Review Article

Syndromes Presenting in the Oral and Maxillofacial Region: A Review

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ABSTRACT

Clinical examination is appropriate when a pertinent condition is ruled out considering all the associated syndromes. It is mandatory for a clinician to have sufficient knowledge about the syndromes for giving the final diagnosis and treatment plan. The aim of this review is to describe various syndromes presenting in the oral cavity.

KEYWORDS: *Abnormality, oral cavity, syndromes*

INTRODUCTION

Dental anomalies are only discovered after the first few years of life. This postpones the dental and orofacial components of the syndromic diagnosis, which are critical for the evaluation of prognostic factors, as well as the right timing and treatment of oral function, aesthetics, and social aspects. Not all syndromes can be clinically detected early, especially when there is no documented family history. Furthermore, due to a lack of medical expertise and variances in dental and craniofacial development, the treatment of these patients is frequently challenging.

Syndrome is defined as "A recognized pattern of malformation, presumed to have the same etiology, constitutes group of symptoms that collectively indicate or characterize a disease, psychological disorder or other abnormal condition."[1]

TREACHER COLLINS SYNDROME

Treacher Collins syndrome is a congenital craniofacial deformity caused by a genetic mutation. This illness is now known as Treacher Collins syndrome in the United States and the United Kingdom, Franceschetti–Klein syndrome in Europe, and mandibulofacial dysostosis elsewhere.[2]

Anomalies of the head and face are the most noticeable features. Down slanting eyes with notched lower lids,[3,4] sunken cheekbones[5,6] and jawbones, pointed nasal prominence,[5,7] large mouth,[6] and high arched palate are among these features. They also have auricular pinnae malformation,[8] conductive hearing loss,[9] and preauricular hair extension. Cleft lip and/or palate are seen in a small percentage of Treacher Collins Syndrome patients.

FRAGILE X SYNDROME

One of the most frequent hereditary diseases is Fragile X syndrome (FXS), also known as Martin-Bell syndrome. This syndrome is linked to certain cognitive, behavioral, and physical changes and accounts for 30% of all cases of inherited mental retardation.[10,11] Macrocephalia, a prominent frontal bone, hypotelorism, strabismus, hypoplasia of the middle part of the face, mandibular protrusion, and the possibility of Pierre-Robin syndrome (micrognathia, glossoptosis, and cleft palate) are all common facial features of FXS.[12,13] An ogival palate, cleft palate, the presence of mesiodens,[14] dental hypomineralization and abrasion of the occlusal surfaces and incisal edges, as well as an increase in the dimensions of the dental crowns in the mesiodistal and vestibulolingual orientation, which results in severe bone-dental discrepancies, are the most common intraoral anomalies.[13,15]

DIGEORGE SYNDROME

The Down syndrome (DS), also known as DiGeorge syndrome (DGS) or velocardiofacial syndrome,[16] is a 22q11 deletion disease. DGS is a phenotypic condition caused by a microdeletion on chromosome 22 at the 22q11.2 region. The pharyngeal pouches, which are

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important for the embryologic development of the middle and external ear, maxilla, mandible, palatine tonsils, thyroid, parathyroids, thymus, aortic arch, and cardiac outflow tract, fail to develop properly as a result of this mutation. Heart defects, recurring infections, aberrant facial features, thymic hypoplasia or aplasia, cleft palate, developmental delay, and hypocalcemia are all the features of DGS.[17]

Pierre Robin Syndrome

The clinical trio of micrognathia (mandibular hypoplasia), glossoptosis (downward displacement of the tongue), and upper airway obstruction characterizes the Pierre Robin sequence (PRS). Clinically, this creates a small, underdeveloped mandible, which allows the base of the tongue to slip back into the throat, potentially compromising the upper airway. It is frequently linked to cleft palate.[18] These symptoms could be part of a syndrome or stand alone. In 1891, the sequence was first published. However, in 1923, Pierre Robin described the first example of a newborn with these traits.[19] Stickler syndrome is the most prevalent of the 34 syndromes linked to syndromic PRS [Table 1].[20]

Stickler Syndrome

The most prevalent syndrome linked to PRS is Stickler syndrome. Stickler syndrome was detected in 47% of patients with syndromic PRS in one research.[20] It is an autosomal dominant disorder caused by a COL gene mutation that affects collagen production. Premature osteoarthritis, ocular involvement, sensorineural hearing loss, distinctive facies with maxillary hypoplasia, midface hypoplasia, long philtrum, and micrognathia and cleft palate are all symptoms of the Stickler syndrome (Pierre-Robin sequence).[21,22] Midline clefting is seen in a quarter of patients (25% of instances). The Pierre-Robin sequence, clefting of the hard/soft palate, and the mildest form of the bifid uvula[23] are all examples of this. Stickler's syndrome is diagnosed in 30%–44% of kids born with the Pierre-Robin sequence. Similarly, if a child has a Pierre-Robin sequence, an ocular examination should be undertaken to rule out Stickler's syndrome.[24]

Parry-Romberg Syndrome

C Parry and M Romberg were the first to define Parry Romberg syndrome, which is also known as progressive hemifacial atrophy, progressive facial hemiatrophy, or idiopathic hemifacial atrophy.[25] It is an idiopathic, progressive craniofacial asymmetry that occurs as subcutaneous tissue, muscles, osseous, and cartilaginous components atrophy. In morphologically normal-born individuals, it shows up in the first two decades. In the trigeminal nerve area, it usually affects one or more dermatomes. It begins with ophthalmic and neurological symptoms and progresses to maxillo-facial or cardiac involvement. Bony alterations include hypoplasia of the maxilla, zygomatic bone, mandible, temporal, and frontal bones (occasionally). Oral signs including unilateral tongue atrophy, gingival atrophy, hard palate atrophy, and abnormal tooth formation are the maxillofacial involvement.

Down's Syndrome

DS, also known as trisomy 21, is a genetic condition caused by a chromosome 21 abnormality. The most prevalent congenital malformation/mental retardation syndrome is this one. Protruded tongue, mouth breathing, open bite, crowding, anterior crossbite, drooling, fissured tongue, malocclusion, low levels of dental caries, and poor oral hygiene are all common orofacial features in DS.[26]

Klippel-Trenaunay-Weber Syndrome

Klippel-Trenaunay-Weber syndrome manifests itself clinically as cutaneous hemangiomas (portwine stain type), varicose veins, and soft tissue and osseous hypertrophy of the extremities.[27] Lymphangiomas, abdominal hemangiomas, syndactyly, polydactyly, oligodactyly, and macrodactyly are among the other abnormalities detected.[28] An enlarged maxilla, tooth displacement, and malocclusions are some of the most common oral cavity abnormalities.[29]

Proteus Syndrome

Proteus syndrome (PS) is an extremely rare condition marked by asymmetric and excessive bone expansion. Skeletal abnormalities are more common in PS than craniofacial abnormalities. Although oral and maxillofacial signs of PS are documented, there are few case reports describing these features. Dental agenesis, impacted teeth, malocclusion, asymmetric dental growth and maturation, frontal line displacement, asymmetric tongue enlargement, exostoses/hyperostosis, degenerative changes in the temporomandibular joint, alterations of maxillary and mandibular vertical and/or horizontal growth, and enlargement of mandibular canal and foramen are some of the oral and maxillofacial manifestations of PS.[30]

McCune-Albright Syndrome

A characteristic trio of polyostotic fibrous dysplasia (FD), café-au-lait macules, and underlying endocrinopathies distinguish McCune-Albright Syndrome (MAS).[31] FD

Table 1: Syndromes and Clinical Features

Syndromes	Clinical features
Treacher Collin syndrome	Down slanting eyes with notched lower lids, sunken cheekbones and jawbones, pointed nasal prominence, large mouth, and high arched palate, cleft lip and cleft palate
Fragile X syndrome	Macrocephalia, hypotelorism, strabismus, hypoplasia of the middle part of the face, mandibular protrusion, micrognathia, glossoptosis, and cleft palate, ogival palate, mesiodens, dental hypomineralization and abrasion of the occlusal surfaces and incisal edges, increase in the dimensions of the dental crowns
DiGeorge syndrome or velocardiofacial syndrome	Heart defects, recurring infections, aberrant facial features, thymic hypoplasia or aplasia, cleft palate, developmental delay, and hypocalcemia
Pierre Robin syndrome	Micrognathia (mandibular hypoplasia), glossoptosis (downward displacement of the tongue), upper airway obstruction, cleft palate
Stickler syndrome	Premature osteoarthritis, ocular involvement, sensorineural hearing loss, distinctive facies with maxillary hypoplasia, midface hypoplasia, long philtrum, and micrognathia; and cleft palate
Parry-Romberg syndrome	Hypoplasia of the maxilla, zygomatic bone, mandible, temporal, and frontal bones (occasionally), unilateral tongue atrophy, gingival atrophy, hard palate atrophy, and abnormal tooth formation are the maxillofacial involvement
Down's syndrome	Protruded tongue, mouth breathing, open bite, crowding, anterior crossbite, drooling, fissured tongue, malocclusion, low levels of dental caries, and poor oral hygiene
Klippel-Trenaunay-Weber syndrome	Cutaneous hemangiomas, varicose veins, and soft tissue and osseous hypertrophy of the extremities. Enlarged maxilla, tooth displacement, and malocclusions
Proteus syndrome	Dental agenesis, impacted teeth, malocclusion, asymmetric dental growth and maturation, frontal line displacement, asymmetric tongue enlargement, exostoses/hyperostosis, degenerative changes in the temporomandibular joint, alterations of maxillary and mandibular vertical and/or horizontal growth, and enlargement of mandibular canal and foramen
McCune-Albright syndrome	Orofacial deformity, bone pain, poor oral health. Dental developmental abnormalities, malocclusion, and a high caries index
Epidermal nevus syndrome	Localized or diffuse verrucous growths on the lips, palate, gingiva, buccal mucosa, and tongue. Hypertrophy of the tongue, cleft palate, high arched palate, bifid uvula, and dental anomalies such as hypodontia, unerupted teeth, malformed teeth, and odontodysplasia
Langer-Giedion syndrome	Multiple bony exostosis, small stature, mental impairment, and typical facial features, sparse scalp hair, a rounded nose, a large philtral area, and a thin upper lip, micrognathia, retrognathia, hypodontia, and malocclusion
Maffucci syndrome	Enchondromatosis (dyschondroplasia) and soft tissue hemangiomas, with a significant risk of malignancy
Segmental odontomaxillary dysplasia	Aberrant growth and maturation of bone, teeth, and gingiva of the afflicted segment
Gardner syndrome	Osteomas in the skull and jaw, fibrous tumors and sebaceous cysts, polyps of the stomach and small bowel, and distinctive retinal pigmentation. Multiple unerupted and supernumerary teeth, odontomas, dentigerous cysts, and hypercementosis are examples of dental abnormalities
Van der Woude syndrome	Lip pits with a cleft lip, cleft palate, or both. Congenital lip pits develop on the vermilion border of the lip, with or without secretion
Peutz-Jeghers syndrome	Gastrointestinal hamartomatous polyps and pigmented mucocutaneous lesions. Mucocutaneous macules appear on the lips, around the mouth, eyes, nose, and buccal mucosa, as well as sparsely on the fingers, soles of the feet, palms, anal area, and intestinal mucosa
Laugier–Hunziker syndrome	Varied number of asymptomatic, lenticular or linear, brown to black mucocutaneous macules, usually less than 5 mm in diameter
Melkersson–Rosenthal syndrome	Recurrent orofacial edema, relapsing facial paralysis, and a fissured tongue, cheilitis granulomatosa
Zimmerman-Laband syndrome	Enlargement of the attached and marginal gingiva, anomalies of the nose, ear, and nails, joint hyperextensibility, hepatosplenomegaly, skeletal abnormalities, and mental impairment
Rutherfurd syndrome	Gingival fibromatosis and corneal degeneration
Cross syndrome	Gingival fibromatosis, microphthalmia, mental retardation, and pigmentary anomalies
Ramon syndrome	Gingival fibromatosis, hypertrichosis, mental retardation, delayed development, epilepsy, and cherubism

lesions in the craniofacial area affect 90% of MAS patients, leading to significant orofacial deformity, dental abnormalities, bone pain, and poor oral health. Dental developmental abnormalities, malocclusion, and a high caries index are also linked to maxillo-mandibular FD.[32]

Epidermal Nevus Syndrome

The epidermal nevus syndromes (ENSs) are a collection of disorders defined by extensive/atypical epidermal nevus with additional cutaneous and extracutaneous characteristics. They are a clinically diverse group

of mosaic skin disorders. The type of accompanying epidermal nevus and the presence or absence of heritability is used to distinguish ENSs.[33]

Localized or diffuse verrucous growths on the lips, palate, gingiva, buccal mucosa, and tongue are the most common oral symptoms documented.[34] Hypertrophy of the tongue, cleft palate, high arched palate, bifid uvula,[35] and dental anomalies such as hypodontia, unerupted teeth, malformed teeth, and odontodysplasia seem to be among the other findings.[34]

Langer-Giedion Syndrome

The deletion of chromosomal material causes Langer-Giedion syndrome, a rare autosomal dominant genetic condition. Multiple bony exostosis, small stature, mental impairment, and typical facial features are all the symptoms. Individuals have sparse scalp hair, a rounded nose, a large philtral area, and a thin upper lip, among other characteristics. Some people with this illness have loose skin during childhood which generally resolves as they become older. Based on cephalometric study, oral and dental manifestations include micrognathia, retrognathia, hypodontia, and malocclusion.[36]

Maffucci Syndrome

It is a rare nonhereditary congenital mesenchymal dysplasia characterized by enchondromatosis (dyschondroplasia) and soft tissue hemangiomas, with a significant risk of malignancy.[37] Multiple enchondromas and hemangiomas appear during the first two decades of life in Maffucci's syndrome, which affects the skin and skeletal system.[38,39]

According to a review of the literature, the head-and-neck region is involved in roughly 5% to 10% of reported cases. Only a few hemangiomas appear in the mouth.[40]

Segmental Odontomaxillary Dysplasia

Segmental odontomaxillary dysplasia is an uncommon maxillary developmental condition marked by aberrant growth and maturation of bone, teeth, and gingiva of the afflicted segment. The complete spectrum of clinical signs of the syndrome is unclear due to its rarity.[41]

Gardners Syndrome

Gardner's syndrome is characterized by several colonic polyps (familial adenomatosis polyposis coli) and a multitude of extracolonic symptoms that frequently occur before diagnosis. Bone abnormalities (osteomas in the skull and jaw), dental abnormalities, skin tumors (fibrous tumors and sebaceous cysts), polyps of the stomach and small bowel, and distinctive retinal pigmentation are among the extracolonic findings. Multiple unerupted and supernumerary teeth, odontomas, dentigerous cysts, and hypercementosis are examples of dental abnormalities. Oral examination may reveal palpable bone swellings or exostoses on the mandibular angles, as well as pain, limited mouth opening in some patients.[42]

Van der Woude Syndrome

Van der Woude Syndrome is the most prevalent variety of syndromic orofacial clefting, accounting for 2% of all occurrences, and has a phenotype that is most similar to nonsyndromic types. With cardinal clinical symptoms of lip pits with a cleft lip, cleft palate, or both, the syndrome has an autosomal dominant genetic pattern with varied expressivity and a high degree of penetrance.[43] Clinically, congenital lip pits develop on the vermilion border of the lip, with or without secretion. They are normally bilateral; however, they can sometimes be unilateral or centrally located on the lower lip.[44] Lower lip pits have been linked to a variety of congenital abnormalities.[45,46] Oral facial digital syndrome type 1, popliteal pterygium syndrome, and kabuki make-up syndrome are some of the other syndromes that have lower lip pits as a defining feature.[47,48] Oral facial digital syndrome is a collection of congenital defects that affect the face, mouth, and fingers.

Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome is an inherited autosomal dominant condition characterized by gastrointestinal hamartomatous polyps and pigmented mucocutaneous lesions.[49] Mucocutaneous macules appear on the lips, around the mouth, eyes, nose, and buccal mucosa, as well as sparsely on the fingers, soles of the feet, palms, anal area, and intestinal mucosa. Pigment-laden macrophages in the dermis create characteristic pigmentations in 95% of individuals. They are usually flat, blue-gray to brown dots that range in size from 1 to 5 mm in diameter. The development of malignant tumors in these conditions is quite rare. Common freckles, on the other hand, never appear in the oral cavity, are scant near the lips and nostrils, and are undetectable at birth. Hyperpigmentation might fade away completely during adolescence. The presence of histopathologically verified hamartomatous polyps, as well as at least two of the following clinical criteria: family history, hyperpigmentation, and polyps in the small bowel are all required for a diagnosis.[50-55]

Laugier–Hunziker Syndrome

In adults, Laugier–Hunziker syndrome is defined by generalized physiological condition of the oral membrane

similarly as longitudinal melanonychia. They occur as macular lesions with a diameter of <5 mm. Laugier–Hunziker syndrome is thought to be a benign condition with no systemic symptoms or neoplastic potential.[56] A varied number of asymptomatic, lenticular (lens-shaped) or linear, brown to black mucocutaneous macules, usually <5 mm in diameter are characteristic with LHS. They might be confluent or singular. The edges may be well defined or vague. Hyperpigmentation appears gradually and spontaneously, and it is considered permanent.[57,58] Lips, buccal mucosa, and hard palate are the most prevalent sites for lesions. The soft palate, tongue, gingiva, and mouth floor are among the less commonly affected areas. Oral pigmentation frequently lasts a long time, but cutaneous lesions fade away during puberty.[59]

The nails are affected in about 50%–60% of instances, and the symptoms typically present as single or double stripes or uniform pigmentation on one-half of the nail or the entire nail (melanonychia).[57,58,60] One or more fingernails and/or, less frequently, toenails are implicated in the absence of nail dystrophy, forming a band. The cause of these pigmentary stripes in LHS is unknown, but it is assumed to be linked to the involvement of the oral cavity.[61,62]

Melkersson-Rosenthal Syndrome

Recurrent orofacial edema, relapsing facial paralysis, and a fissured tongue are the symptoms of Melkersson-Rosenthal syndrome. The typical trio is not always present at the same time, and some forms of the disease, such as cheilitis granulomatosa, might be detected in partial forms.[63]

Fissured tongue (lingua plicata) is characterized as 2 mm deep and 15 mm long grooves on the dorsum of the tongue.[64] In 30%–80% of MRS instances, it is present.[65] Secondary infections, hypertrophy, papillae loss, loss of taste, and dysesthesia are all potential risks of fissuring. Fissuring is a condition that can be passed on through the generations.

Zimmerman-Laband Syndrome

Zimmerman-Laband syndrome is an uncommon condition marked by enlargement of the attached and marginal gingiva, anomalies of the nose, ear, and nails, joint hyperextensibility, hepatosplenomegaly, skeletal abnormalities, and mental impairment on occasion. Gingival enlargement, which appears early in children, is the most prominent symptom of this syndrome. Gingival enlargement caused by idiopathic causes usually appears after the permanent teeth have erupted. This syndrome is not a life-threatening condition.[66]

Rutherfurd Syndrome

The Rutherfurd syndrome establishes the link between gingival fibromatosis and corneal degeneration as an autosomal dominant feature.[67]

Cross Syndrome

Gingival fibromatosis, microphthalmia, mental retardation, and pigmentary anomalies are all features of Cross syndrome, which is probably an autosomal recessive condition.[68]

Ramon Syndrome

Ramon syndrome is a disorder that includes gingival fibromatosis, as well as hypertrichosis, mental retardation, delayed development, epilepsy, and cherubism and is considered to be autosomal recessive.[69]

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Conflicts of interest

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