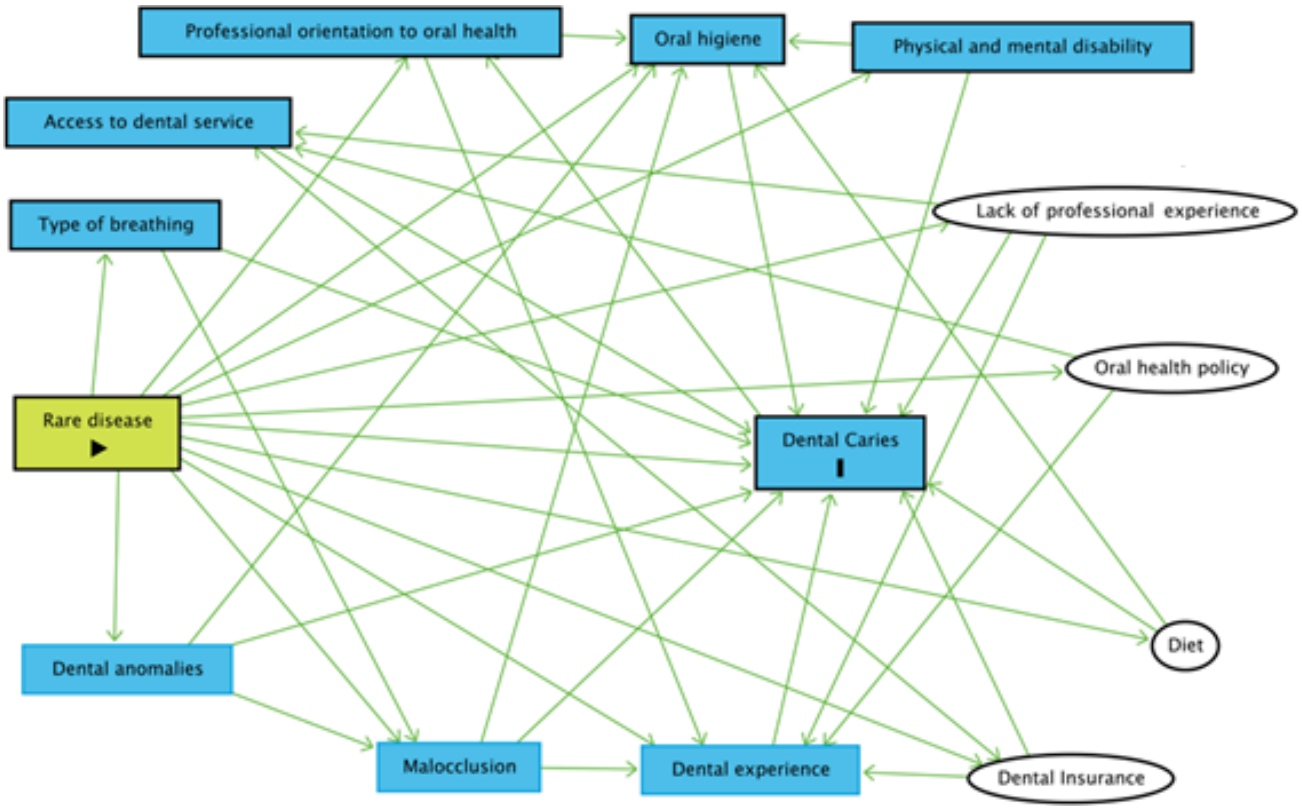


Figure 1: A directed acyclic graph showing the influence of different factors in rare diseases on the apparition of dental caries. Amongst these factors, mouth breathing, malocclusions, as well as dental anomalies can increase the likelihood of the development of dental caries. (4)

The study and observation of rare diseases in the oral cavity has a long history. For example, *Dentinogenesis imperfecta,* was first recorded in the nineteenth century. (5) Research suggests approximately fifteen percent of rare diseases present orofacial manifestations, and in the over five thousand genetically inherited syndromes, over nine hundred show a maxillofacial, dental, or oral association. The Orphanet Journal on Rare Diseases records over 2153 diseases with head and neck affectation. Across different countries, many initiatives have been created to better categorise and understand such rare diseases. The diverse range of manifestations in these diseases' present unique

challenges in their understanding. Novel genetic research has been known to cause recategorization of such diseases. (3,6)

One such project is the creation of the ROMSE (*recording of orofacial manifestations in people with rare diseases*) database, which began in 2011 in Germany, which categorises diseases with such manifestations that were recorded in the Orphanet Journal of Rare Diseases by the specific manifestations they present. The ten principal

categories employed by this database are shown below. (6)

Main groups of orofacial manifestations in ROMSE	No. of diseases
Anomalies of the lips (without clefts)	43
Craniofacial malformations	12
Dysgnathia	145
Haemorrhagic diathesis	10
Neoplasia	24
Changes in the oral mucosa and tongue	135
Bone diseases	11
Anomalies of the cleft	145
Dental anomalies	187
Other	26

Figure 2: The ten principal categories of orofacial signs on the ROMSE database and the number of diseases that show them. (6)

The ROMSE database enables diseases to be categorised with their primary and secondary characteristics, which can be easily searched. The database has proven to be a very useful tool and has been mentioned in some of the case reports that will be referenced later in this article. The system of categorisation mentioned above will be employed in this review.

Alongside reduced awareness, significant disparities in access to appropriate medical diagnosis, care and treatment exist. In a French study, poorer health outcomes were

seen in rural areas than in the capital city for rare diseases of the Head, Neck and Teeth, requiring patients to travel long distances. Better national co-ordination and improvement was suggested. (3)

Descriptions of conditions

The rare orofacial diseases discussed in this review are described in the following principal categories set out above. Due to the multisystemic nature of many diseases, some of the diseases described below may also exhibit characteristics of other categories. Special emphasis has been made towards orofacial symptoms of these diseases, which in many cases are multi-systemic.

Anomalies of the lips (without clefts)

Hereditary haemorrhagic telangiectasia

A vascular disorder causing the transfer of blood from arterial vessels to veins instead of capillaries. This causes the apparition of abnormal red spots on the surface of the lips, mouth surfaces, tongue, and skin surfaces. The condition is autosomal dominant. (7)

Craniofacial malformations

These conditions refer to malformations in the skull and face. The etiological origins for these syndromes are congenital abnormalities in embryological layers caused primarily by genetic aberrations. (8)

Cleft Lip and Palate

Cleft Lip and Palate are two congenital conditions, sometimes combined, in which a failure of union in the formation of the lip and/or palate occurs. The condition is

multifactorial and can affect speaking as well as feeding and may affect tooth development. (9)

Craniosynostosis

A condition where bones in the skull fuse early. As a result, normal growth of the skull is impeded, and morphological changes are observed in the face, with skeletofacial and orthodontic manifestations. The condition is autosomal dominant or recessive. (10)

Dysgnathia

This term refers to situations in which the development of the jaw and masticatory system is altered.

Congenital ectodermal dysplasia

A systemic condition with childhood onset where the ectodermal embryological layer is altered, causing alterations to ectodermal structures which include tooth size, shape, and structure, and might also cause missing teeth (hypodontia). Asialism (reduced salivary secretion) is also observed. The condition is of autosomal dominant inheritance. (2)

Williams syndrome

Also a systemic condition with childhood onset, where alterations such as micrognathia, defects in tooth enamel, and malocclusions can be observed. The condition is also of autosomal dominant inheritance. (2)

Congenital erythropoietic porphyria

A form of porphyria. Complications can include cicatrisation and blistering. Etiologically, the condition is caused by disruptions in the haem group (of Blood) synthesis pathway. It is an autosomal recessive condition. The condition can result in lesions in the upper and lower maxillae, as well as the cranium. Onset varies from early childhood to adulthood. (2,11)

Haemorrhagic diathesis

These refer to conditions where the likelihood of spontaneous bleeding is increased, many due to clotting disorders. These diseases may be congenital and inherited or acquired. (12)

Haemophilia A and B

These refer to two congenital coagulation disorders, in which clotting factors (VIII and IX respectively) are deficient. The two are related to mutations on the X chromosome. (13)

von Willebrand's disease

This refers to a genetic coagulation disorder resulting from a deficiency in a clotting factor known as von Willebrand Factor (vWF). It is an autosomal dominant trait. (13)

Neoplasia

Neoplasias refer to conditions in which tumours (areas of abnormal tissue growth) are present. Neoplasias may be benign or malignant, with the latter being an area of far greater concern, due to uncontrolled growth and metastasis. (14)

Leukaemia

A type of blood cancer caused by increased leucocyte count due to over synthesis in the bone marrow. (15)

Changes in the oral mucosa and tongue

Hereditary gingival fibromatosis

A hereditary condition causing gingival hyperplasia in the maxilla and mandible and consequent dislocation of teeth. (16)

Mucous membrane pemphigoid

A condition causing erosion and blistering in the subepithelial layer, which affects the skin and oral mucosa. It can cause cicatrisation. Complications may include loss of sight and in some cases, death. (17)

Epidermolysis bullosa acquisita

A systemic autoimmune condition resulting in blistering in mucous membranes. It can also cause cicatrisation. Complications may include loss of sight and in some cases, death. (17)

Papillon–Lefèvre syndrome

A condition causing a very early onset periodontitis, gingivostomatitis, and thickening of the keratin layer of the skin. The condition may lead to early loss of the primary and permanent dentition. The onset of the condition is multifactorial, with autosomal recessive inheritance. (18)

Bone diseases

These refer to conditions affecting the bones of the skeletal system. In Dentistry, conditions affecting the bones of the skull can manifest in a number of different ways, including periodontal destruction and orthodontic complications.

Langerhans cell histiocytosis

A systemic condition in which an excess of Langerhans-type cells are produced, which can replicate the conditions of aggressive periodontal inflammation and destruction. The lesion may also cause lesions in the skull and viscera. (2,19)

Osteogenesis imperfecta

A systemic condition in which bone fragility is increased through mutations in the collagen synthesis pathway. Osteogenesis imperfecta may cause malocclusions, gingival hyperplasia, as well as delayed dental eruption. It is closely linked with Dentinogenesis imperfecta type 1 (which is mentioned on the next page). Genetically, it is inherited in an autosomal dominant manner, but may also arise from novel mutations. (2,5,20)

Prader-Willi syndrome

Prader-Willi syndrome is a syndrome of multisystemic affectation which may cause intellectual disability, as well as low bone density and osteoporosis. It also is known for causing dental erosions and causing feeding problems in children. (1,21)

Hypophosphatemic rickets

This refers to a condition in which mineralisation of teeth and bone is altered by disrupted absorption of Calcium and Vitamin D. This can lead to weak and fracturable bones, as well as poor periodontal attachment, causing loss of teeth. (2,19)

Marfan syndrome

Marfan syndrome refers to a connective tissue disease with systemic manifestations. Most commonly caused by a mutation, with symptoms that include dental and orofacial alterations. (2,22)

Cri du Chat syndrome

A syndrome resulting from a partial chromosomal deletion. Alongside intellectual disability, the syndrome may cause dental and skeletofacial abnormalities. The condition may also be responsible for generalised chronic periodontal inflammation, in addition to inadequate oral hygiene due to the difficulty in cleaning the altered dental anatomy as well as intellectual challenges with learning how to take care of oral health. In some cases, cleft palate can also be observed. (1,23)

Dental anomalies

This refers to anomalies in dental shape, size, or number.

Bardet-Biedl Syndrome

An autosomal recessive condition resulting in a number of dental and craniofacial abnormalities. (24)

Otodental syndrome

A systemic condition which involves hearing loss, and the key diagnostic criterion is globodontia (enlarged teeth with a bulbous morphology). (25)

Dentinogenesis imperfecta

An autosomal dominant condition affecting both deciduous and permanent teeth. The condition has three types, the first of which (as previously mentioned) is associated with osteogenesis imperfecta. The second exhibits similar symptoms but without such association, and the third is extremely rare and geographically localised. (5)

Others

These refer to other types of rare diseases which have orofacial manifestations. Many of these are systemic diseases.

Loeys- Dietz syndrome

A connective tissue disorder. The orofacial characteristics of this disease have not yet been researched adequately but include orthodontic and dental manifestations. The syndrome also manifests in temporomandibular joint problems. (26)

Granulomatosis with Polyangiitis

A systemic autoimmune condition causing periodontal inflammation and gingival hyperplasia due to blood vessel inflammation, as well as manifestations in other viscera. (19)

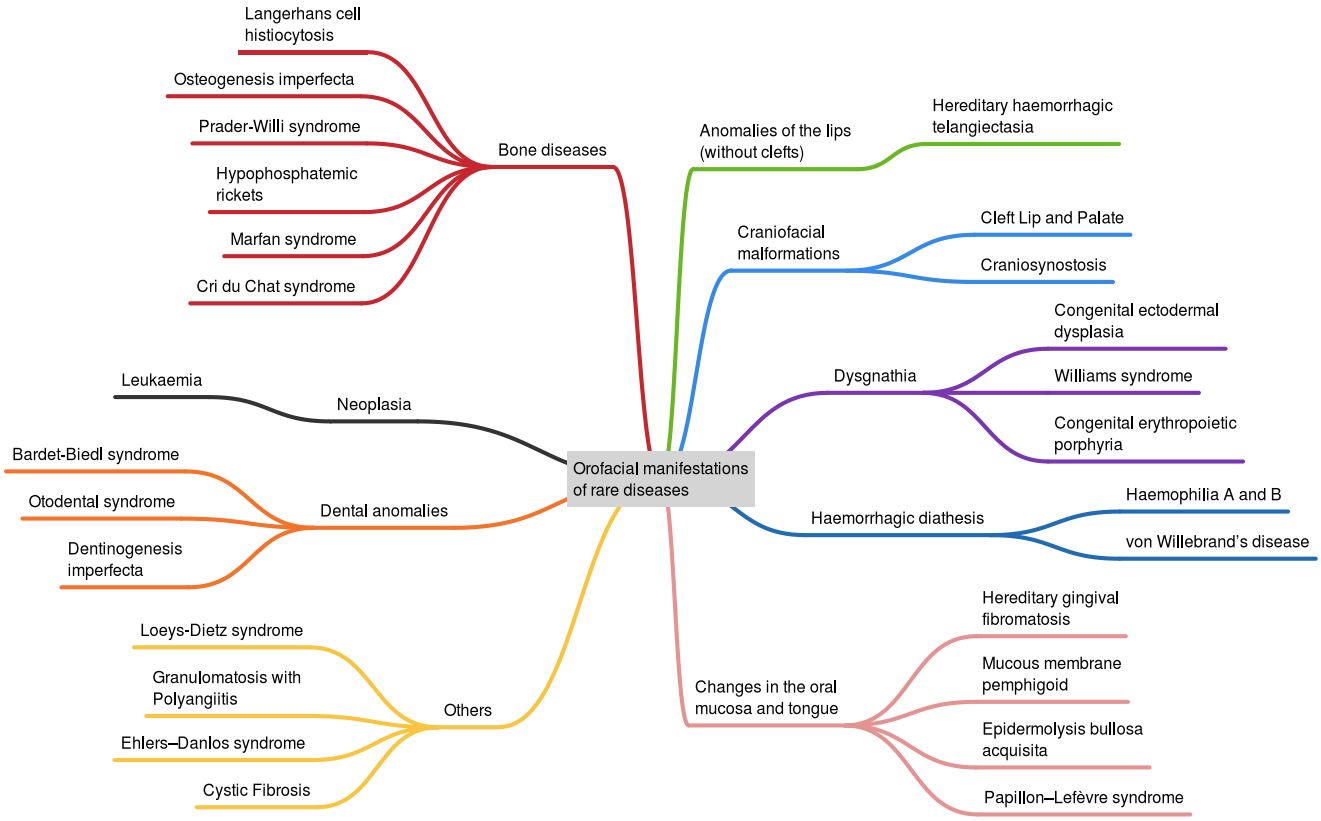
Ehlers–Danlos Syndrome

A systemic connective tissue disorder. It also has manifestations in joints, cicatrisation, and the skin and is known to cause advanced periodontal destruction. (19)

Cystic Fibrosis

A systemic condition predominantly known for the production of viscous mucous, but also with significant oral manifestations in terms of salivary production, and increased risk of dental caries. (1,27)

Summary



Condition	**Symptomatology**	**Frequency** (28)
Hereditary haemorrhagic telangiectasia	Vascular disorder causing abnormal red spots.	1 per 10,000
Cleft Lip and Palate	Failure of union in the formation of the lip and/or palate.	5 per 10,000
Craniosynostosis	Premature fusion of bones in the skull.	3-5 per 10,000
Congenital ectodermal dysplasia	Alterations to ectodermal structures which include tooth size, number, shape, and structure.	~ 1 per 100,000 live births
Williams syndrome	Causes micrognathia, defects in tooth enamel, and malocclusions.	~ 1 per 10-20,000
Congenital erythropoietic porphyria	Scarring and blistering as well as lesions in the upper and lower maxillae.	<1 per 1,000,000
Haemophilia A and B	Two congenital coagulation disorders where clotting factors (VIII and IX) are deficient.	~ 2 per 10,000
von Willebrand's disease	A genetic coagulation disorder where levels of von Willebrand factor (vWF) are reduced.	~ 3 per 10,000
Hereditary gingival fibromatosis	Gingival hyperplasia in the maxilla and mandible and tooth dislocation.	1 per 175,000
Mucous membrane pemphigoid	Erosion and blistering in the subepithelial layer. Can cause ciciatrisation and potentially death.	1 per 500,000 to 770,000
Epidermolysis bullosa acquisita	Causes blistering in mucous membranes, and cicatrisation. Complications include loss of sight and potentially, Death	1 per 96,200
Papillon–Lefèvre syndrome	Causes premature onset periodontitis, gingivostomatitis, and thickening of the keratin layer of the skin. It may lead to early loss of the primary and permanent dentition	1-9 per 1,000,000

Loeys-Dietz syndrome	Poorly researched. Includes malocclusions (overbite and crowding), enamel defects, and a narrow, high palate. It also manifests in TMJ problems.	*Unknown*
Granulomatosis with Polyangiitis	A systemic condition causing periodontal inflammation and gingival hyperplasia due to blood vessel inflammation.	1-9 per 100,000
Ehlers–Danlos Syndrome	A systemic disorder. As well as manifestations in joints, cicatrisation, and the skin, it is known to cause advanced periodontal destruction.	~2 per 10,000
Cystic Fibrosis	A systemic condition known to produce viscous mucous, but also significant oral manifestations such as salivary production, and increased risk of dental caries.	1-9 per 100,000
Bardet-Biedl syndrome	A condition causing a high arched palate, as well as reduced tooth number, reduced root size, and tooth crowding.	1-9 per 1,000,000
Otodental syndrome	A systemic condition. It involves hearing loss and is diagnosed through globodontia (enlarged bulbous teeth). Also involves enamel hypoplasia and greater morphology on molar fissures - both of which increase caries risk. Associated with dentinogenesis imperfecta.	<1 per 1,000,000
Dentinogenesis imperfecta	A condition affecting both the primary and secondary dentitions. The first type is associated with osteogenesis imperfecta. The second exhibits similar symptoms but without such association, and the third is extremely rare and geographically localised.	1-5 per 10,000
Leukaemia	A type of blood cancer caused by increased leucocyte count due to over synthesis in the bone marrow	22-57 per 100,000
Langerhans cell histiocytosis	Where an excess of Langerhans-type cells are produced, which can cause aggressive periodontal inflammation and destruction. May also cause lesions in the skull and viscera.	1-9 per 100,000
Osteogenesis imperfecta	Where bone fragility is increased. Osteogenesis imperfecta may cause a Class II division 1 malocclusion, gingival hyperplasia, as well as delay dental eruption. Closely linked with Dentinogenesis imperfecta type 1.	1-5 per 10,000
Prader-Willi syndrome	A syndrome of multisystemic affectation which may cause intellectual disability, as well as low bone density and osteoporosis. Also causes dental erosions and feeding problems in children.	1-9 per 100,000
Hypophosphatemic rickets	Where mineralisation of teeth and bone is altered by disrupted absorption of Calcium and Vitamin D. Can lead to weak bones with fracture risk, as well as poor periodontal attachment, causing tooth loss.	>1 per 20,000
Marfan syndrome	A systemic disease. Symptoms include dysgnathia, a highly arched palate morphology with dental crowding, hyperplasia in the upper and lower maxillae, mandibular retrognathia, altered number of teeth, as well as malocclusions (including overbite and dental crowding).	1-5 per 10,000
Cri du Chat syndrome	Alongside intellectual disability, the syndrome may cause malocclusion, mandibular migroretrognathia, and enamel hypoplasia. Can also cause chronic periodontal inflammation, inadequate oral hygiene and delayed dental eruption. Cleft palate is seen in some cases.	1 per 15,000 to 45,000

To conclude, this study proposes that it is important that dental and other oral health professionals are able to understand the impact of these diseases with the objective of providing relevant oral healthcare planning and advice for their patients. Practitioners should assist patients to reduce the symptomatology of these diseases where possible and identify and educate patients on risk factors they should keep in mind that may not be acutely present in the general population as a whole, in order to have a direct impact on the oral health of these patients.

Objectives

The objectives that we will review are as follows:

Primary Objective

To educate and inform on a number of rare diseases to oral health professionals. This is intended to:

a. Raise awareness and provide increased understanding of the specific needs of patients with these conditions. The specific and unique needs of patients with these diseases should be better known as a result.
b. Enable better, and earlier recognition of signs and symptoms of such diseases, especially in situations where oral health professionals are the best placed to identify such diseases (such as in developmental alterations).

Secondary Objectives

In addition to our primary objective, we intend to:

a. Encourage oral health professionals to use this information to provide guidance and advice for patients. In doing so, we hope to diminish many risk factors associated with the diseases covered in this review. One aim is to reduce the incidence of irreversible damage to the oral cavity, such as tooth decay and periodontal disease in the case of patients with Cystic Fibrosis and Prader-Willi syndrome.
b. Provide bespoke health strategies where appropriate, for patients with complex or numerous healthcare demands and requirements. An oral care plan can be devised; where necessary, other health care professionals can also be consulted in a multi-disciplinary approach.

Materials and Methods

The scientific articles chosen in this review have been selected using an exhaustive inclusion and exclusion criteria. These criteria include:

a. the language of publication (in either English or Spanish)
b. the time of publication (within the last ten years)
c. having full-text available
d. an individual assessment of the quality of the article, using
    a. the journal's impact factor
    b. the number of citations for the article itself
e. whether any existing or potential biases or conflicts of interest may have influenced the results of the study in question
f. relevance and scope with respect to the objectives of this review

Key words and MeSH terms were used during research, which include "rare diseases", "oral health", "orthodontics", "oral medicine", and "periodontics". Such research was conducted using a number of different databases, including PubMed, Google Scholar, MedLine, the Cochrane Database of Systematic Reviews, and the UEM Biblioteca CRAI.

Furthermore, the oral diseases chosen have been categorised depending on the types of manifestation they present (mucosal, periodontal, developmental alterations to hard tissues, and others).

The reliability of the research referenced in this article is underscored by the use of journals with high impact factors, such as the Orphanet Journal of Rare Diseases (IF 3.61), International Journal of Oral Science (IF 3.05), Cochrane Database of Systematic Reviews (IF 3.09), Clinical Oral Investigations (IF 2.9), Journal of Oral Pathology & Medicine (IF 2.82), and Journal of Oral Rehabilitation (IF 2.70).

Figure 3: The article research and selection process for this review

Results

In this section, we will discuss the different strategies for management of the rare diseases that have been described in this study. Recommendations will be made for general dental practitioners, as well as for specialised dental practitioners, such as orthodontists, periodontists, as well as paediatric dentists.

Of the twenty-six diseases studied, twelve had periodontal and gingival manifestations, eight craniofacial manifestations, and nine orthodontic manifestations. Furthermore, six had implications for mucosal pathologies and nine for increased cariogenicity.

Periodontal and Mucosal symptoms

Many rare diseases exhibit signs and symptoms of periodontal destruction. The pathological presentation of Langerhans cell histiocytosis resembles the conditions of aggressive periodontitis (19), causing gingival inflammation, periodontal destruction, bleeding, recession, and loss of alveolar bone. In different scenarios, a variety of treatment options may be employed. One case report involved the use of scaling and root planning in conjunction with chlorhexidine rinses and prescription of antibiotics. (29) Another described the use of chemotherapy alongside gingival debridement and tooth splinting as a method of arresting alveolar bone destruction. (30)

Hereditary gingival fibromatosis and Granulomatosis with Polyangiitis refer to conditions in which gingival hypertrophy is observed. In Hereditary gingival fibromatosis, this was accompanied with other observations including supragingival biofilm, crown destruction, periodontal ligament widening and tooth displacement. Surgical treatments were used. These consisted of gingivectomies and gingivoplasties. The

surface of cicatrisation was protected from mechanical trauma using an acetate splint adhered to study models using surgical cement.(16) Gingival hyperplasia may also be seen as a minor manifestation in Marfan syndrome. (2,22)

Granulomatosis with Polyangiitis on the other hand, presents a gingivitis which may include also a "strawberry appearance" in both maxillae as well as periodontal inflammation. As a disease which can cause death if not detected within time, it is crucial for a fast diagnosis. Treatment consists of immunosuppressants. (31)

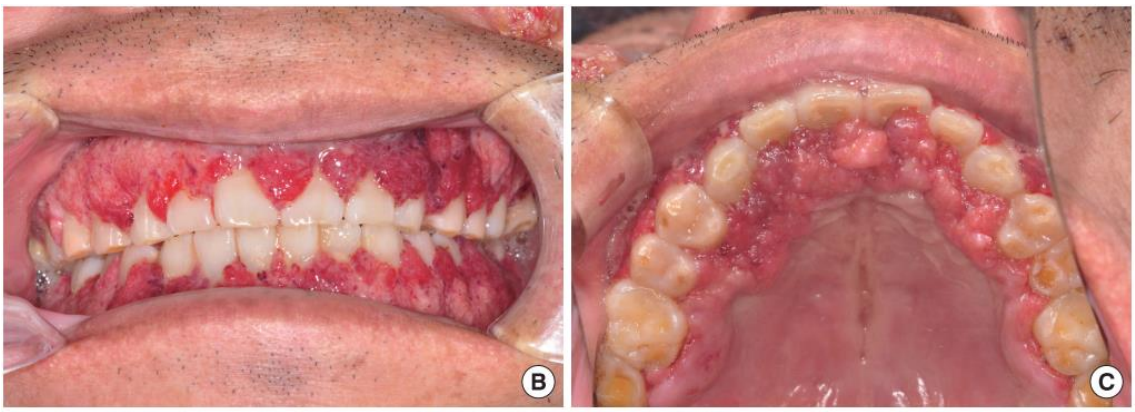


Figure 4: The clinical appearance for Granulomatosis with Polyangiitis. The "strawberry"-like inflammation in the upper and lower gingivae can be seen. (31)

As previously mentioned, Papillon–Lefèvre syndrome is associated with periodontitis, and gingivostomatitis which may lead to early loss of both dentitions. Treatment consists of the use of scaling and root planning in conjunction with chlorhexidine rinses and prescription of antibiotics. Furthermore, extraction of primary teeth may be indicated in prognostically poor cases. Fabrication of prosthetic appliances during the mixed dentition phase to restore occlusion may be required. (18)

One type of Ehlers–Danlos Syndrome is associated with advanced periodontal destruction, spontaneous haemorrhagia intramucosally and gingivally, as well as

reduced thickness of gingival and mucosal tissue. Treatments consist of a combination of educative measures, as well as non-surgical periodontal measures which may include prophylactic treatment. Where necessary, antibiotic prescription as well as administration of topical fluoride may be indicated. (19,32)

Hypophosphatemic rickets also causes poor periodontal health. The periodontal situation of patients should be carefully monitored by the responsible oral care professional. (2,19,33)

In contrast to the diseases mentioned above, Cystic Fibrosis is linked with a lower risk of gingival inflammation. (27,34)

Epidermolysis bullosa acquisita and Mucous Membrane Pemphigoid are rare diseases which present manifestations in the oral mucosa with scarring/cicatrisation and may produce respiratory complications that may cause disability and threaten life. Both conditions are detected using immunofluorescence. Treatment consists of corticosteroid prescription (which may be either oral or topical). When undertaking dental treatment, fillings should be very polished, short instruments and burs used, and great care must be taken to avoid blister formation during the placement of anaesthetic. (17,35)

Haemophilia A and B, and Von Willebrand's disease refer to systemic bleeding disorders. They can cause symptoms which include postponed bleeding, spontaneous gingival bleeding, as well as ecchymosis and nasal bleeding. Furthermore, poor periodontal health is observed, and the presence of dental caries is often found in patients with these conditions, which may originate in anxiety over the production of bleeding during toothbrushing by these patients, and consequently avoiding essential aspects of oral

health care. Desmopressin is prescribed to increase coagulation factors in cases of Haemophilia A and Von Willebrand's disease, whilst concentrates of Prothrombin are prescribed for Haemophilia B. (13)

Hereditary haemorrhagic telangiectasia refers to a vascular disease. It is most commonly noted due to the symptom of red spots in the labial, lingual, palatal and gingival surfaces. Basic dental treatments, such as prophylactic cleaning, toothbrushing or use of dental floss may cause spontaneous haemorrhagia. When undertaking dental treatment, antibiotic prophylaxis may be required. A medical professional will use medical imaging to check the prognosis of the condition, and interconsultation with the physician in charge is recommended. Treatments may include embolisation, laser therapy and coagulation. (7,13,36)

Whilst manifesting more greatly in the scope of dental and skeletofacial malformations, Cri du Chat syndrome also causes generalized chronic periodontitis. Due to poor oral health, calculus and dental recession may be observed. To preserve oral health, restorative treatments (such as caries removal) are required, along with preventive treatments (such as demonstrating to the child and their parents an adequate tooth brushing technique). (23)

Developmental alterations: Orthodontic, Skeletofacial and Dental

A number of rare diseases in this review present manifestations of developmental importance. As previously mentioned, in Cleft Lip and Palate a failure of union in the formation of the lip and/or palate occurs. The condition causes problems with phonation and may result in disrupted tooth development (with dental malformations), and/or tooth agenesis. In addition, increased angulation of the palate may be observed. Treatment involves surgery between 12-18 months of age, as well as dental and orthodontic treatments. (2,9)

In Craniosynostosis, premature bone fusion causes impediment of normal growth of the skull, resulting in facial morphological changes. Alongside this, Maxillary Hypoplasia (underdevelopment of the upper maxillae), and a Class III malocclusion may be seen alongside dental alterations. The disease may also be caused by hypophosphatemic rickets. Early diagnosis is crucial in ensuring developmental damage is prevented. Diagnosis is often conducted by a medical professional based on discomfort the child faces, often due to increased intracranial pressure. Surgical treatment is necessary, primarily cranial surgery, but also orthognathic surgery. Such treatment will involve orthodontic, dental and craniofacial surgery professionals working together. (2,10)

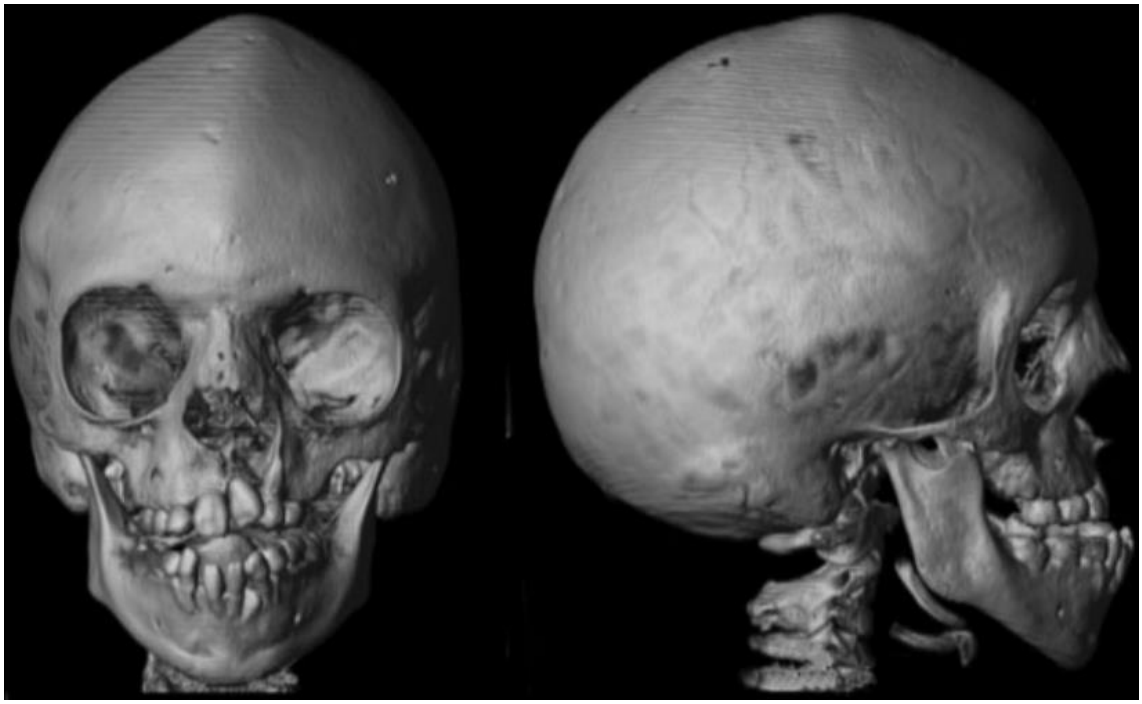


Figure 5: A computer tomography-based reconstruction of the face of a six-year-old boy with Craniosynostosis. Along with an anterior open bite, maxillary hypoplasia and a Class III malocclusion can be observed. (10)

Congenital ectodermal dysplasia is a developmental disease which causes a number of dental changes. These include hypodontia, and altered tooth morphology, in terms of a more pointed or pegged shape, taurodontism (enlarged crown and pulp anatomy with reduced root size), and enamel hypoplasia. Reduced salivary flows are observed. (2) Treatment may involve the use of prosthetic appliances or implants, even at a very young age. (37)

Williams syndrome results in a smaller upper maxillary width, reduced tooth size and defects in enamel, and malocclusions. Cranial alterations, such as flattened zygomatic bones, wider mouth size, and reduced jaw size are also observed. There is currently an absence of adequate treatment protocols for the disease, and contemporary treatment options involve medical vigilance, pharmacotherapy, surgical treatment, as well as phonatory and behavioural treatment. (2)

Osteogenesis imperfecta is known to cause bone fragility and deformity. It also however may cause an orthodontic Class II division 1 malocclusion, gingival hyperplasia, as well as postponed dental eruption. No cure for the condition is available, but orthodontic treatment is commonly indicated. (2,20)

As previously mentioned, the disease is related to dentinogenesis imperfecta type 1, a condition which causes malocclusion and postponed dental eruption. (2)

Marfan syndrome symptoms include dysgnathia, a highly arched palate morphology with a long skull, dental crowding, hyperplasia in the upper and lower maxillae, mandibular retrognathia, altered number of teeth, as well as malocclusions (including overbite and dental crowding). The syndrome has no treatment, but orthognathic and orthodontic surgeries may be used to reduce tooth crowding and retrognathia of the mandible. (2,22)

Alongside the previously mentioned periodontal manifestations, the Cri du Chat syndrome presents malocclusion, mandibular microretrognathia, anterior open-bite, and enamel hypoplasia, as well as inadequate oral hygiene and delayed dental eruption. In some cases, cleft palate can also be observed. Surgical treatment for malocclusion correction is indicated to improve the functional occlusion of the patient. (1,23)

Bardet-Biedl Syndrome is a rare disease with a high arched palate, as well as gingival hyperplasia, reduced tooth number, reduced root size, and tooth crowding. The condition also presents malocclusions and may result in Xerostomia due to mouth breathing. Treatment is complicated by behavioural changes (as patients may exhibit an autism-like behaviour) with attention deficit and cognitive impairment. Behavioural techniques such as “tell-show-do” are useful. Furthermore, treatment is complicated

by the systemic conditions the disease manifests. Patients maybe taking dialysis, in which case, the nephrologist must be consulted before invasive procedures such as gingivectomies. Antibiotic prophylaxis and the use of local anaesthetics without vasoconstrictors (such as Mepivacaine) are recommended. (24)

Loeys - Dietz syndrome is an extremely rare disease requiring further research. It is however known that symptoms include malocclusions (overbite and crowding), a bifid uvula, enamel defects, and a narrow, high palate. The syndrome also manifests in temporomandibular joint problems.(26)

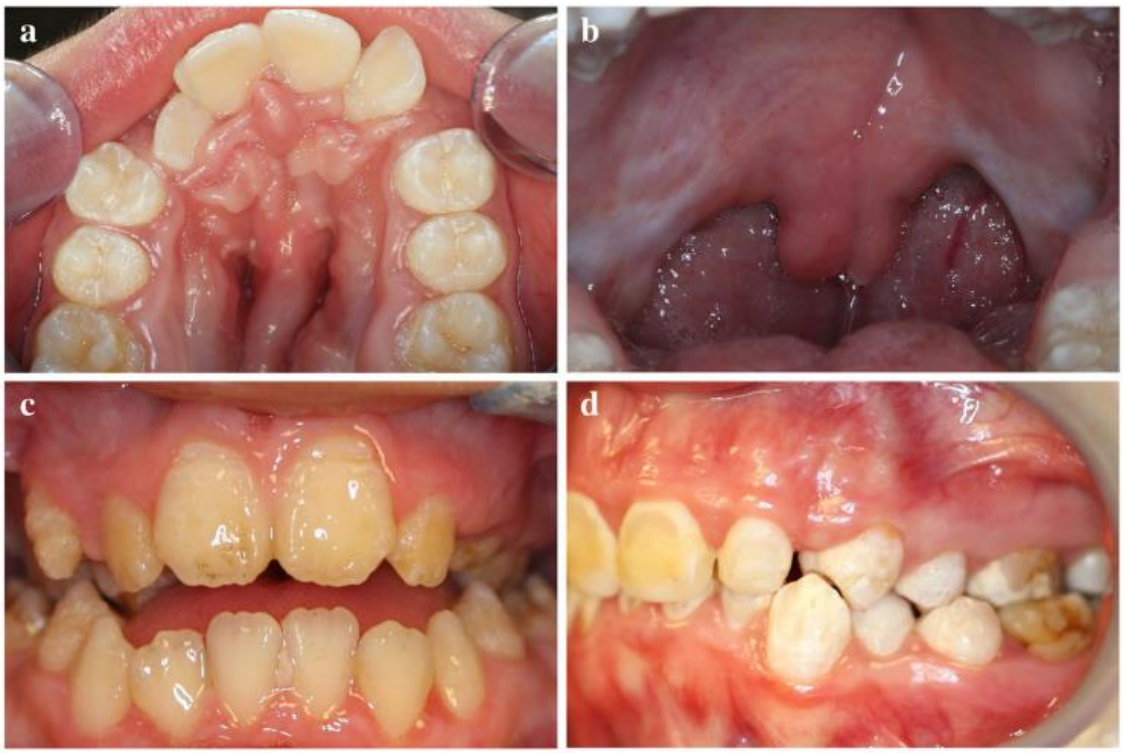


Figure 6: The clinical appearance of the Loeys - Dietz syndrome. The narrow, high palate, bifid uvula, along with structural defects in enamel and malocclusion can be recognised. (26)

Congenital erythropoietic porphyria may cause lesions in the upper and lower maxillae, cranium, and red pigmentation in the teeth. Treatments include transfusions of blood, as well as transplantation of stem cells and bone marrow. (2,11)

Multifactorial

Prader-Willi syndrome manifests a micro-mandible, reduced mouth size, low bone density and osteoporosis, however the main concern for oral health professionals relates to dental caries, erosions, candidiasis, periodontitis, gingivitis, abscesses, oral mucosal alterations such as angular chelitis, and feeding problems in children. Hypotonia also causes problems with phonation. In addition, the condition manifests sialorrhea and mouth breathing. (1,21)

Leukaemia, a blood cancer, can cause a number of manifestations, such as localised or generalised gingival hyperplasia, petechiae and bruising in the soft and hard palate, as well as spontaneous gingival haemorrhagia. Furthermore, the side effects of chemotherapy may cause immunodepression and increased cariogenicity. Chemotherapy may also cause candidiasis, pain and xerostomia. In children who have received chemotherapy, enamel hypoplasia may be seen along with distorted root development. If possible, it is important to conduct dental treatments prior to radiation. Radiographs are used as a diagnostic tool. Interconsultation with the oncologist is necessary. (38)

It is also extremely important to explain to the patient the types of changes they will see after their surgical treatment and radiation, ranging from mucositis and xerostomia to cavities, trismus, dysphagia, and in the longer term, osteonecrosis. As a result, we should advise the patient to adjust their diet as appropriate if they experience mucositis;

and use topical anaesthesia and artificial saliva which can be purchased in pharmacies, as well as 0.05% clobetasol propionate. (39)

We should also advise the patient to take 100 ml of water with salt and bicarbonate to help prevent candidiasis infections. (39)

Sodium fluoride gel 1% as well as reinforcing hygiene techniques can help prevent caries by radiation, which is a significant risk due to the patient's prior abundance of plaque.(39) It is advised that the patient wears a superior and inferior leaded prosthesis, impressions of which will be sent to the lab (one week prior to radiotherapy). (40)

Dental decay

Otodental syndrome presents globodontia (enlarged teeth with a bulbous morphology) as the key diagnostic sign. The condition involves enamel hypoplasia, which combined with the accentuated morphology on molar fissures, increases risk of caries. It has been associated with dentinogenesis imperfecta. In a case report, masticatory problems were observed. Teeth with globodontia also present an increased risk of endo-perio lesions due to accentuated coronal and pulpal morphology. Thus, preventive measures to arrest risk of caries development are crucial, such as the application of topical fluoride. (25,41)

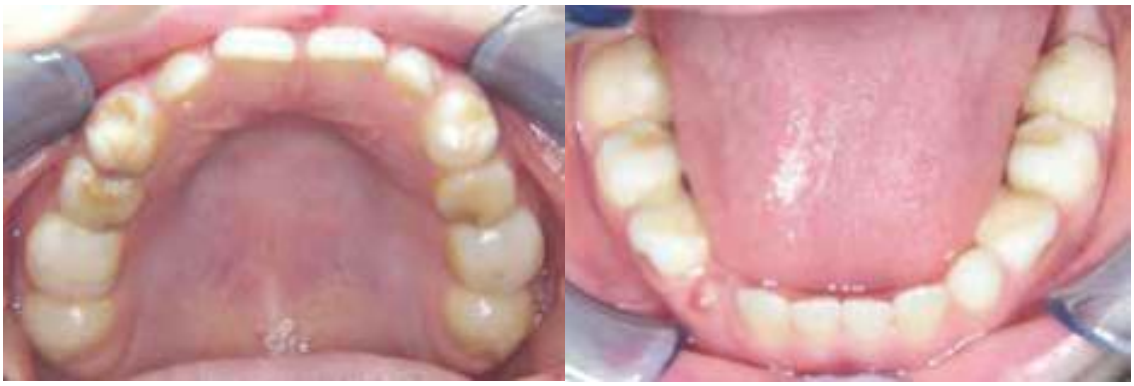


Figure 7: An intraoral patient examination of the upper and lower arches in otodental syndrome. The characteristic sign of globodontia is visible in the molars.

(41)

Another systemic disease, Cystic Fibrosis, is known to increase risk of dental decay and calculus. It has been suggested that increased salivary production may disturb the saliva buffer rate and salivary antibacterial properties. Other challenges include gastroesophageal reflux, changes to enamel structure and the requirement of increased calorie intake to maintain an adequate weight. Preventative measures are recommended. (1,27)

Discussion

In this section, we have analysed the concerns of patients with respect to their quality of life in different studies, and the ramifications of these with respect to treatment programmes for oral care professionals. We suggest certain recommendations about strategies to be adopted.

A study by *Toupenay et al* focused on the quality of life and care provided to patients by surveying patients with questionnaires. The study included two groups, the first with patients who had a disease including a dental component and the second where the patients had a rare disease without such component. The study found a clear association between dental problems such as absence of teeth, periodontal problems, untreated cavities, and a negative consequence for quality of life, along with other personal and environmental factors.

Patients suffering from a rare disease with a dental component were four times less likely to have fewer than twenty natural teeth. Within this group of patients, prosthetic rehabilitation requirements were high, but only satisfied in 17.4% of cases, which may be related to the cost of such treatments.

In terms of impacts on quality of life described by patients, psychological distress was the main factor, with limitations in function, social disability and physical discomfort also being recorded. (42)

In a separate questionnaire study by *Friedlander et al* in children and adolescents, poorer oral health quality of life levels were found in girls than in boys due to the social pressure towards self-appearance, and patients and parents reported challenges

towards their oral health in their daily life, which include problems brushing teeth, pain, complications with mastication, changes in tooth pigmentation, restrictions in the aperture of the mouth, a reduced surface for chewing as well as lower levels of saliva. The feeling of isolation and being different to other children was also a key factor in relation to lower levels of quality of life. Rarer diseases resulted in a greater likelihood of renouncing oral care.

Peculiarly, patients with cleft-related diseases reported a higher quality of life than those with non-cleft related dental rare diseases. This may be due to well organised and funded treatment plans, including psychological support for patients with such diseases whilst such strategies do not yet exist for patients with non-cleft related dental rare diseases. (3)

To build better oral health communities, more work must be done to achieve greater equity in access to healthcare and assistance and reduce disparities with the general population.

As part of our research, we suggest treatment plans to be used as a basis for approaching rare diseases with each of the following categories, and any potential interconsultations with other healthcare professionals that may be needed:

Type of rare disease	Treatment plan	Potential interconsultations required
Periodontal	Recognise the individual rare disease in question and any medications being taken along with medical and family history. Refer the patient for specialist care where you are the first to identify a condition. Where required, enact a plan of action for regular check-ups, periodontal studies, and reducing periodontal and gingival inflammation, including the use of prophylactic cleaning, scaling and root planning, gingival debridement and chlorhexidine rinses in conjunction with other healthcare professionals. Educate the patient on the additional actions they must take to preserve their periodontal and general oral health, and where increased likelihood of bleeding causes anxiety, reassure the patient to continue their oral health routine (such as tooth brushing) despite this.	General medical practitioners Periodontists (for advanced periodontal treatment) Hygienists (prophylactic cleaning) Haematologists (where significantly increased bleeding is present) Oral and general pathologists Special care dentistry Medical geneticists Paediatric dentistry (where applicable)

		Medical and psychological support
Mucosal	Identify the type of mucosal condition present. Review the medications being taken (such as corticosteroids) along with the medical history of the patient. Refer the patient for specialist care where you are the first to identify a condition and liaise to create an appropriate plan of action for dental treatment. Be careful not to provoke inflammation or blister formation during treatment where this is a risk. Such a risk can be mitigated through care towards selection of appropriate dental instruments, burs, and precaution on placing anaesthetic. If the mucosal condition causes bleeding, the patient should be aware of this and be reassured as with in periodontal conditions.	General medical practitioners Oral and general pathologists (mucosal) Haematologists (where significantly increased bleeding is present) Dermatologists Paediatric dentistry (where applicable) Special care dentistry Medical and psychological support

Skeletofacial, Orthodontic and Dental	Recognise the individual rare disease in question and any medications being taken along with medical and family history. Refer the patient for specialist care where you are the first to identify a condition. In skeletal and orthodontic conditions, this can include referral for orthodontic or maxillofacial care. Liaise with the medical and dental specialists to create a plan of action. In dental related diseases, such referrals can include orthodontic (for correction of malocclusions), restorative (where dental tissue structures need restoration and/or decay is present), and prosthetic and/or implant dentistry (to resolve agenesis or teeth in a poor prognostic condition).	General medical practitioners Orthopaedic medicine Maxillofacial surgeons Orthodontists Medical geneticists Paediatric dentistry (where applicable) Special care dentistry Dental Prosthetists, Implantologists and Restorative Dentists (dental related rare diseases) Medical and psychological support

Multifactorial	Recognise the individual rare disease in question and any medications being taken along with medical and family history. Refer the patient for specialist care where you are the first to identify a condition. Multifactorial diseases will present systemic manifestations. For this reason, it is especially important to be aware of medical treatments planned or undertaken. For example, in the case of patients treated for cancer, it is advisable to resolve issues of dental decay prior to the start of chemotherapy. A bespoke plan of action should be created in consultation with the appropriate healthcare professionals. Where necessary, special care dentists may be best placed to undertake such a plan of action.	General medical practitioners Specialist medical, dental and psychological support (depending on specific case, includes pathologists, haematologists, oncologists, medical geneticists, internal medicine and many other specialities along with surgeons)

Conclusions

Dentists are often the primary care providers who can make a diagnosis in cases of rare diseases, which manifest themselves in a disparate number of ways. For this reason, it is essential that increased training about their manifestations and their further management is provided. Furthermore, there is a prescient need for dentists to better understand the requirements of such patients to better assist them with their oral health needs. This requires a multi-disciplinary approach integrating the support of medical professionals, general dental practitioners, and specialist oral health care providers. Effort should be made to provide care within a local setting where possible to maximise patient comfort.

The research undertaken demonstrates that rare diseases have unique requirements with challenges. Quality of life surveys demonstrated unhappiness, concerns and dissatisfaction, especially where aesthetic alterations (such as alterations or agenesis of teeth) were present, which caused great psychological distress to patients and was ranked of greater concern by patients than alterations in function. Of greatest concern was the inequitable level of support for patients with certain rare diseases over others, as noted in the study by *Friedlander et al*, where patients with a less “visible” condition (non-cleft related rare diseases) reported a lower quality of life than those presenting a more visible condition (cleft related rare diseases). Properly addressing issues of patient self-esteem and satisfaction must therefore be key in any treatment undertaken.

The information provided in this study provides an opportunity for change and improvement in the approach taken to sufferers of such conditions. We hope that increased communication between oral health professionals and medical professionals can produce a unified approach, with greater understanding and empathy towards patients.

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Annexes

Journal section: Medically compromised patients in Dentistry
Publication Types: Review

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Impact of rare diseases in oral health

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Abstract

Background: Rare diseases (RD) are those that present a lower prevalence than 5 cases per 10.000 population. The main objective of this review was to study the effect on oral health in rare diseases, while the secondary objective of the study is theme upgrade.

Material and Methods: Comparative observational case-control studies were analysed and a systematic review was conducted in PubMed. Each rare disease listed on the statistical data record of the Health Portal of the Ministry of Equality, Health and Social Policies Board of Andalusia was associated with "oral health". The variables studied included dental, oral mucosa and occlusion alterations, oral pathologies (caries, periodontal disease) and other alterations (mouth breathing, parafunctional habits, etc). A bias analysis of the variable caries was conducted.

Results: Six RD were selected through our inclusion and exclusion criteria (hypogammaglobulinemia, Rett syndrome, Marfan syndrome, Prader-Willi syndrome, cystic fibrosis and Cri du chat syndrome) in a total of 8 publications, of which four trials were classified as high risk of bias and one of them as medium risk. There were not trials with low risk of bias.

Conclusions: The main statistically significant differences found by Syndrome compared to a control group were in Hypogammaglobulinemia with a greater tendency to enamel hypoplasia and dry mouth. The Rett syndrome had, as well, a greater tendency to an anterior open bite, ogival palate, bruxism, mouth breathing and tongue thrusting. Prader-Willi syndrome had a tendency of dental erosion, and Cri du chat syndrome showed a higher association to *Tannerella forsythia*.

Key words: *Rare diseases, oral health.*

REVIEW ARTICLE OPEN

Dental-craniofacial manifestation and treatment of rare diseases

En Luo[1], Hanghang Liu[1], Qiucheng Zhao[1], Bing Shi[1] and Qianming Chen[1]

Rare diseases are usually genetic, chronic and incurable disorders with a relatively low incidence. Developments in the diagnosis and management of rare diseases have been relatively slow due to a lack of sufficient profit motivation and market to attract research by companies. However, due to the attention of government and society as well as economic development, rare diseases have been gradually become an increasing concern. As several dental-craniofacial manifestations are associated with rare diseases, we summarize them in this study to help dentists and oral maxillofacial surgeons provide an early diagnosis and subsequent management for patients with these rare diseases.

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INTRODUCTION

Recently, the National Health and Health Committee of China first defined 121 rare diseases in the Chinese population. The list of these rare diseases was established according to prevalence, disease burden and social support, medical technology status, and the definition of rare diseases in relevant international institutions. Twenty million people in China were reported to suffer from these rare diseases.

A rare disease is any disease or condition that affects a small percentage of the population, and most of them are genetic and life-threatening diseases.[1,2] Most rare diseases appear early and throughout the person's life, and 30% of those affected will die before 5 years of age.[3] However, there has been no single, widely accepted definition for rare diseases until now. According to national conditions, each country or region may have different criteria for rare disease identification. In the United States, a rare disease is defined by the Rare Diseases Act of 2002, which relies solely on prevalence: 'any disease or condition that affects fewer than 200 000 people in the United States', or ~1 in 1 500 people.[4] In the European Union, the European Commission defines rare disease as a life-threatening or chronically debilitating disease with a population prevalence of less than 1 in 2 000.[4]

In several parts of the world, rare disease is used as a synonym of 'orphan disease', indicating a lack of a sufficiently large market to obtain source and support for discovering and investigating-related therapies. Paradoxically, rare diseases are common.[5] More than 7 000 rare diseases, approximately 10% of the total human diseases, have been identified with advances in our knowledge regarding the human genome, and more than 2 000 million people worldwide are living with one of the 7 000 diseases defined as "rare".[6] In recent years, several rare diseases have been gaining a large amount of attention, such as amyotrophic lateral sclerosis. Increased concern and a correct understanding of rare diseases would promote mechanistic, diagnostic and therapeutic advances.

In this review, we aim to summarize the related manifestations and treatment of dental-craniofacial disorders related to rare diseases, thus helping to improve understanding and certainly diagnostic capacity for dentists and oral maxillofacial surgeons.

DENTAL-CRANIOFACIAL DISORDER-RELATED RARE DISEASES

Tooth dysplasia

Congenital ectodermal dysplasia. Ectodermal dysplasias (EDs) are a group of more than 150 different genetic disorders deriving from ectodermal structural abnormalities.[7,8] Ectodermal dysplasias have been described as 'heritable conditions in which there are abnormalities of two or more ectodermal structures, such as the hair, teeth, nails, sweat glands, salivary glands, cranial-facial structure, digits and other parts of the body'.[7] The abnormality in the development of tooth buds frequently results in congenital hypodontia (both primary and permanent dentitions) and/or changes in tooth morphology or size, such as peg-shaped or pointed teeth, taurodontism and enamel defects, including hypoplasia.[9] The degree of tooth missing is always in the mild to moderate range, and a wide variation is observed regarding which teeth are missing; however, the most frequently reported missing teeth are the first molars, upper central incisors and canines[10–14] (Table 1). Accordingly, composite restorations or crowns are almost always necessary for children as early as 2 years of age, and multiple denture replacements are often needed as the child grows, with dental implants providing a potential option in adolescence when the jaw is fully grown. The current option of extracting teeth and substituting them with dental implants is quite common.[15] Additionally, orthodontic treatment is further necessary during the early teenage years as part of the best multi-disciplinary approach. Furthermore, several studies have also reported reduced salivary secretion in ED patients, accompanied by a reduced buffering ability and increased bacterial counts.[16–20] Therefore, a systematic preventive plan including fluoride use and

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RESEARCH Open Access

Oral health related quality of life of children and adolescents affected by rare orofacial diseases: a questionnaire-based cohort study

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Abstract

Background: Rare diseases affecting the teeth, the oral cavity and the face are numerous, each of them present specific characteristics, and is a life-long condition. The aim of the study was to assess the association between Oral health-related quality of life (OHRQoL), and demographic characteristics, clinical and dental factors, and psycho-social characteristics to investigate that oral symptoms are not the main factors underlying a decrease in OHRQoL.

Material and methods: We conducted a national cohort study in French centres for rare diseases (RD) specialized in orofacial diseases. The inclusion criteria were: to have received care in RD centres over the last 5 years (2012–2017) and to have been between 6 and 17 years of age on September 1, 2017. Patients were invited to answer a questionnaire composed of socio-demographic, clinical and dental questions, psychosocial questions and then fill in the Child-OIDP Index. At the end of the questionnaire, a free space was left for the patient to add a verbatim comment to provide qualitative data. Thematic analysis was used to analyze the verbatim answers.

Results: Complete data were available for 110 patients. The sample included 44.5% boys and 55.5% girls. Ages ranged from 6 to 17 years old and 68.2% were between 6 to 12 years old and 31.8% were between 13 and 17 years old. Factor associated with a lower OHRQoL were: being a girl ($p = 0.03$), renouncement to dental care for financial reasons ($p = 0.01$), having syndromic disease ($p = 0.01$), having a problem with tooth shape and color ($p = 0.03$), feeling isolated, alone and different from other children ($p = 0.003$ and $p = 0.02$). Qualitative analysis highlighted very little recourse to psychological care and patients reported great anxiety and fear about the future.

Conclusion: OHRQoL of children suffering from these diseases is impaired, especially from the psychosocial point of view but also from that of the course of treatment and access to care. There is a need to improve the legibility of care pathways and the financial coverage of treatments.

Keywords: Rare disease, Cleft, Oral manifestation, Teeth, Oral health-related quality of life (OHRQoL), Child, CHILD-OIDP

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Orphanet Journal of Rare Diseases

RESEARCH Open Access

Assessing a possible vulnerability to dental caries in individuals with rare genetic diseases that affect the skeletal development

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Abstract

Background: Individuals diagnosed with a rare genetic disease that affects skeletal development often have physical limitations and orofacial problems that exert an impact on oral health. The aim of the present study was to analyze the possible vulnerability to dental caries in individuals with rare genetic diseases that affect skeletal development.

Methods: A paired cross-sectional study was carried out with a sample of 140 individuals [70 with rare genetic diseases affecting skeletal development: mucopolysaccharidosis (MPS) ($n = 29$) and osteogenesis imperfecta (OI) ($n = 41$) and 70 without rare diseases] and their parents/caregivers. The participants in the first group were recruited from two reference hospitals specialized in rare genetic diseases in the city of Belo Horizonte, Brazil. All participants were examined for the evaluation of breathing type, malocclusion, dental anomalies, oral hygiene and dental caries. The parents/caregivers answered a structured questionnaire addressing the individual/behavioral characteristics and medical/dental history of the participants. Statistical analysis involved the chi-square test and multiple logistic regression analysis for the dependent variable (dental caries) ($\alpha = 5\%$). This study received approval from the Human Research Ethics Committee of the Universidade Federal de Minas Gerais.

Results: The mean age of the individuals was 10.34 ± 6.55 years (median: 9.50 years). Individuals with inadequate oral hygiene were 4.70–fold more likely to have dental caries (95% CI: 2.13–10.40) and those with the rare genetic diseases (MPS/OI) were 2.92-fold more likely to have dental caries (95% CI: 1.38–6.17).

Conclusion: Individuals with inadequate oral hygiene and those with MPS and OI had a greater chance of belonging to the group with dental caries. Based on the present findings, individuals with the rare genetic diseases may be considered vulnerable to caries.

Keywords: Rare diseases, Genetic diseases, Disabled persons, Oral health, Dental caries

Background

The World Health Organization (WHO) defines rare diseases as all diseases for which the prevalence is less than 65 cases per 100,000 inhabitants [1]. Rare diseases are characterized as debilitating and chronically degenerative and require continuous medical follow up. Affected individuals often have impaired physical, mental, sensorial and behavioral capacities, which can compromise their autonomy with regard to performing activities of daily living [2–6].

Mucopolysaccharidoses (MPS) and osteogenesis imperfecta (OI) are two rare genetic diseases that compromise skeletal development and affect general health. The two diseases lead to dental problems. Studies show that malocclusion, tooth agenesis, tooth rotation and microdontia are common in this population. These diseases are also associated with alterations in genes that

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Dentinogenesis imperfecta: an early treatment strategy

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Abstract

Dentinogenesis imperfecta (DI) type 2 is a disease inherited in a simple autosomal dominant mode. As soon as the teeth erupt the parents may notice the problem and look for a pediatric dentist's advice and treatment. Early diagnosis and treatment of DI is recommended, as it may prevent or intercept deterioration of the teeth and occlusion and improve esthetics.

The purpose of this article is to present the objectives, treatment options, and problems encountered in the treatment of DI in the early primary dentition. A two-stage treatment of a toddler under general anesthesia is described and discussed.

This paper recommends for severe cases of DI two treatment stages performed under general anesthesia. Stage 1 is early (around age 18-20 months) and is directed to covering the incisors with composite restorations and the first primary molars with preformed crowns. Stage 2 (around age 28-30 months) seeks to protect the second primary molars with preformed crowns and cover the canines with composite restorations. (Pediatr Dent 23:232-237, 2001)

Dentinogenesis imperfecta (DI) or hereditary opalescent dentin, was first described in the late 19th century.[1,2] It is a localized mesodermal dysplasia affecting both the primary and permanent dentition. The disease is inherited in a simple autosomal dominant mode with high penetrance and a low mutation rate.[3] The reported incidence in the USA is 1:8000 births.[4] Shields et al proposed three types of dentinogenesis imperfecta: DI type 1 is associated with osteogenesis imperfecta. DI type 2 has essentially the same clinical radiographic and histological features as DI type 1 but without osteogenesis imperfecta; DI type 3 is rare and is only found in the triracial Brandywine population of Maryland.[5] It has been suggested that DI type 2 and DI type 3 are different expressions of the same gene.[6,7]

Clinically, with DI both dentitions are affected. The color of the teeth varies from brown to blue, sometimes described as amber or gray, with an opalescent sheen.[3] The enamel may show hypoplastic or hypocalcified defects in about one-third of the patients and, in an affected patient, tends to crack away from the defective dentin. The exposed dentin may undergo severe and rapid attrition.[3]

Radiographically, the teeth have bulbous crowns with constricted short roots. Initially, pulp chambers may be abnormally wide and resemble "shell teeth," but they will progressively obliterate.[5] Histologically, the enamel, although normal in structure, tends to crack. The dentin-enamel junction is not scalloped. In most cases the structure of the mantle dentin is normal,[8] whereas the dentinal tubules of the circumferential dentin are coarse and branched and the total number of tubules is reduced.[8] The presence of an atubular area in the dentin with reduced mineralization and a reduced number of odontoblasts are consistent findings.[8] Pulpal inclusions and much interglobular dentin are also frequent.[8]

The biochemical characteristics of the dentin include a collagen defect and a primary defect in the calcifying matrix.[9] Takagi and Sasaki suggested that the dentin in DI type 2 is deficient in the phosphorous ion, which is important in the early stage of odontoblastic differentiation and its mineralization.[10] Susuki et al published a case describing DI type 2 with absent enamel prisms and abnormal mantle dentin.[11]

The purpose of this article is to present the objectives, treatment options and problems encountered in the treatment of DI in the early primary dentition. A two-stage treatment of a toddler under general anesthesia is described and discussed.

Dental treatment

In DI, the primary dentition appears more severely affected than the permanent dentition, evidenced by rapid wear of the teeth.[3] This attrition may cause pulpal involvement with dental abscesses,[9] and the short, constricted roots might break under load, thus necessitating extraction. The severe attrition may result in a rapid decrease in the occlusal height. In the early primary dentition, these appear to be the most immediate problems, and soon after eruption it is generally necessary to protect the primary molars with stainless steel crowns.[12]

In the restorative treatment of pediatric patients, glass ionomer with fluoride-releasing and chemically attaching materials are recommended for occlussally non-stressed areas.[13] An acid etch technique followed by composite restoration is proposed as an alternative for restoration of the anterior teeth.[13,14] Polycarbonate crowns may offer an alternative for the restoration of the anterior primary teeth.[15] An acrylic overlay denture, resting over the remnants of crowns and roots of the primary dentition, also has been used successfully.[16]

Wright has stated that the dental approach for managing dentinogenesis imperfecta will vary with the severity of the clinical expression, while intracoronal restoration and bonded veneers for anterior teeth may be acceptable in mild cases, they might not last in severe cases exhibiting enamel fracturing and rapid wear.[17]

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Development of a database to record orofacial manifestations in patients with rare diseases: a status report from the ROMSE (recording of orofacial manifestations in people with rare diseases) database

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Abstract

The aim of this working group was to establish a ROMSE (recording of orofacial manifestations in people with rare diseases) database to provide clinicians, patients, and their families with better information about these diseases. In 2011, we began to search the databases Orphanet, OMIM® (Online Mendelian Inheritance in Man®), and PubMed, for rare diseases with orofacial symptoms, and since 2013, the collected information has been incorporated into a web-based, freely accessible database. To date, 471 rare diseases with orofacial signs have been listed on ROMSE, and 10 main categories with 99 subcategories of signs such as different types of dental anomalies, changes in the oral mucosa, dysgnathia, and orofacial clefts, have been defined. The database provides a platform for general clinicians, orthodontists, and oral and maxillofacial surgeons to work on the best treatments.

Keywords: rare disease; orofacial manifestation; database; interdisciplinary dentistry; European Council recommendation

Introduction

In the European Union (EU), a disease is considered rare if it affects fewer than 2000 people,[1] which means that roughly 30 million people are affected in the 28 member states, and four million of them are in Germany. Globally, around 8000 rare diseases are recognised, and 80% of them are genetic,[2] but because there are so few patients, it is not usually possible to conduct clinical trials with evidence-based results. Studies have shown that around 15% may be accompanied by orofacial signs,[3,4] and there is dental, oral, or maxillofacial involvement in over 900 of the 5000-plus syndromes that are genetic.[5] Changes in the oral cavity or perioral region can be of special relevance in the early diagnosis of such diseases,[6] and they need to be treated to improve a patient's quality of life.

In 2009 the Council of the EU recommended that member states develop and implement plans and strategies to man-

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Hereditary hemorrhagic telangiectasia

From Genetics Home Reference. Learn more

Description

Hereditary hemorrhagic telangiectasia is a disorder that results in the development of multiple abnormalities in the blood vessels.

In the circulatory system, blood carrying oxygen from the lungs is normally pumped by the heart into the arteries at high pressure. The pressure allows the blood to make its way through the arteries to the smaller vessels (arterioles and capillaries) that supply oxygen to the body's tissues. By the time blood reaches the capillaries, the pressure is much lower. The blood then proceeds from the capillaries into veins, through which it eventually returns to the heart.

In hereditary hemorrhagic telangiectasia, some arterial vessels flow directly into veins rather than into the capillaries. These abnormalities are called arteriovenous malformations. When they occur in vessels near the surface of the skin, where they are visible as red markings, they are known as telangiectases (the singular is telangiectasia).

Without the normal buffer of the capillaries, the blood moves from the arteries at high pressure into the thinner walled, less elastic veins. The extra pressure tends to strain and enlarge these blood vessels, and may result in compression or irritation of adjacent tissues and frequent episodes of severe bleeding (hemorrhage). Nosebleeds are very common in people with hereditary hemorrhagic telangiectasia, and more serious problems may arise from hemorrhages in the brain, liver, lungs, or other organs.

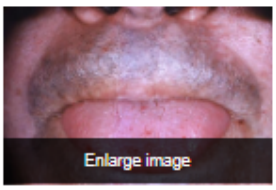
There are several forms of hereditary hemorrhagic telangiectasia, distinguished mainly by their genetic cause but with some differences in patterns of signs and symptoms. People with type 1 tend to develop symptoms earlier than those with type 2, and are more likely to have blood vessel malformations in the lungs and brain. Type 2 and type 3 may be associated with a higher risk of liver involvement. Women are more likely than men to develop blood vessel malformations in the lungs with type 1, and are also at higher risk of liver involvement with both type 1 and type 2. Individuals with any form of hereditary hemorrhagic telangiectasia, however, can have any of these problems.

Juvenile polyposis/hereditary hemorrhagic telangiectasia syndrome is a condition that involves both arteriovenous malformations and a tendency to develop growths (polyps) in the gastrointestinal tract. Hereditary hemorrhagic telangiectasia types 1, 2 and 3 do not appear to increase the likelihood of such polyps.

Frequency

Causes

Inheritance



Related Health Topics

Arteriovenous Malformations
Genetic Disorders

MEDICAL ENCYCLOPEDIA

Genetics
Osler-Weber-Rendu syndrome

Understanding Genetics

What is the prognosis of a genetic condition?
How can gene variants affect health and development?
What does it mean if a disorder seems to run in my family?
What are the different ways a genetic condition can be inherited?
How are genetic conditions treated or managed?

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Invited Review

INVITED REVIEW

New insights into craniofacial malformations

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Abstract

Development of the human skull and face is a highly orchestrated and complex three-dimensional morphogenetic process, involving hundreds of genes controlling the coordinated patterning, proliferation and differentiation of tissues having multiple embryological origins. Craniofacial malformations that occur because of abnormal development (including cleft lip and/or palate, craniosynostosis and facial dysostoses), comprise over one-third of all congenital birth defects. High-throughput sequencing has recently led to the identification of many new causative disease genes and functional studies have clarified their mechanisms of action. We present recent findings in craniofacial genetics and discuss how this information together with developmental studies in animal models is helping to increase understanding of normal craniofacial development.

Introduction

The head is the most complex structure of the body. The skull, including bones that enclose and protect the brain and sensory organs, also acts as a scaffold for the face to support the functions of feeding and breathing in combination with connective tissue, musculature, vasculature and associated innervation. Collectively these tissues are derived from endoderm, mesoderm, ectoderm and cranial neural crest cells (CNCCs) and their derivatives (1). Signalling between these cellular components and to the craniofacial mesenchyme (formed primarily by CNCCs with a mesodermal contribution) provides positional cues and regulates growth and differentiation (Fig. 1). These dynamic spatio-temporal processes are highly complex and susceptible to dysregulation as evidenced by the high proportion of congenital defects that involve the skull and face (2). We will summarise recent molecular insights into development of the skull and face, then discuss the latest discoveries in the genetic basis of human craniofacial malformations including craniosynostosis, facial exostoses and cleft lip and/or palate. Newly identified disease genes underlying these pathologies are listed in Table 1.

New Insights into Craniofacial Development

The mammalian skull is formed from both mesoderm and neural crest (NC)-derived mesenchyme (22,23). Following induction of the NC at the lateral edges of the neural plate, CNCCs undergo an epithelial-to-mesenchymal transition and migrate to different destinations depending on their position along the anteroposterior axis of the neural tube (Fig. 1).

The cranial sutures that separate the flat bones of the skull perform a vital role in coordinating growth with rapid brain expansion. Sutures contain mesenchymal stem cells (MSCs), progeny of which divide and mature to osteoblasts at the adjacent bone fronts (24). In the mouse the MSC precursors of the coronal suture originate from cephalic paraxial mesoderm arising at the mesencephalon/diencephalon boundary at embryonic day (E)7.5, in response to sonic hedgehog (SHH) signalling from the adjacent notochord (25) (Fig. 1). Subsequently, the MSCs migrate to an organizing centre located above the developing eye at the base of the future coronal suture (supra-orbital regulatory centre, SRC) (25). Here they lie between cephalic mesodermal cells (parietal bone-forming) and CNCCs (frontal bone-forming). Crucially this arrangement is maintained during growth so that, as the coronal suture develops, it is populated purely by mesodermal derivatives, whereas NC-derived cells do not cross from the frontal bone territory (25). Using conditional labelling with a *Gli1* driver, a population of MSC within the suture was recently demonstrated postnatally; these cells are critical for skull growth as their ablation leads to suture fusion (26).

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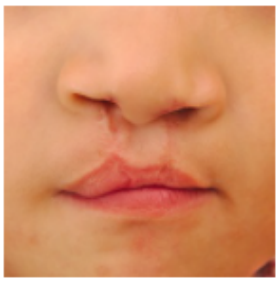
Cleft Lip and Palate



Summary

Cleft lip and cleft palate are birth defects that occur when a baby's lip or mouth do not form properly. They happen early during pregnancy. A baby can have a cleft lip, a cleft palate, or both.

A cleft lip happens if the tissue that makes up the lip does not join completely before birth. This causes an opening in the upper lip. The opening can be a small slit or a large opening that goes through the lip into the nose. It can be on one or both sides of the lip or, rarely, in the middle of the lip.

Children with a cleft lip also can have a cleft palate. The roof of the mouth is called the "palate." With a cleft palate, the tissue that makes up the roof of the mouth does not join correctly. Babies may have both the front and back parts of the palate open, or they may have only one part open.

Children with a cleft lip or a cleft palate often have problems with feeding and talking. They also might have ear infections, hearing loss, and problems with their teeth.

Often, surgery can close the lip and palate. Cleft lip surgery is usually done before age 12 months, and cleft palate surgery is done before 18 months. Many children have other complications. They may need additional surgeries, dental and orthodontic care, and speech therapy as they get older. With treatment, most children with clefts do well and lead a healthy life.

Centers for Disease Control and Prevention

Start Here

- Cleft Lip and Cleft Palate (March of Dimes Birth Defects Foundation)
  Also in Spanish
- Cleft Lip and Cleft Palate (Mayo Foundation for Medical Education and Research)
  Also in Spanish
- Facts about Cleft Lip and Cleft Palate (Centers for Disease Control and Prevention)
  Also in Spanish
- Introduction to Cleft and Craniofacial Conditions (Cleft Palate Foundation)
- Orofacial Clefts (For Parents) (Nemours Foundation)
  Also in Spanish

Treatments and Therapies

- Cleft Lip and Palate Surgery (American Association of Oral and Maxillofacial Surgeons) - PDF
- Information about Treatment for Adults with Cleft Lip and Palate (Cleft Palate Foundation)
  Also in Spanish

MEDICAL ENCYCLOPEDIA

- Aarskog syndrome
- Cleft lip and palate
- Cleft lip and palate repair
- Cleft lip and palate repair - discharge
- Cleft lip repair - slideshow

National Institutes of Health

The primary NIH organization for research on *Cleft Lip and Palate* is the National Institute of Dental and Craniofacial Research

Syndromic Craniosynostosis

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Abstract

Although most cases of craniosynostosis are nonsyndromic, craniosynostosis is known to occur in conjunction with other anomalies in well-defined patterns that make up clinically recognized syndromes. Patients with syndromic craniosynostoses are much more complicated to care for, requiring a multidisciplinary approach to address all of their needs effectively.

This review describes the most common craniosynostosis syndromes, their characteristic features and syndrome-specific functional issues, and new modalities utilized in their management. General principles including skull development, the risk of developing increased intracranial pressure in craniosynostosis syndromes, and techniques to measure intracranial pressure are discussed. Evolving techniques of the established operative management of craniosynostosis are discussed together with more recent techniques including spring cranioplasty and posterior cranial vault distraction osteogenesis.

Keywords

- syndromic craniosynostosis
- intracranial pressure
- posterior vault distraction
- spring cranioplasty
- midface distraction

Craniosynostosis can occur as an isolated event resulting in nonsyndromic craniosynostosis, or it can occur in conjunction with other anomalies in well-defined patterns that make up clinically recognized syndromes. Patients with syndromic craniosynostoses are much more complicated to care for, requiring a multidisciplinary team to address all of their needs effectively. These are typically genetic in nature, and may demonstrate autosomal dominant, autosomal recessive, and X-linked patterns of inheritance. Although busy tertiary care centers will encounter a broad range of syndromes, the more commonly identified craniosynostosis syndromes seen by plastic surgeons include Crouzon, Saethre-Chotzen, Apert, Pfeiffer, and Muenke syndromes. These variably share some common features in addition to craniosynostosis including exophthalmos, midface hypoplasia, cranial base anomalies, abnormal facies, and limb anomalies. In fact, the craniofacial features of the various syndromes can be so similar that the digital anomalies may be the sole differentiating physical finding to allow a clinical diagnosis.

Surgery for craniosynostosis dates from the 19th century, but early operations carried high complication rates with poor long-term outcomes. Cranial vault reconstruction did not gain widespread acceptance until 1967 when Paul Tessier revolutionized the field by introducing his intracranial approach that allowed accurate osteotomy, mobilization, and repositioning of the recessed forehead and supraorbital regions. Since that time, several significant advances including surgical intervention in infancy, the advent of computed tomography, introduction of rigid and later resorbable plating systems, and distraction osteogenesis have fueled the evolution of our approach to the treatment of patients with syndromic craniosynostosis. The goal of this article is to review the salient features of the commonly encountered craniosynostosis syndromes and both the traditional and cutting-edge approaches to treatment.

General Considerations

Craniofacial growth generally follows a craniocaudad pattern with an initial rapid calvarial growth during infancy, followed by orbital and midface growth in the first decade and mandibular growth in adolescence. Over the first year of life, the brain triples in volume to reach two thirds of its adult size. It continues to grow rapidly over the next 2 years, then growth continues more gradually with the brain reaching adult size between 6 and 10 years of age. Skull growth occurs

Congenital erythropoietic porphyria

Información en español

Other Names: Porphyria, congenital erythropoietic; CEP; Günther disease; See More

Categories: Blood Diseases; Congenital and Genetic Diseases; Kidney and Urinary Diseases; See More

This disease is grouped under: Porphyria

Summary

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Congenital erythropoietic porphyria (CEP) is the rarest type of porphyria and is commonly seen in infancy.[1] It is characterized by severe skin photosensitivity that may lead to scarring, blistering, and increased hair growth at the face and back of the hands.[2][3] Photosensitivity and infection may cause the loss of fingers and facial features.[1] Symptoms of CEP range from mild to severe and may include excessive hair growth throughout the body (hypertrichosis), reddish discoloration of the teeth, anemia, and reddish-colored urine.[4] In CEP, there is a defect in the synthesis of heme within the red blood cells of bone marrow.[3][4] This defect leads to an increase in the buildup and, therefore, waste of porphyrin and its precursors, which leads to the signs and symptoms.[3] Inheritance is autosomal recessive. It is caused by mutations in the *UROS* gene.[3] Treatment for CEP may include a bone marrow transplant and hematopoietic stem cell cord blood transplantation.[2][1] Blood transfusions or spleen removal may also reduce the amount of porphyrin produced by the bone marrow. Affected people must avoid sunlight exposure.[1]

Last updated: 3/22/2017

Symptoms

Listen

This table lists symptoms that people with this disease may have. For most diseases, symptoms will vary from person to person. People with the same disease may not have all the symptoms listed. This information comes

What to Know About Bleeding Diathesis: Causes, Symptoms, Treatment

Medically reviewed by Alana Biggers, M.D., MPH — Written by Marjorie Hecht on September 24, 2019

Bleeding diathesis means a tendency to bleed or bruise easily. The word "diathesis" comes from the ancient Greek word for "state" or "condition."

Most bleeding disorders occur when blood doesn't clot properly. Symptoms of bleeding diathesis can range from mild to severe.

The causes of bleeding and bruising can vary widely, including:

- a normal response to injury
- an inherited disorder
- a response to some drugs or herbal preparations
- abnormalities in blood vessels or connective tissue
- an acute disease, such as leukemia

Keep reading to learn about common symptoms and causes of bleeding diathesis, along with their diagnosis and treatment.

Fast facts about bleeding diathesis

- An estimated 26 percent to 45 percent of healthy people have a history of nosebleeds, gum bleeding, or easy bruising.
- About 5 percent to 10 percent of women of reproductive age seek treatment for heavy periods (menorrhagia).
- More than 20 percent of the population reports at least one bleeding symptom.

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Bleeding Disorders of Importance in Dental Care and Related Patient Management

Anurag Gupta, BDS; *Joel B. Epstein*, DMD, MSD, FRCD(C); *Robert J. Cabay*, MD, DDS

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ABSTRACT

Oral care providers must be aware of the impact of bleeding disorders on the management of dental patients. Initial recognition of a bleeding disorder, which may indicate the presence of a systemic pathologic process, may occur in dental practice. Furthermore, prophylactic, restorative and surgical dental care of patients with bleeding disorders is best accomplished by practitioners who are knowledgeable about the pathology, complications and treatment options associated with these conditions. The purpose of this paper is to review common bleeding disorders and their effects on the delivery of oral health care.

MeSH Key Words: blood coagulation/physiology; blood coagulation disorders/complications; dental care

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Dentists must be aware of the impact of bleeding disorders on the management of their patients. Proper dental and medical evaluation of patients is therefore necessary before treatment, especially if an invasive dental procedure is planned. Patient evaluation and history should begin with standard medical questionnaires. Patients should be queried about any previous unusual bleeding episode after surgery or injury, spontaneous bleeding and easy or frequent bruising. For the purpose of history-taking, a clinically significant bleeding episode[1] is one that:

- continues beyond 12 hours
- causes the patient to call or return to the dental practitioner or to seek medical treatment or emergency care
- results in the development of hematoma or ecchymosis within the soft tissues or
- requires blood product support.

Most reported bleeding episodes are minor and do not require a visit to the dentist or the emergency department and do not affect dental treatment significantly.

The patient should be asked for any history of significant and prolonged bleeding after dental extraction or bleeding from gingivae. A history of nasal or oral bleeding should be noted. Many bleeding disorders, such as hemophilia and von Willebrand's disease, run in families; therefore, a family history of bleeding disorders should be carefully elicited.

A complete drug history is important. If a patient is taking anticoagulant drugs, it will be important to consult his or her physician before any major surgical procedure. In addition, a number of medications may interfere with hemostasis and prolong bleeding. Drugs of abuse, such as alcohol or heroin, may also cause excess bleeding[2] by causing liver damage resulting in altered production of coagulation factors. Illicit injection drug use carries an increased risk of transmission of viral pathogens that may lead to viral hepatitis and altered liver function.

A general examination of the patient might indicate a tendency to bleed. Multiple purpurae of the skin, bleeding wounds, evident

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Cancer

Also called: Carcinoma, Malignancy, Neoplasms, Tumor

On this page

Summary

Cancer begins in your cells, which are the building blocks of your body. Normally, your body forms new cells as you need them, replacing old cells that die. Sometimes this process goes wrong. New cells grow even when you don't need them, and old cells don't die when they should. These extra cells can form a mass called a tumor. Tumors can be benign or malignant. Benign tumors aren't cancer while malignant ones are. Cells from malignant tumors can invade nearby tissues. They can also break away and spread to other parts of the body.

Cancer is not just one disease but many diseases. There are more than 100 different types of cancer. Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. The spread of cancer from one part of the body to another is called metastasis. Symptoms and treatment depend on the cancer type and how advanced it is. Most treatment plans may include surgery, radiation and/or chemotherapy. Some may involve hormone therapy, immunotherapy or other types of biologic therapy, or stem cell transplantation.

NIH: National Cancer Institute

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- Cancer (American Academy of Family Physicians)
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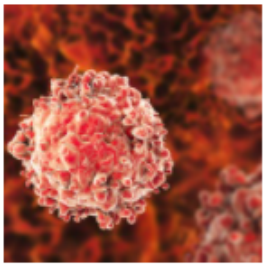
Leukemia



Summary

Leukemia is cancer of the white blood cells. White blood cells help your body fight infection. Your blood cells form in your bone marrow. In leukemia, the bone marrow produces abnormal white blood cells. These cells crowd out the healthy blood cells, making it hard for blood to do its work.

There are different types of leukemia, including

- Acute lymphocytic leukemia
- Acute myeloid leukemia
- Chronic lymphocytic leukemia
- Chronic myeloid leukemia

Leukemia can develop quickly or slowly. Chronic leukemia grows slowly. In acute leukemia, the cells are very abnormal and their number increases rapidly. Adults can get either type; children with leukemia most often have an acute type. Some leukemias can often be cured. Other types are hard to cure, but you can often control them. Treatments may include chemotherapy, radiation and stem cell transplantation. Even if symptoms disappear, you might need therapy to prevent a relapse.

NIH: National Cancer Institute

Start Here

- Leukemia (Mayo Foundation for Medical Education and Research)
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- Understanding Leukemia (Leukemia & Lymphoma Society) - PDF
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Diagnosis and Tests

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Fibromatosis gingival hereditaria: una rara enfermedad. Reporte de una familia

Hereditary Gingival Fibromatosis: A Rare Disease. A Family Report

Fibromatose gengival hereditária uma estranha doença: reporte de uma família

Edwin Guzmán Rivera, OD[1];
Ary López Álvarez, OD[2];
Jonathan Harris Ricardo OD, MSc*[1,2]

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Resumen

Introducción: la fibromatosis gingival hereditaria es un desorden genético raro que produce un sobrecrecimiento gingival y el desplazamiento dental asociado, la patogénesis y la base molecular de la enfermedad sigue siendo desconocida. Dado que es una enfermedad poco frecuente, es importante que el profesional en el área de la salud oral conozca las características clínicas, histológicas y genéticas de la enfermedad con el objetivo de realizar un correcto diagnóstico, plan de tratamiento y orientación sobre la condición de la patología. *Presentación del caso*: se reporta informe de una familia con tres generaciones afectadas con fibromatosis gingival hereditaria, en la que se describen las características clínicas, histopatológicas y tratamiento. *Conclusión*: la fibromatosis gingival hereditaria es un trastorno poco frecuente que genera diversos grados de aumento en el volumen gingival, los compromisos estéticos y funcionales a menudo requieren intervención quirúrgica, histológicamente es común la presencia de abundantes haces de colágeno y fibroblastos.

Palabras clave: fibromatosis gingival, familia, genética, cirugía bucal.

Abstract

Introduction: Hereditary gingival fibromatosis is a rare genetic disorder that produces a gingival overgrowth and the associated dental displacement, the pathogenesis and the molecular basis of the

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REVIEW

Papillon–Lefèvre syndrome: clinical presentation and management options

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Number of times this article has been viewed

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Abstract: Papillon–Lefèvre syndrome (PLS) is a rare autosomal recessive disorder, characterized by diffuse palmoplantar keratoderma and precocious aggressive periodontitis, leading to premature loss of deciduous and permanent dentition at a very young age. Various etiopathogenic factors are associated with the syndrome, like immunologic alterations, genetic mutations, and the role of bacteria. Dentists play a significant role in the diagnosis and management of PLS as there are characteristic manifestations like periodontal destruction at an early age and an early eruption of permanent teeth. Here, we are presenting an elaborate review of PLS, its etiopathogenesis, clinical presentation, and management options.

Keywords: deciduous and permanent dentition, modified complete dentures, palmoplantar keratoderma, periodontitis

Video abstract

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Introduction

Papillon–Lefèvre syndrome (PLS) was first described by two French physicians, Papillon and Lefèvre, in France.[1] It is an autosomal recessive inherited disorder of keratinization,[2] characterized by redness, thickening of the soles and palms, and severe destructive periodontal disease affecting both primary and permanent teeth, caused by mutations in *cathepsin C* (CTSC) gene.[3,4] Other symptoms include hyperhidrosis, arachnodactyly, intracranial calcification, increased susceptibility to infections, and mental retardation.[5,6] The pedigree study reveals the mode of inheritance of the disease. PLS is inherited as an autosomal recessive disorder and if both parents are carriers of the defective gene there is a 25% risk for their children to be affected.[7] The incidence of PLS is one to four per million with no sex and racial predominance. Between two and four people per thousand are heterozygous for the PLS gene and therefore they become carriers of the disorder; this results in a population prevalence of one to four per million people.[7–9] Greater frequency of occurrence in consanguineous offspring has been noted in approximately one-third of the cases.[10] The disease becomes apparent by 2–3 years of age as an oral manifestation affecting the deciduous teeth with periodontal involvement leading to premature exfoliation of the same teeth. As the permanent dentition erupts, the same sequence of events recur, leading to the early shedding of the permanent dentition. Approximately 20%–25% of PLS cases suffer from increased susceptibility to infections other than periodontitis; most of them show predisposition to mild skin infections such as furunculosis or pyodermas. Occasionally, severe infections such as liver abscess or pneumonia occurs.[11]

PLS is caused by genetic defect located on chromosome 11q14.1-q14.3, which involves mutations of the CTSC gene.[12] Various studies in PLS patients have shown

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Article

Rare Diseases with Periodontal Manifestations

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Abstract: *Background*: The object of this paper was to provide an overview of rare diseases (RDs) with periodontal manifestations and allocate them to relevant categories. *Methods*: In ROMSE, a database for "Rare Diseases with Orofacial Involvement", all 541 entities were analyzed with respect to manifestations of periodontal relevance. Inclusion criteria were periodontally relevant changes to the oral cavity, in accordance with the 2018 version of the Classification of Periodontal and Peri-Implant Diseases and Conditions. Rare diseases were recorded, using the methodology described, and subsequently compared with the Orphanet Classification of Rare Diseases. *Results*: A total of 76 RDs with periodontal involvement were recorded and allocated in accordance with the Classification of Periodontal and Peri-Implant Diseases and Conditions. Of the 541 RDs analyzed as having known orofacial manifestations, almost 14 percent indicated a periodontally compromised dentition. *Conclusions*: Around 14 percent of RDs with an orofacial involvement showed periodontally relevant manifestations, which present not only as a result of gingivitis and periodontitis, but also gingival hyperplasia in connection with an underlying disease. Thus, dentists play an important role in therapy and early diagnoses of underlying diseases based on periodontally relevant manifestations.

Keywords: rare diseases; periodontal manifestations; oral manifestations of systemic diseases; oral manifestations; classification of periodontal and peri-implant diseases and conditions

1. Introduction

According to the European Union (EU) definition, a disease is classified as "rare" when fewer than one in 2000 people are affected by it. At least 30 million people in the 28 member states of the EU are affected [1]. Worldwide, between 5000 and 8000 different rare diseases (RD) are known, 80 percent of which have a genetic cause [2,3]. Around four million people in the Federal Republic of Germany are affected by RDs [2]. Since 2009, there has been an increase in public awareness of RDs in the EU after the Council of the European Union called upon member states to draw up, at the appropriate level, plans and strategies for RDs [4]. In most cases, exact epidemiological data are not available as a result of incomplete registrations of RDs in national and international databases. To improve this situation, the German Ministry of Health set up a "Nationaler Aktionsplan für Menschen mit Seltenen

Dental management of osteogenesis imperfecta: a case report

Ghada Al Muhaidib[a], Abdullah S. Al Mushayt[b] and Zeinab Darwish[c,d]

Osteogenesis imperfecta is an inherited disorder of connective tissue caused by type I collagen defects, thus all tissues rich in type I collagen are affected. The present report describes a 10-year old Saudi female child with osteogenesis imperfecta and dental problems. Oral and para-oral examination as well as general evaluation was done to the patient. The patient was found to have mandibular osteoporotic changes, delayed eruption of some teeth, caries and malocclusion. Dental treatment was carried out with a follow up of more than 2 years. Based on the previous, patients with osteogenesis imperfecta should be followed up by the dentist collaborated with the treating physician to treat the existing dental problems and to avoid oral and para-oral complications. ***Egypt J Oral Maxillofac Surg***

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Keywords: bisphosphonates, congenital disorders, osteogenesis imperfecta, osteoporosis

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Introduction

Osteogenesis imperfecta (OI) is a congenital disorder characterized by increased bone fragility and low bone mass. It results from mutations in the genes COL1A1 and COL1A2 that encode for either chain of type 1 collagen [1]. The disease causes either a decrease in collagen synthesis or the production of abnormal collagen; thus, all tissues rich in type 1 collagen can be affected [1]. Patients therefore present with multiple long bone fragility (osteoporosis), bone deformity, joint laxity and hypermobility, blue sclera, hearing loss, skin thinness, and growth deficiency [2]. The original classification of OI into four types (OI type I, II, III, and IV) was based on clinical and radiological findings and mode of inheritance [3]. Type I includes patients who have the mild form, almost normal stature, and blue sclera. Type II is considered the most severe form and is lethal in the prenatal period. Type III includes patients with the classic disease manifestation, usually with moderate deformity at birth, and progressively deforming bones. Type IV includes patients with extensive phenotypic variability, including mild to severe forms of OI [3]. Although these clinical features provide the bases for classifications, a significant proportion of patients cannot be classified in this way [4]. In 2004 and 2007, this classification was expanded with OI types V–VIII because of distinct clinical features and/or different causative gene mutations [5,6].

There are significant oral problems that occur in different types of OI including dentinogenesis imperfecta (DI), class III dental malocclusion, and delay in dental development [2,7,8]. DI is sometimes associated with OI, but no relationship has been found between the numbers of bone fractures or deformity and the degree to which the teeth are affected [8]. In contrast, other patients with OI have normal teeth [7].

The purpose of this case report is to present the systemic and the dentofacial features of OI and discuss special considerations that should be kept in mind in the case of dental management of this condition.

Case description and management

A 10-year-old Saudi female child was referred by her pediatrician to the medically compromised Pediatric Dentistry Clinic at the Faculty of Dentistry, King Abdulaziz University in Jeddah, Saudi Arabia (Fig. 1). The patient's main dental complaint was bleeding upon brushing, swollen gums, and broken teeth. She is the eldest among two siblings. Parents are first-degree cousins. The mother had full-term pregnancy and the patient was delivered by normal vaginal delivery. Medical history indicated that the patient is a known case of OI and osteoporosis. There was no history of a similar family condition. After birth, she was discovered to have facial bone fracture, but she had normal white sclera of eye and did not experience any discoloration. She had multiple bony fractures of both hands in her first year of life. After the first year, she was started on infusion doses of bisphosphonate (Zoledronic acid 0.05 mg/kg over 30 min) every 3 months to increase bone density. She is on a daily dose of vitamin D and calcium syrup (Osteocare, Vitabiotics Ltd., London, United Kingdom). She started to walk at 2 years of age. She had a ventricular septal defect that was corrected by surgery when she was 6 years old. Before 2 years, she complained of a swelling in the sole of the right foot, with severe pain upon walking. It was surgically removed under general anesthesia, and biopsy report indicated the diagnosis of neuofibroma. This lesion has recurred after 1 year and excisional biopsy was performed, which indicated the same diagnosis of neurofibroma. She is on regular recall visits with both the pediatric endocrinologist and the pediatric cardiologist. The patient had only one previous dental visit, where the dentist refused to treat her because of her medical problems.

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REVIEW

Oral health in patients with Prader-Willi syndrome: current perspectives

This article was published in the following Dove Press journal:
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Abstract: Prader-Willi syndrome (PWS) is a rare complex multisystem disorder and presents several aspects related to dentistry. The purpose of this review is to present current perspectives about oral health in patients with PWS. Delay development, hyperphagia, foamy and highly viscous saliva raise the risk of caries and contribute to tooth wear. Cariogenic foods uncontrolled consumption allows to obesity and dental problems progress worsening systemic disorders. These factors can be controlled. The success in follow-ups with caries free and oral health controlled demonstrate the importance of multidisciplinary team intervention corroborated by support at home from birth to adulthood. Thereby, current perspective on the disease is that there is possibility of proper maintenance of oral health in PWS patients. Guided care interferes positively with the overall well-being and quality of life of the individual with PWS and their family. A multidisciplinary team with a focus on teaching patients and family members will help minimize eventual problems.
Keywords: Prader-Willi syndrome, oral health, patient care management

Introduction

Prader-Willi syndrome (PWS) presents odontological aspects of interest. Many deleterious effects on the oral cavity were associated with this behavioral and endocrine disorder that may cause surgery and/or worsening of the clinical condition.[1]

History

First described by Dr. Langdom Down in 1887, it was named "polysardia" and documented by Andrea Prader, Heinrich Willi, and Alexis Labhart in 1956.[2] Besides Prader-Willi syndrome, others scientific names are Willi-Prader syndrome, Prader-Labhart-Willi syndrome,[3,4] and Prader-Labhart-Willi-Fanconi's syndrome.[4]

Definition, prevalence and, genetics

PWS is a complex and rare multisystem disorder,[5] it occurs at a similar prevalence between genders with an incidence of 1/15,000 to 1/25,000.[6] A lack of expression of Paterno's gene in chromosome 15q11–q13[5,7–11] causes PWS, and it is characterized by hypothalamic dysfunction.[7]

Genetic testing is performed to confirm the diagnosis.[11] There is a relationship between the clinical characteristics and the age range of the PWS carrier. This criterion is used to facilitate the analysis for the later request of DNA tests (Table 1). Feeding problems are a feature in infancy whereas hypogonadism is a problem in adolescence.[12]

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Article

Oral Health-Related Quality of Life in People with Rare Hereditary Connective Tissue Disorders: Marfan Syndrome

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Abstract: Background: The aim of this study was to analyze data on oral health-related quality of life (OHRQoL) in people with Marfan syndrome and to obtain information on the diagnosis period, orthodontic treatment, and oral symptoms. Methods: A questionnaire was developed consisting of open questions and the standardized German version of the OHIP-14 (Oral Health Impact Profile) questionnaire for the evaluation of OHRQoL. The age of diagnosis, time period from the first signs of the disease to diagnosis, and OHIP-values were compared between male and female participants. Additionally, the OHIP-values between participants who were orthodontically treated and those who were not treated were assessed. The statistical analysis was performed using the Mann–Whitney test with a significance level at $p = 0.05$. Results: A total of 51 questionnaires were evaluated, which included 34 female and 17 male participants. Overall, 84% of respondents reported oral symptoms. Male respondents tended to diagnose the disease earlier ($p = 0.00$), with a smaller period between the first symptom and the diagnosis ($p = 0.04$). The OHIP-14 score was gender-neutral at 13.65 ± 13.53 points. Conclusion: In Marfan syndrome, many years (12.01 ± 11.61) elapse between the onset of first symptoms and correct diagnosis of the disease. People with Marfan syndrome have a worse OHRQoL than do the general population.

Keywords: rare diseases; oral health-related quality of life; OHRQoL; Marfan; patient reported outcome; OHIP-14

1. Introduction

In the European Union, a disease is considered "rare" if it affects less than one in 2000 people [1]. Hereditary connective tissue diseases such as Marfan syndrome are therefore classified as rare diseases. The prevalence of Marfan syndrome is 1:5000 for both genders [2,3].

Marfan syndrome is a genetic systemic connective tissue disorder with varied and combined symptoms of the heart, circulation, muscles, skeleton, eyes, and lungs [2]. The cause of most Marfan syndromes is a mutation in the fibrillin-1 gene on chromosome 15q21 [3,4]. The oral symptoms of Marfan syndrome include a narrow, highly arched palate with crowding of the teeth [5,6], dysgnathia, malocclusion [7], temporomandibular dysfunction [8], and changes in the number of teeth [9].

To date, only a few studies have been carried out on oral health-related quality of life (OHRQoL) in people with rare diseases [10], who report reduced OHRQoL. With respect to Marfan syndrome, the authors were unable to find any publications that reported on OHRQoL.

For this reason, a survey questionnaire composed of free text questions and the standardized German version of the OHIP-14 (Oral Health Impact Profile) was developed (Table S1).

Dentistry

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Case Report Open Access

Cri Du Chat Syndrome: Dental Management and Case Report

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Abstract

Cri du chat Syndrome (CdCS) is a rare genetic condition with an incidence of 1:50,000 live births. It is a severe disease resulting from a deletion of the short arm of chromosome 5 and is characterized by intellectual disabilities and delayed physical development. The basic medical disorder includes dysmorphic facies, mental retardation, and a striking catlike cry in infancy. Because of significant oral anomalies and difficulty in behaviour management, the syndrome is of particular interest to dental practitioners. The aim of this paper was to report a case of a 12-year-old patient with CdCS referred to a paediatric dental clinic for dental treatment.

Keywords: 5p deletion; Cri du chat syndrome; Paediatric dentistry; Etiology; Classification; Analysis; Diagnosis

Introduction

Cri du chat syndrome (CdCS), discovered by Lejeune et al. in 1963 [1], is a genetic disease resulting from a deletion of the short arm of chromosome 5 (5p-). It is a rare disease with an incidence of 1:50,000 live-born infants [1]. The main character of this syndrome is a high-pitched catlike cry (hence the name of the syndrome), which was thus described by Grouchy and Turleau in 1977 [2], due to malformation of the larynxes of children with this syndrome. However, it is believed that with advancing age, such sound becomes less characteristic, making it difficult to diagnose this condition [3]. CdCS is characterized by intellectual disabilities and delayed physical development, including abnormalities of the airways [4]. The clinical features at birth are low weight, microcephaly, round face, large nasal bridge, hypertelorism, epicanthal folds, downward slanting palpebral fissures, down-turned corners of the mouth, low-set ears, micrognathia, and abnormal dermatoglyphics (transverse flexion creases) [5]. Diagnosis of this syndrome is defined by the clinical characteristics and examination of the cytogenetic-affected child, with a guideline available for the parents [6]. Patients with this syndrome may present orofacial anomalies, including mandibular microretrognathia, dental biprotrusion, dental malocclusions, high but rarely cleft palate, anterior open bite, poor oral hygiene, enamel hypoplasia, generalized chronic periodontitis, and retardation of tooth eruption [6,7]. Taking into consideration the relevance of CdCS, the objective of this study was to report the dental treatment performed on a patient with a CdCS diagnosis.

Case Report

A 12-year-old male patient diagnosed with CdCS attended the clinic of the Acolher/PNE project at Fluminense Federal University for dental treatment. The patient's mother sought dental care because the patient, who has a speech disability, showed pain in the lower region of the teeth. The patient used to show his mother where it hurts by placing his hand on his face, near the acking teeth. Anamnesis and clinical examination were performed. The patient's mother reported that she was 25 years old when she became pregnant and had a pregnancy without complications or the use of medicine. The mother also reported no presence of congenital anomalies in other family members.

The medical history revealed hospitalization for bacterial pneumonia for five months, a seizure, anaemia, and a tracheostomy. The patient uses drugs such as levothyroxine sodium (once a day) for treatment of congenital hypothyroidism and risperidone (once a day) for anxiety control and altered behaviour; he started taking these medications at three years old. The manufactures claim these medications have no side effects in oral cavity. In addition, the patient undergoes occupational therapy as a means of cognitive development and presents a deficit of learning and communication; however, he hears in a normal tone.

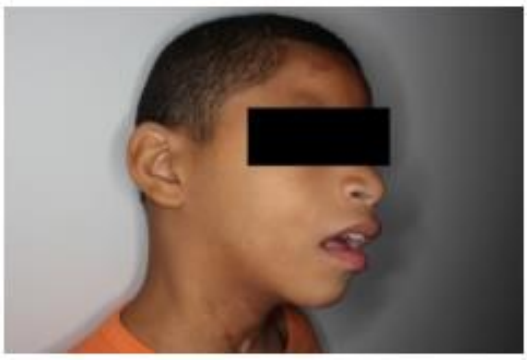

Figure 1: Side view of patient's face.

The patient's dysmorphic features included microcephaly, a broad forehead, a depressed nasal bridge, bilateral low-set ears, a high-arched

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Oral and Craniofacial Anomalies of Bardet-Biedl Syndrome: Dental Management in the Context of a Rare Disease

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Abstract

Standardized guidelines for the oral health management of patients with rare diseases exhibiting morphologic anomalies are currently lacking. This review considers Bardet-Biedl syndrome (BBS), a monogenic autosomal recessive nonmotile ciliopathy, as an archetypal condition. Dental anomalies are present in a majority of individuals affected by BBS due to abnormal embryonic orofacial and tooth development. Genetically encoded intrinsic oral structural anomalies and heterogeneous BBS clinical phenotypes and consequent oral comorbidities confound oral health management. Since the comorbid spectrum of BBS phenotypes spans diabetes, renal disease, obesity, sleep apnea, cardiovascular disease, and cognitive disorders, a broad spectrum of collateral oral disease may be encountered. The genetic impact of BBS on the anatomic development of oral components and oral pathology encountered in the context of various BBS phenotypes and their associated comorbidities are reviewed herein. Challenges encountered in managing patients with BBS are highlighted, emphasizing the spectrum of oral pathology associated with heterogeneous clinical phenotypic expression. Guidelines for provision of care across the spectrum of BBS clinical phenotypes are considered. Establishment of integrated medical-dental delivery models of oral care in the context of rare diseases is emphasized, including involvement of caregivers in the context of managing these patients with special needs.

Keywords: ciliopathies, cilia, mutation, registries, Wnt signalling pathway, maxillofacial abnormalities

Introduction

Bardet-Biedl syndrome (BBS) is a pleiotropic autosomal recessive genetic disorder with vast genetic heterogeneity (Forsythe et al. 2003). To date, causal mutations of 21 genes (*BBS1* to *BBS21*; see Fig. 1A; Forsythe et al. 2003; Heon et al. 2016; Schaefer et al. 2016) have been identified, accounting for approximately 80% of individuals meeting diagnostic criteria for BBS. Relative frequency of genetic mutations seen in BBS was summarized in a recent review by Haws et al. (2015), with *BBS1* and *BBS10* showing the highest prevalence and approximately 20% remaining undefined to date (see Fig. 1B). The clinical diagnosis is established if 4 primary features, or 3 primary and 2 secondary features, are evident. Table 1 summarizes primary and secondary features of BBS (Beales et al. 1999; Forsythe and Beales 2013). Improved understanding of dental anomalies associated with BBS is essential to informing proper dental treatment planning and providing supportive oral care for affected patients, which is often complicated by coexisting renal, cardiac, metabolic, and developmental abnormalities. The focus of this review is as follows: 1) to summarize current knowledge on primary craniofacial abnormalities and oral manifestations associated with BBS and secondary oral manifestations that may arise from other clinical manifestations associated with BBS; 2) expand on current understanding of pathophysiology of dental abnormalities encountered in BBS; and 3), in the absence of clinical practice guidelines for management of patients with ciliopathies, highlight considerations surrounding care planning and oral health management of patients with BBS presenting with primary and secondary oral manifestations.

Epidemiology

First described by Georges Louis Bardet and Artur Biedl in the early 1920s, BBS is characterized as a condition with an array of clinical characteristics (Forsythe et al. 2003). Incidence of BBS is very rare, and few studies have assessed

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Otodental syndrome: a case presentation in a 6-year old child

ABSTRACT

Background *Otodental syndrome is a rare condition characterised by globodontia, and sensorineural high frequency hearing loss. To date, only 20 cases of otodental syndrome have been reported.*

Case report *A 6 year-old girl presented with a chief complaint of delay in the eruption of primary canines. Following clinical, radiographic and audiologic evaluations, the patient was diagnosed with otodental syndrome.*

Conclusion *Globodontia is a diagnostic feature of the otodental syndrome, which often provides the path to discovery of the associated hearing loss. Missing teeth, arch-size discrepancies, chewing problems and teething disturbances are the other major complications.*

Keywords *Globe-shaped teeth; Globodontia; Hearing loss; Otodental syndrome.*

Introduction

Otodental syndrome is a rare anomaly, inherited on an autosomal dominant basis [Hennekam et al., 2010]. The condition has also been reported under various names, including familial otodentodysplasia [Toledo et al., 1971] and otodental dysplasia. [Levin et al., 1975; Chen et al., 1988]. Otodental syndrome is characterised by globodontia [Witkop et al., 1976] and sensorineural high frequency hearing loss [Hennekam et al., 2010]. Globodontia is a striking dental phenotype, characterised by abnormal bulbous enlargement of tooth crown with almost no discernable cusps, which is both pathognomonic and diagnostic of the otodental syndrome [Hennekam et al., 2010]. Globodontia occurs in both primary and permanent dentition, affecting canine and posterior teeth [Witkop et al., 1976]. Primary and permanent incisors are not affected and display normal shape and size.

After Winter [1983] reported an associated ocular trait, the condition was later named oculo-oto-dental syndrome (OOD) by Vierra et al. [2002]. However, that particular family which exhibited ocular coloboma is considered as a different condition, since no other case in the literature has presented the same ocular trait [Hennekam et al., 2010]. Gregory-Evans et al. [2007] evaluated 3 families with globodontia, one being the original case presented by Winter [1983]. Following molecular tests, the authors suggested that FGF3 haploinsufficiency is likely the cause of otodental syndrome and that FADD haploinsufficiency accounts for the associated ocular coloboma [Gregory-Evans et al., 2007].

Other reported dental findings of otodental syndrome include localised enamel defects (hypoplasia) on canines, missing or microdontic premolars, odontomas and conically-shaped supernumerary teeth [Hennekam et al., 2010; Bloch-Zupan et al., 2006]. Delayed eruption is a frequent finding in both primary and permanent dentitions [Bloch-Zupan et al., 2006].

In otodental syndrome, bilateral sensorineural hearing deficiency to about 65dB is found at all frequencies but is more pronounced at about 1000 Hz. [Hennekam et al., 2010]. The age of onset of the hearing loss ranges from early childhood to middle age [Cook et al., 1981; Jorgenson et al., 1975; Colter et al., 2005]. Regardless of the age of onset, hearing loss is progressive but it usually plateaus by the fourth decade [Cook et al., 1981].

The present case report describes the clinical features of otodental syndrome in a 6-year-old girl.

Case report

A 6-year-old girl was referred to the Paediatric Dentistry Department with a chief complaint of delay in the eruption of her primary canines. According to the hospital records, the child had experienced an emergency intervention at the age of 4 due to a piece of cake lodged in her throat. The cake was uneventfully removed with a nasogastric tube, but thereafter the child consistently reported difficulty in chewing.

Intraoral examination showed that the maxillary and

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RESEARCH Open Access

Oral health-related quality of life in Loeys-Dietz syndrome, a rare connective tissue disorder: an observational cohort study

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Abstract

Background: Loeys-Dietz syndrome (LDS) is a rare connective tissue disorder whose oral manifestations and dental phenotypes have not been well-characterized. The aim of this study was to explore the influence of oral manifestations on oral health-related quality of life (OHRQoL) in LDS patients.

Material and methods: LDS subjects were assessed by the craniofacial team at the National Institutes of Health Clinical Center Dental Clinic between June 2015 and January 2018. Oral Health Impact Profile (OHIP-14) questionnaire, oral health self-care behavior questionnaire and a comprehensive dental examination were completed for each subject. OHRQoL was assessed using the OHIP-14 questionnaire with higher scores corresponding to worse OHRQoL. Regression models were used to determine the relationship between each oral manifestation and the OHIP-14 scores using a level of significance of $p \leq 0.05$.

Results: A total of 33 LDS subjects (51.5% female) aged 3–57 years (19.6 ± 15.1 years) were included in the study. The OHIP-14 scores ($n = 33$) were significantly higher in LDS subjects (6.30 [SD 6.37]) when compared to unaffected family member subjects (1.50 [SD 2.28], $p < 0.01$), and higher than the previously reported scores of the general U.S. population (2.81 [SD 0.12]). Regarding oral health self-care behavior ($n = 32$), the majority of LDS subjects reported receiving regular dental care (81%) and maintaining good-to-excellent daily oral hygiene (75%). Using a crude regression model, worse OHRQoL was found to be associated with dental hypersensitivity ($\beta = 5.24$; $p < 0.05$), temporomandibular joints (TMJ) abnormalities ($\beta = 5.92$; $p < 0.01$), self-reported poor-to-fair oral health status ($\beta = 6.77$; $p < 0.01$), and cumulation of four or more oral manifestations ($\beta = 7.23$; $p < 0.001$). Finally, using a parsimonious model, self-reported poor-to-fair oral health status ($\beta = 5.87$; $p < 0.01$) and TMJ abnormalities ($\beta = 4.95$; $p < 0.01$) remained significant.

Conclusions: The dental hypersensitivity, TMJ abnormalities, self-reported poor-to-fair oral health status and cumulation of four-or-more oral manifestations had significant influence on worse OHRQoL. Specific dental treatment guidelines are necessary to ensure optimal quality of life in patients diagnosed with LDS.

Keywords: Rare diseases, Rare connective tissue disorders, Loeys-Dietz syndrome (LDS), Oral health-related quality of life (OHRQoL), Oral health impact profile (OHIP-14)

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Oral cavity health among cystic fibrosis patients: Literature overview

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of article

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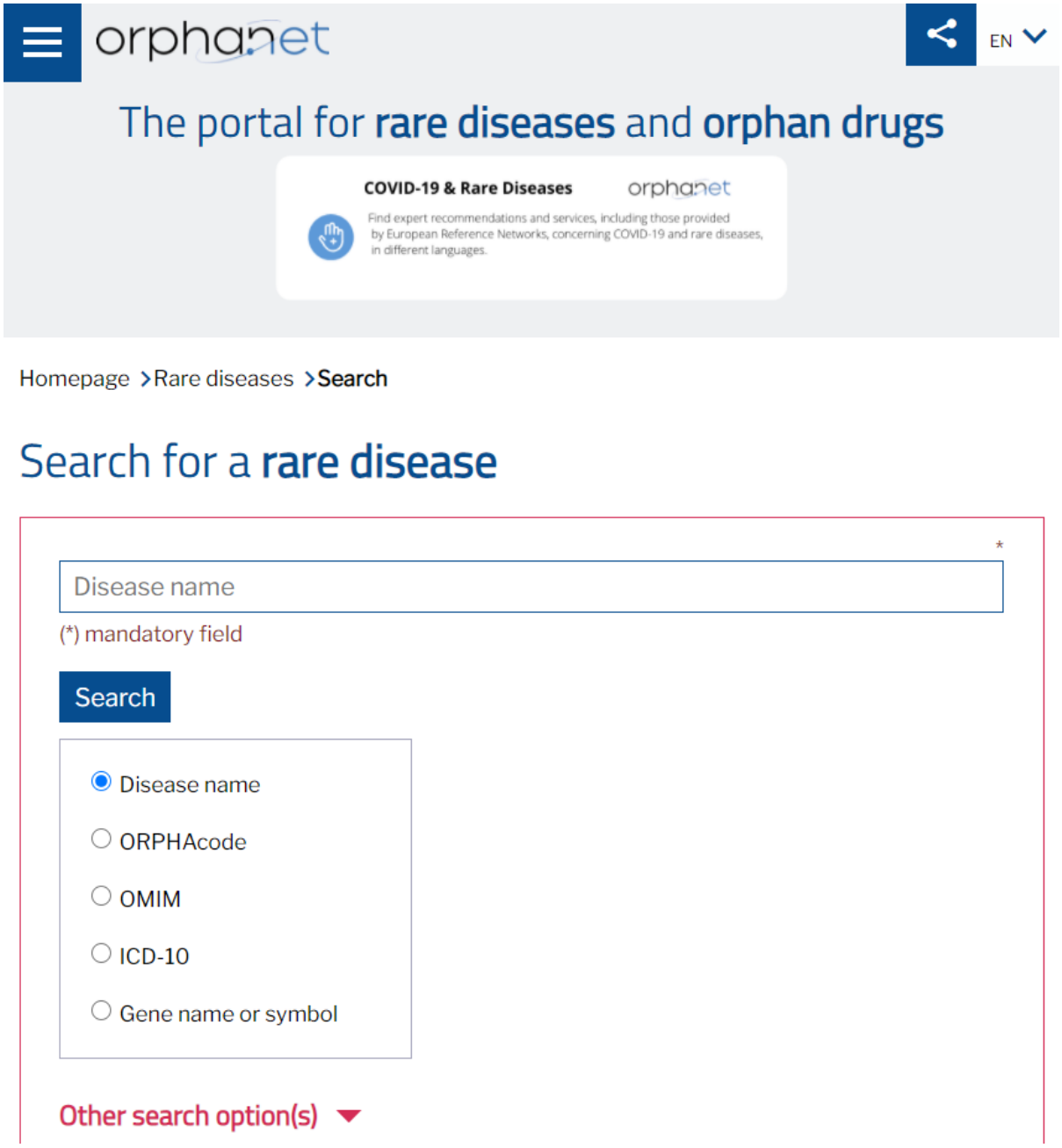
Abstract

Cystic fibrosis is a genetic disorder in which the mutation of the Cystis Fibrosis Transmembrane Conductance Regulator (CFTR) gene that codes the protein forming a chloride channel of epithelial cells results in its distorted functioning. The manifestations of the disorder are mainly observed in the respiratory and digestive system. Accumulation of sticky and thick mucus is the dominant clinical symptom; it leads to chronic infections and gradual tissue destruction. Although cystic fibrosis remains incurable, it is currently feasible to extend patients' life expectancy thanks to modern therapy possibilities. As cystic fibrosis is no longer the domain of pediatricians, health care to CF patients needs to be provided by doctors of various specializations. The multidisciplinary team of doctors should include a dentist aware of specific prevention and treatment needs of this group of patients. It results from the fact that in the course of cystic fibrosis it is possible to observe a variety of changes in the oral cavity environment. The study presents dental issues observed in CF patients and reported in literature. Particular attention was paid to dental caries, mineralization disorders of hard dental tissues, gingivitis and the change in the content and properties of saliva; moreover, prevention and treatment options regarding oral cavity health is this group of patients were taken into consideration.

Key words: cystic fibrosis, gastrointestinal disorders, oral disease, genetic markers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Case Report

Role of multidisciplinary approach in a case of Langerhans cell histiocytosis with initial periodontal manifestations

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Abstract: Introduction: Langerhans cell histiocytosis (LCH) is a rare inflammatory myeloid neoplasia of unknown etiology occurring in both children and adults. This condition is characterized by an abnormal proliferation of Langerhans cells that may virtually affect all sites in the human body. Oral manifestations of LCH could be the first clinical sign of disease and its periodontal localization could be easily mistaken for other more common entities, such as chronic periodontitis, aggressive periodontitis, and necrotizing ulcerative periodontitis. Case presentation: A 32-years old female visited a private dental practice with a chief complaint of sensitivity in the mandibular left first molar. Clinical and radiographic examination revealed deep periodontal pocket, recession, furcation involvement, mobility, severe alveolar bone destruction and a diagnosis of aggressive periodontitis was rendered. Multiple tooth extractions were carried out due to progressive periodontal destruction with impaired healing and development of ulcerative lesions. Multidisciplinary investigation demonstrated that the periodontal involvement was a manifestation of an underlying systemic disease. A biopsy of a bone lesion was therefore performed, revealing the presence of multifocal single system LCH. Conclusion: The identification of periodontal LCH is not trivial given that it may clinically resemble other periodontal disease entities. The dentist can be the first health care personnel to unravel the presence of an underlying systemic LCH.

Keywords: Langerhans cell histiocytosis, systemic disease, bone lesions, periodontal disease

Introduction

Langerhans cell histiocytosis (LCH) is the most common histiocytic disorder, which is characterized by an abnormal proliferation of CD1a-positive histiocytes, *i.e.* Langerhans cells [1]. This exceedingly rare inflammatory myeloid neoplasia may affect virtually all organ systems of the human body, with no predilection of gender [1, 2]. Despite affecting any age group, from newborns to elders, the incidence of LCH is higher in children compared to adults, with a median age of presentation of 30 months [3]. In particular, young Caucasian individuals are reported to be the highest-risk population [4]. Although the etiology of LCH remains enigmatic, possible causative factors have been proposed, including disturbance in immunoregulation, genetic factors, thyroid diseases and smoking [5-8]. The biology underpinning LCH is still a subject of debate; however, recent advances in the genomic characterization of this rare condition revealed the presence of an activating hotspot V600E somatic mutation in the proto-oncogene B-Raf (*BRAF*) in up to 57% of cases [9]. Moreover, activation of extracellular-signal-regulated kinases (ERKs) appeared to be universal in LCH in recent molecular studies [10].

The clinical course of LCH is highly variable and unpredictable, existing along a spectrum of disease that may involve a single site (unifocal), multiple sites (multifocal) in a single organ system or multiple organ systems (multisystem) which could affect a limited number of organs or either be disseminated and life threatening [2, 11]. Bone is the most commonly involved tis-

Vasileios Panis

Langerhans cell histiocytosis mimicking aggressive periodontitis: Challenges in diagnosis and management

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Objective: Langerhans cell histiocytosis (LCH) is a rare disorder characterized by clonal proliferation of Langerhans cells that affects various organs. Oral involvement may simulate periodontal disease and cause significant diagnostic and management difficulties. Here, we present an interesting LCH case with severe periodontal destruction in a young woman in order to facilitate early recognition of this aggressive disease and successful participation of the general practitioner in the management of such patients. **Case Presentation:** A 21-year-old woman was referred for evaluation of recurrent episodes of dull pain in the gingiva for the last 9 months, which had not been successfully managed by her general practitioner. Clinical and radiographic examination showed extensive alveolar bone loss. Histopathologic examination revealed diffuse aggregates of Langerhans cells, while a complete work-up did not demonstrate evidence of systemic involvement. A diagnosis of LCH limited to the oral cavity was established. The patient received systemic chemotherapy in combination with appropriate dental care including gingival debridement and tooth immobilization. Following chemotherapy completion, comparative clinical, radiographic, and microscopic evaluation showed complete remission. During an 18-month follow-up period, frequent oral examinations and appropriate dental interventions confirmed the lack of LCH recurrence and guaranteed the stabilization of periodontal tissues. **Conclusions:** Oral soft and hard tissue involvement may be the only manifestation of LCH. The present case exemplifies the importance of close collaboration between general dentistry and its disciplines (periodontology, restorative dentistry, oral medicine, oral and maxillofacial pathology, and oral radiology), and hematology-oncology for diagnosis, management, treatment monitoring, and decision-making. *(Quintessence Int 2016;47:731–738; doi: 10.3290/j.qi.a36568)*

Key words: aggressive periodontitis, general practitioner, jaws, Langerhans cell histiocytosis, multidisciplinary approach, osteolytic lesions

Frequently, the general practitioner encounters cases characterized by gingival inflammation and periodontal tissue destruction that cannot be easily attributed to local factors alone. Especially in younger patients, the appearance of extensive alveolar bone loss, tooth mobility, and swollen and painful gingiva should raise the possibility of an underlying systemic condition causing or exacerbating rapid periodontal destruction. In this context, various possible systemic causes must

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The case report was presented at the Joint meeting of the American Academy of Oral and Maxillofacial Pathology and the American Academy of Oral Medicine, San Diego, USA, 18–24 April 2015.

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Role of gingival manifestation in diagnosis of granulomatosis with polyangiitis (Wegener's granulomatosis)

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Purpose: This report describes a case of granulomatosis with polyangiitis (GPA) in which the gingival manifestation was crucial in both making an early diagnosis and possibly in deciding the approach to treatment.
Methods: A 57-year-old sailor presented to the Department of Dentistry at Ulsan University Hospital complaining of gingival swelling since approximately 2 months. He had orofacial granulomatous lesions and the specific gingival manifestation of strawberry gingivitis.
Results: The diagnosis of GPA was made on the basis of clinical symptoms and signs, and confirmed by the presence of the anti-neutrophil cytoplasmic antibody and a positive biopsy. The patient was admitted to the hospital and subsequently placed on a disease-modifying therapy regimen that included methotrexate and prednisone.
Conclusions: Identification of the gingival manifestation of the disease permitted an early diagnosis and prompt therapy in a disease in which time is a crucial factor. Because of its rapid progression and potentially fatal outcome, an early diagnosis of GPA is important. Therefore, dentists should be aware of the oral signs and symptoms of such systemic diseases.

Keywords: Diagnosis, Gingiva, Granulomatosis with polyangiitis, Orofacial.

INTRODUCTION

Several systemic diseases exhibit oral and gingival manifestations, and thus dentists can play an important role in the early diagnosis of these diseases. Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is one such disease that may have gingival manifestations. GPA is a potentially life-threatening disease characterized by necrotizing granulomatous inflammation and small vessel vasculitis. The precise etiology of GPA remains unknown. It chiefly affects the upper and lower respiratory tract and kidneys, but can affect any part of the body or any of its organs [1-3]. Inflammation of the blood vessels leads to damage to vital organs. Without treatment GPA usually runs a rapid and fatal course with most patients not surviving more than a year after diagnosis [4-6].

Oral involvement of GPA has been observed in approximately 6%–13% of patients [7] and its manifestation includes oral mucosal ulcerations and nodules. However the most characteristic oral lesion is hyperplastic gingivitis presenting with a "strawberry like" appearance [5,8]. Occasionally oral lesions are observed before multi-organ involvement occurs. The diagnosis of GPA is made based on clinical symptoms and signs, the presence of the anti-neutrophil cytoplasmic antibody (ANCA), and a positive biopsy [9]. Because of its

Caring For Patients with Ehlers-Danlos Syndrome

By Darlene J. Swigart, EPDH, MS on December 14, 2016

PURCHASE COURSE

This course was published in the February 2018 issue and expires February 2021. The authors have no commercial conflicts of interest to disclose. This 2 credit hour self-study activity is electronically mediated.

EDUCATIONAL OBJECTIVES

After reading this course, the participant should be able to:

1. Describe and define Ehlers-Danlos syndrome.
2. Discuss the diagnosis of EDS.
3. Identify the oral health issues that may present in patients with EDS.

Ehlers-Danlos syndrome (EDS) represents a rare group of inherited connective tissue disorders involving the biosynthesis of collagen—the major protein building material in the body.[1-3] EDS is a multisystemic disorder affecting patients both physically and psychologically with a wide range of symptoms. The most common manifestations include hyperelasticity of the skin (Figure 1A), hypermobility (Figure 1B) and joint pain, frail soft tissue with bruising and scarring, and chronic fatigue.[1,4-7,8]

Due to advances in genotyping, gene mutations have been isolated in many types of EDS, supporting the theory that an inheritable factor exists in this rare disorder.[3,9-13] Identification through genetic testing is not always

CRITICAL REVIEWS IN ORAL BIOLOGY & MEDICINE

Rare Bone Diseases and Their Dental, Oral, and Craniofacial Manifestations

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Abstract: *Hereditary diseases affecting the skeleton are heterogeneous in etiology and severity. Though many of these conditions are individually rare, the total number of people affected is great. These disorders often include dental-oral-craniofacial (DOC) manifestations, but the combination of the rarity and lack of in-depth reporting often limit our understanding and ability to diagnose and treat affected individuals. In this review, we focus on dental, oral, and craniofacial manifestations of rare bone diseases. Discussed are defects in 4 key physiologic processes in bone/tooth formation that serve as models for the understanding of other diseases in the skeleton and DOC complex: progenitor cell differentiation (fibrous dysplasia), extracellular matrix production (osteogenesis imperfecta), mineralization (familial tumoral calcinosis/hyperostosis hyperphosphatemia syndrome, hypophosphatemic rickets, and hypophosphatasia), and bone resorption (Gorham-Stout disease). For each condition, we highlight causative mutations (when known), etiopathology in the skeleton and DOC complex, and treatments. By understanding how these 4 foci are subverted to cause disease, we aim to improve the identification of genetic, molecular, and/or biologic causes, diagnoses, and treatment of these and other rare bone conditions that may share underlying mechanisms of disease.*

Key Words: fibrous dysplasia of bone, osteogenesis imperfecta, familial hypophosphatemic rickets, hypophosphatasia, hyperphosphatemic familial tumoral calcinosis, Gorham-Stout disease.

Introduction

Hereditary diseases affecting the skeleton, which we define to include the craniofacial and dental structure, are heterogeneous in etiology, onset, and severity. Although many of these conditions are individually rare (affecting less than 1 in 200,000), the total number of people affected is great (see the National Organization for Rare Disorders at www.rarediseases.org and the Rare Bone Disease Patient Network at http://www.usbji.org/projects/RBDPN_op.cfm). Rare disorders are difficult to diagnose and are easily misdiagnosed; those of the skeleton are no exception. While progress has been made in our understanding of the underlying causes, pathologies, and mechanisms of bone diseases, those of the dental-oral-craniofacial (DOC) complex are frequently overlooked or superficially reported. This has implications in terms of understanding, diagnosing, and treating affected individuals, in turn affecting health and quality of life.

Proper formation of the skeleton and dentition requires integration of numerous processes beginning in early embryonic development. These include patterning of the head, limbs, and skeletal/dental elements, cell migration and proliferation, differentiation to specialized cells, matrix secretion, biomineralization of bones and teeth, and remodeling of bone. For purposes of this review, we discuss 4 processes directly affecting the formation and function of craniofacial bones and teeth (Fig. 1) that can serve as models for an

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Review article

Periodontal and oral health status of people with Cystic Fibrosis: a systematic review

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ABSTRACT

Introduction and Objectives: People with Cystic Fibrosis (PWCF) may be presumed to be at lower risk of periodontal disease due to long term antibiotic use but this has not been comprehensively investigated. The oral hygiene and periodontal status of PWCF in comparison to the general population is not well established.
The objective of this systematic review was to critically evaluate the literature on periodontal and oral hygiene status in PWCF to see if this group are at increased risk of periodontal disease (gingivitis or periodontitis).
Data Sources: 5 databases were searched: Scopus, MEDLINE, Embase, Cochrane Library and Web of Science.
Study Selection: The search resulted in 614 publications from databases with one more publication identified by searching bibliographies. 13 studies were included in the qualitative analysis.
Conclusions: The majority of studies showed better oral hygiene, with lower levels of gingivitis and plaque among people with Cystic Fibrosis (PWCF) than controls. Interestingly, despite this, many studies showed that PWCF had higher levels of dental calculus. Three studies found there was no difference in Oral Hygiene between PWCF and controls. One study found that PWCF aged between 6 and 9.5 years had increased levels of clinical gingivitis, and one study showed that PWCF with gingivitis had more bleeding on probing than people without CF. The vast majority of PWCF examined were children- only five studies included people over 18 years, and only one looked exclusively at adults. There is a need for further study into the periodontal health of PWCF- particularly those over the age of 18.
Clinical Significance: There are currently no guidelines referring to oral care in PWCF. Studies have suggested that the oral cavity acts as a reservoir of bacteria which may colonise the lungs.
If PWCF are at increased risk of periodontal disease, they should attend for regular screenings to facilitate early detection.

1. Introduction

Cystic fibrosis (CF) is the most common lethal genetic disease in white populations [1]. It was first recognised as a separate disease entity in 1938 when Dorothy Andersen's study distinguished a disease of mucus plugging of the glandular ducts from that of coeliac disease [2]. The genetic basis for this disease is a well-characterized, severe monogenic recessive disorder, found mainly in Caucasian populations of European ancestry, which arises from mutations in the cystic fibrosis transmembrane conductance regulator (*CFTR*) gene on chromosome 7 [3]. More than 1500 CFTR mutations have been identified, but the functional importance of only a small number is known [1]. ΔF508 is the most common CF mutation worldwide, accounting for approximately 66% of the cases of CF [4]. The mutations of the CFTR epithelial chloride channel dehydrates secretions in the airways, the pancreatic ducts, and in other organ systems which results in progressive organ damage. The main impact can be seen in the Respiratory/Pulmonary System (e.g. repeated infective pulmonary exacerbations, bronchiectasis, pneumothorax, haemoptysis), Pancreatic Disease (e.g. pancreatic insufficiency, Cystic Fibrosis Related Diabetes), Hepatobiliary Disease (e.g. Liver disease, Cirrhosis), Gastrointestinal Tract (e.g. GORD, malabsorption of fat), Kidney Disease (including chronic renal insufficiency), Genitourinary (including male infertility), Bone Disease (e.g. osteopenia, osteoporosis) and Cutaneous Diseases (including urticaria and vasculitis) [5–7]. The manifestations of CF can impact significantly on quality of life, which tends to deteriorate as the severity of the disease increases [8].

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Case Report Open Access

Oral Manifestations of a Patient with Epidermolysis Bullosa

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Abstract

Epidermolysis bullosa acquisita (EBA) is a chronic autoimmune bullous disease characterized by the presence of IgG and IgM antibodies at the level of basement membrane. It is rare in humans and animals with an incidence ranging from 0.2 to 0.5 new cases per million and per year. This dermatological condition is a severe autoimmune disease. Scarring of the extensor surfaces of the extremities, hands and feet are typical; milia occur frequently; and nails often become thick and dystrophic or are lost. The disorder affects both sexes equally and occurs in all racial and ethnic groups.

Keywords: Adherent fingers; Absent nails; Microstomia; Bullae; Preventive care

Introduction

Epidermolysis Bullosa (EB) is a group of rare inherited disorders, usually detected at birth or early childhood [1-4]. Köbner coined the term 'epidermolysis bullosa' in 1886, but even before this time, Legg and Brocq had already provided a clinical description of the disease. Epidermolysis bullosa characterized by extreme fragility of the skin and mucous membranes, which gives rise to the formation of blisters following minor trauma [5]. This dermatological condition is a severe autoimmune disease [6,7]. Scarring of the extensor surfaces of the extremities, hands and feet are typical; milia occur frequently; and nails often become thick and dystrophic or are lost. The disorder affects both sexes equally and occurs in all racial and ethnic groups [8]. Epidermolysis bullosa has been classified into three major types depending upon the histological level of tissue separation [9]:

I. Epidermolysis bullosa simplex is characterized by discontinuities in the epithelial keratinocyte layer;

II. Junctional epidermolysis bullosa involves separation within the basement membrane; and

III. Dystrophic epidermolysis bullosa is characterized by discontinuities in the underlying connective tissue.

Each type of EB has various subtypes and these may vary in severity [10]. Skin biopsies are needed for appropriate diagnosis and classification for affected subjects.

Case Report

A 12-year-old female patient diagnosed with severe generalized junctional EB was referred to the Department of oral medicine and Radiology. The patient complaints of dental pain, halitosis, severe crustation of lips and limited mouth opening with ulcerations of buccal mucosa. The patient had one sister, aged 6 years old, who was unaffected by the disease. Her parents were also unaffected and were not consanguineous. Both sets of grandparents came from the nearby areas of same state. This type of illness had not previously appeared in the family Physical examination revealed generalized worn-out skin, blistering and scar formation, with blisters and vesicles present especially on the head and neck .The patient's few fingers were adherent, and her nails were absent (Figures 1 & 2). Scar formation had resulted in the formation of microstomia (Figure 3). The patient's maximum mouth opening was 14 mm. Clinical examination showed multiple missing teeth, decay and poor oral hygiene (Figure 4), due in part to a soft diet and hand contractures.

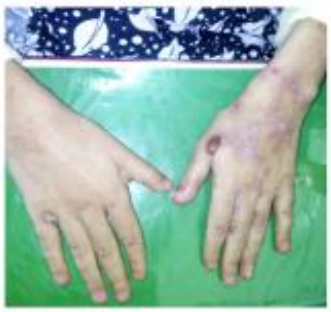

Figure 1: Nails absent.

Miscellaneous Latest CE Courses

The Signs and Symptoms of Hereditary Hemorrhagic Telangiectasia

Though this genetic disorder is relatively rare, the first manifestations often appear in the oral cavity, so dental professionals need to be prepared to recognize them.

By Aleksandra Pavolotskaya, LDH, MS — On Nov 13, 2013 — 0

PURCHASE COURSE

This course was published in the November 2013 issue and expires November 2016. The author has no commercial conflicts of interest to disclose. This 2 credit hour self-study activity is electronically mediated.

EDUCATIONAL OBJECTIVES

After reading this course, the participant should be

Hereditary hemorrhagic telangiectasia (HHT) is a relatively uncommon autosomal dominant genetic disorder that causes multiple arteriovenous malformations (AVMs) of the nose, skin, lung, brain, liver, and gastrointestinal (GI) tract, which can significantly impede blood circulation (Figure 1).[1] This medical condition is also referred to as Osler-Weber-Rendu Syndrome, after the names of the authors who first described the clinical symptoms and hereditary occurrences of the disease. In 1896, Rendu described the disease as a pseudo hemophilia related to hereditary epistaxis (nosebleeds). In 1901, Osler described the clinical symptoms of the syndrome and hereditary occurrence. In 1907, Weber separated

HHT from

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Mini-implants: Alternative for Oral Rehabilitation of a Child with Ectodermal Dysplasia

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Ectodermal dysplasia is a rare congenital disease that affects several structures of ectodermal origin. The most commonly related oral characteristics are hypodontia, malformed teeth and underdeveloped alveolar ridges. New alternative treatments are needed due to the failure of the conventional prosthesis retention. This case report outlines the oral rehabilitation treatment of a 9-year-old girl with ectodermal dysplasia. The treatment was performed with conventional prosthesis upon mini-implants. The mini-implants provided prosthetic retention. The patient reported a good adaptation of the dental prosthesis and satisfaction with the treatment. The increased self-esteem improved the socialization skills of the girl. In this case report, use of prosthesis with mini-implants was satisfactory for prosthetic retention. However, clinical studies with long-term follow-up are needed to test the mini-implants as an alternative for oral rehabilitation of children with ectodermal dysplasia.

Key Words: ectodermal dysplasia, child, oral rehabilitation.

Introduction

Ectodermal dysplasia (ED) is a rare congenital disease linked to a recessive gene from X chromosome. It affects several structures of ectodermal origin, such as hair, skin, nails and teeth. This disease has an incidence of 1:100,000 births, is more common among boys and has a 30% mortality rate in childhood due to intermittent hyperthermia (1-3).

The patient with ED presents specific facial and oral characteristics, such as saddled nose, decreased vertical dimension, facial depth, labial protuberance, little hair, lack of eyelashes and eyebrows, hypodontia, malformed and conical teeth, diastema, underdeveloped alveolar ridges, lack of teeth on both deciduous and permanent dentitions (4).

Dental prosthesis is the conventional oral rehabilitation of patients with ED. Due to the lack of areas for prosthesis retention and stability in these patients, some alternatives of rehabilitation are needed. Dental implants have been used as an alternative to increase the support or retention of definitive prostheses (5-8). Mini-implants, frequently used for orthodontic anchorage and prosthesis abutments, have been suggested as conventional implants with smaller dimensions. Patients treated with mini-implants as dental abutments demonstrated more satisfaction with their rehabilitation than those treated with conventional prostheses (9). The authors reported better retention and adaptation, and masticatory efficiency and comfort, resulting in a positive impact on their quality of life. There are two reports on the use of mini-implants for prosthetic rehabilitation of children (10,11) and recently, Sfeir et al. (12), described the use of mini-implants in children with ED.

This paper presents a case of oral rehabilitation of a child with ED using dental prosthesis supported by mini-implants.

Case Report

A 9-year-old girl presented with chief complaint of missing teeth and speech and mastication impairment. During review of clinical history, the mother reported that the child had been examined by a pediatrician and diagnosed with ED. History of lack of retention and stability of a previously used dental prosthesis was also reported.

Extraoral examination revealed visible loss of facial vertical dimension, hypotonicity of the perioral musculature, with a senile facial appearance. The patient presented dry and rough skin, sparse scalp hair, missing eyelashes and eyebrows, and severe hypohidrosis (Fig. 1A). Intraoral examination was observed hypodontia, with the presence of four erupted teeth (#55, #65, #75 and #85), and two conical teeth (#11 and #21) (Fig. 1B), besides reduced vertical dimension, xerostomia, and diastema between maxillary anterior teeth. Dental germs of the mandibular first molars were identified on the panoramic radiograph (Fig. 1C).

In the first treatment approach, the dentists had recommended the restoration of the maxillary incisors and adaptation of a conventional partial removable

Review Article

Dental Treatment in Patients with Leukemia

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Dental treatment of patients with leukemia should be planned on the basis of antineoplastic therapy which can be chemotherapy with or without radiotherapy and bone marrow transplantation. Many are the oral manifestations presented by these patients, arising from leukemia and/or treatment. In addition, performing dental procedures at different stages of treatment (before, during, or after) must follow certain protocols in relation to the haematological indices of patients, aimed at maintaining health and contributing to the effectiveness of the results of antineoplastic therapy. Through a literature review, the purpose of this study was to report the hematological abnormalities present in patients with leukemia, trying to correlate them with the feasibility of dental treatment at different stages of the disease. It is concluded in this paper that dental treatment in relation to haematological indices presented by patients with leukemia must follow certain protocols, mainly related to neutrophil and platelet counts, and the presence of the dentist in a multidisciplinary team is required for the health care of this patient.

1. Introduction

The insertion of dentistry in the multidisciplinary context of hematology-oncology is an important part of the success of cancer treatment. Oral complications can compromise the protocols of chemotherapy, possibly making it necessary to decrease the administered dose, the change in treatment protocol, or even discontinuation of antineoplastic therapy, directly affecting patient survival [1, 2].

The feasibility to perform certain dental procedures in leukemia patients depends on the overall state of health of the patient, as well as the stage of the disease and/or antineoplastic therapy or hematopoietic stem cell transplantation. Despite the expectation of finding a vast literature on the leukemia/dental relationship, the bibliographic survey conducted (PubMed, BIREME, Journals Portal CAPES, and SciELO) resulted in a few articles involving the amplitude of this relationship. Facing the need to establish protocols for the dental care of oncohematological patients at University Hospital, Federal University of Santa Catarina, a simplified guide for the guidance of residents in dentistry in the evaluation and treatment of these patients was developed. The guide consists of tables correlating phases of chemotherapy and hematopoietic stem cell transplantation to the most common dental procedures (classification adapted from Sonis et al. [3]).

2. General Considerations regarding Leukemia

Leukemia is a malignant disease of the blood, where the uncontrolled proliferation of immature blood cells that originate from hematopoietic stem cell mutation occurs. Eventually these aberrant cells compete with normal cells for space in the bone marrow, causing bone marrow failure and death [4].

Oral Complications of Chemotherapy and Head/Neck Radiation (PDQ®)–Health Professional Version

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ON THIS PAGE

Efectividad de las prótesis intrabucales protectoras emplomadas en teleterapia y braquiterapia

Effectiveness of Intraoral Protective Leaded Prostheses in Teletherapy and Brachytherapy

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Proyecto de investigación de la Red Métodos Alternativos para la Preservación de la Salud Bucal, financiado por Convocatoria 2011 de Redes Temáticas de Colaboración Académica, Subsecretaría de Educación Pública, Programa de Mejoramiento del Profesorado (Promep).

RESUMEN

Antecedentes: se presentan las primeras fases de pruebas *in vitro* que refutan la hipótesis de que el material de 2-3 mm de plomo utilizado como protector en prótesis radíferas, durante radioterapia en pacientes oncológicos de cabeza y cuello, ayuda a reducir el depósito de dosis en los órganos sanos o de riesgo. *Propósito*: comprobar la efectividad del plomo para reducir la radiación terapéutica. *Métodos*: se realizaron pruebas *in vitro* con dos placas de plomo de 1 mm x 5 cm x 5 cm sobre una película radiocrómica Gafchromic RQTA2 "10 x 10". Se aplicó, con acelerador lineal, una energía de 6 MeV en dosis promedio de 192 cGy de una fracción de dosis aplicables en teleterapia. También se efectuaron pruebas de contacto de 0,168 MeV de iridio 192 (braquiterapia) para una dosis de 300 c*Gy*, la cual se aplica fraccionada bajo una cubierta de agua sólida (polímero de 2 cm de espesor con la misma densidad del agua). Se realizaron pruebas similares sin la protección de plomo en ambos casos (campo abierto) como control. *Resultados*: con la lectura de densidades de la película se encontró que en el tratamiento con iridio 192 y 2 mm de plomo hubo una diferencia de aumento de radiación del 7,25 % con respecto al campo abierto (sin plomo). En el tratamiento con acelerador lineal a 6 MeV con 2 mm de plomo se observó un aumento de 16,25 % con respecto al campo abierto.

PALABRAS CLAVE
Cirugía oncológica; protector bucal; prótesis bucomaxilofacial; radioterapia

ÁREAS TEMÁTICAS
Radiología oral y maxilofacial; oncología

ABSTRACT

Background: We present early-stage in vitro evidence supporting the hypothesis that 2-3 mm lead plaques used as shielding in prosthesis for the radiotherapy in head-and-neck cancer patients help reduce deposit dose in healthy or at risk organs. *Purpose*: To test the effect of lead in reducing therapeutic radiation. *Methods*: *In vitro* tests were performed with two 1 mm x 5 cm x 5 cm lead plates on a Gafchromic RQTA2 "10 x 10" chromic film. 6 MeV energy doses of 192 cGy applied with a linear accelerator as a fraction of applicable doses of teletherapy to test contact. Likewise, 168 MeV Iridium 192 (brachytherapy) were used for a 300 c*Gy* dosis under a cover of solid water (2 cm thick polymer with the same density as water). Similar tests were performed without the lead protection in both cases (open field) as a control. *Results*: The density readings of the films showed, for the treatment with 2 mm lead Iridium 192, an increased difference of radiation of 7.25% compared to the open field. The treatment with linear accelerator with 6 MeV energy and 2 mm lead increased 16.25% compared to the open field.

KEYWORDS
Mouth guard; oncological surgery; oral maxillofacial prosthesis; radiotherapy

THEMATIC FIELDS
Oral and maxillofacial radiology; oncology

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Sinead Enright

A Karen Humphrys, Gillian Rea and Jacqueline A James

Globodontia in the Otodental Syndrome: A Rare Defect of Tooth Morphology Occurring with Hearing Loss in an Eight-Year-Old

Abstract: Otodental syndrome is a hereditary disorder comprising globodontia and sensorineural hearing loss. Globodontia is characterized by distinctively bulbous, enlarged crowns of molar and primary canine teeth. Anomalies including taurodontism and hypodontia also occur. We report on the dental treatment and multidisciplinary management of an eight-year-old girl with this rare condition. Referral to Clinical Genetics and Oral Pathology was instrumental in establishing a diagnosis of otodental syndrome for this young patient and her mother, who had similar dental defects.

CPD/Clinical Relevance: To increase awareness among practitioners of this rare dental disorder and highlight the need for multidisciplinary management of such cases.

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Globodontia is a gross morphologic dental anomaly characterized by 'globe'-shaped teeth.[1] The condition affects the size, shape and number of teeth with the most distinctive feature being bulbous, enlarged crowns of primary canine, primary molar and permanent molar teeth. Taurodontism, hypodontia, delayed eruption, malocclusion and dysmorphic facial characteristics have also been noted. The features of globodontia are summarized in Table 1.

Globodontia is a pathognomonic feature of otodental syndrome,[2,3] a disorder of ectodermal origin first described by Levin *et al* in 1975.[4] Synonymous terms include otodental dysplasia, familial otodentodysplasia and globodontia-deafness syndrome. In this rare, autosomal dominant condition, globodontia occurs with hearing loss.[5]

Nine families with otodental syndrome have been documented in the literature, including one kindred in which ocular coloboma segregates with the disease (oculo-oto-dental syndrome).[2] Single nucleotide polymorphism (SNP) genome scanning of three affected families localized otodental syndrome to chromosome 11q13.[3] Haplotype analysis revealed overlapping hemizygous microdeletions and subsequently haploinsufficiency of *FGF3* was implicated as the likely cause of otodental syndrome.

Hearing impairment in otodental syndrome is sensorineural in nature and most pronounced in the high frequency range.[3,4,6] Hearing deficit appears to plateau by the fourth decade.[6] The combination of hearing loss and dental anomalies is seen in over 200 genetic syndromes[7] and

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Rare diseases with oral components: care course and quality of life

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Aim: To describe links between the care course of individuals suffering from rare diseases and socio-behavioural risk factors and to ascertain the impact of dental conditions on the quality of life. ***Design:*** A cross–sectional comparative study involving self-reported questionnaire was performed. Care course was evaluated using Predisposing, Enabling and Needs factors. The impacts of dental conditions on quality of life were measured with the OHIP 14 questionnaire. Proportions were compared by Chi-square test. Logistic regression for multivariate analysis assessed statistical association between variables. ***Results:*** Responses were received from 355 subjects (mean age 36.9 years, 67.6% females). Thirty-three rare diseases were recorded. Respondents were classified as group A, individuals suffering from rare diseases with a dental component (n=207, 58.3%), and group B, without dental component. Group A reported earlier diagnosis, more positive attitude toward dentists, functional limitation and higher prosthetic treatment needs. Only 17.4% of subjects having fewer than 20 teeth wear prosthetics. A higher percentage of individuals claiming pain, physical disability, psychological discomfort and social disability, was found among group B ($p<0.001$). Logistic regression analysis retained two impact factors: psychological disability (Exp(B)=8.66; 95% CI 1.86-40.34) and social wellbeing (Exp(B)=0.06; 95% CI 0.02-0.215). ***Conclusion:*** Rare diseases with a dental component benefited from earlier identification of symptoms. Dentists could contribute to patients' quality of life by helping in early diagnosis, reducing functional limitation and improving social wellbeing.

Key words: *rare diseases, stomatognathic diseases, dental care, quality of life*

Introduction

The impact of chronic dental diseases on the quality of life of individuals and societies has been a topic investigated for decades. Poor oral health affects the most basic needs of human beings such as eating, drinking, smiling and communicating and can therefore potentially harm quality of life. Missing teeth, periodontal disease, untreated caries, social, behavioural, financial and environmental factors were found to be associated with a negative impact on the quality of life measured by the OHIP questionnaire (John *et al.*, 2004; Leao and Sheiham, 1996; McGrath and Bedi, 2001).

However, studies measuring the impact of the health status of people suffering from rare diseases with an oral component on their access to treatment and quality of life are scarce. A large number of original articles describe distinct cases of rare diseases and their dental phenotypes. Indeed, numerous rare diseases affect the development of hard tissue around teeth and dental anomalies are known components of many syndromes (Bailleul-Forestier *et al.*, 2008a; 2008b). Among 5,000 known genetic rare diseases, approximately 700 harbour dental, oral or craniofacial components (John Hopkins University, 2011). Since tooth germ development depends on epithelial-mesenchymal interactions, dental abnormalities such as tooth agenesis are prominent in ectodermal syndromes such as Ectodermal Dysplasias (Mikkola, 2009).

In their study, Locker and Matear (2001) supported the opinion that oral abnormalities can have impacts on the quality of life of patients, thereby affecting the well-being of individuals and society. Most studies of rare diseases are either studies of clinically identified cases or observational studies of populations of patients affected by a specific disease. The main explanation for this is the rarity of the cases and their diversity. Another reason is the limited medical knowledge on oral health in these specific conditions. Until now, little has been published on the situation of individuals affected by rare diseases with an oral component. More specifically, few epidemiological and socioeconomic data are available. A rare disease in the European Union is one that occurs in under 5 per 10,000 individuals, 27 to 36 million of European people are affected, which corresponds to a prevalence between 6 and 8% for all the rare diseases. In France, nearly 4 million people (5%) are affected (EURORDIS, 2005). Rare diseases are often complex, requiring multidisciplinary approaches for providing adequate care for patients. However, the care-course of patients with rare diseases is hampered by major problems: e.g. delays between the onset of the symptoms and diagnosis, the lack of standardised diagnostic procedures. The scarcity of clinical and natural history data due to the low prevalence of these diseases results from a lack of priority from the pharmaceutical industry and difficulty in establishing accurate diagnoses. Only ~300 of 3000 ORPHANET listed diseases benefit from disseminated knowledge, so most are insufficiently known by health professionals, a problem exacerbated by these diseases'