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Syndromes of head and neck region associated with gingival findings

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Abstract
The part of the oral mucosa that covers the alveolar processes of the jaws and also surrounds the neck of the teeth is known as gingiva. The word syndrome is derived from the Greek syn (together) and dromos (running) and refers to a 'running together' or concurrence of symptoms. Even after taking into account local inflammatory conditions and drug use, occasional instances with a syndromic origin have been recorded. Present review tries to combine the relevant features of syndromes associated with gingival findings into a systemic review.

Keywords: Syndromes, head and neck, gingiva, gingival enlargement

Introduction
In genetics, 'syndrome' refers to a pattern of multiple malformations that are thought to be pathogenetically related [1]. Cohen & Kreiborg, who stated that in medical genetics, Multiple abnormalities that arise in embryonically disjointed regions are known as a syndrome [2]. Head and neck syndromes represent a complete set of anomalies that involve signs and symptoms associated with various other systems in human body along with distinct head and neck features.

Syndromes involving the gingiva are as follows [3]

1. Syndromes associated with gingival enlargement

Gingival enlargement or gingival overgrowth, a common trait of gingival disease, is characterized by an increase in the size of gingiva. This group includes syndromes as follows along with relevant findings of each one of them as follows:

a. Cowden's syndrome/Cowden disease/Multiple hamartoma syndrome
It is associated with mutations in the PTEN gene on chromosome arm 10q [4]. Multiple papules on the gingiva has been noted giving an appearance of a cobblestone pattern. Other findings include nose, lips and ears showing popular lesions, periodontitis, gross dental caries, thyroid adenoma and gastrointestinal hamartomas [5].

b. Sturge–Weber syndrome
Caused by a mutation in the GNAQ gene. Gingival lesions vary from slight vascular enlargement to massive gingival growths [6]. Other intraoral findings include the buccal mucosa, palate, tongue, the floor of mouth, gingiva, and lips showing angiomatosis which may show purplish-red discoloration [7]. Other extraoral findings characteristic port wine stains-confined to skin supplied by trigeminal nerve along with brain calcifications, ocular disorders, hemiplegia and epilepsy.

c. Klippel–Trenauny–Weber syndrome
This syndrome is associated with mutations in AGGF1 (Angiogenic Growth Factor 1). Intraoral gingival findings include capillary hemangiomas, vascular hypertrophy, gingival fibroma, fibromatosis, and hyperplasia. There is also unilateral increase in size of periodontal tissues [8]. Other intraoral findings include capillary hemangiomas on tongue, unilateral macroglossia, increase in size of fungiform papillae, unilateral increase in size of the lips, hyperplastic tissue responses on cheeks, tooth malformation which includes diastema formation. Delayed exfoliation of primary teeth along with premature eruption

of teeth on affected side and early mineralization of roots on affected side [8].

d. Hurler's syndrome

This syndrome is characterized by anterior region showing gingival overgrowth with hyperplastic gingiva. There is also enlargement of tongue, shortening and widening of mandible, areas of bone destruction in jaws, high-arched palate, localized dentigerous cyst-like radiolucencies [9].

e. Ellis–Creveld syndrome

Ellis–Creveld syndrome is characterized by mutation in EVC and EVC2 gene [10]. Characteristic features include upper lip fused to the gingiva with disappearance of mucobuccal fold, absence of sulcus, partial hare lip, prenatal eruption of the teeth, conical teeth, hypoplasia of enamel and hypodontia [10]. Extraoral findings include dwarfism and finger nail abnormalities.

f. Robinow syndrome / Fetal face syndrome

This syndrome is commonly associated with mutations in ROR2 gene on chromosome 9q22 [11]. Gingival enlargement along with upper lip with inverted V appearance, midline clefting of lower lip, malposition of primary and permanent teeth and ankyloglossia is noted.

g. Oro-facial-digital syndrome type 1

This syndrome is associated with mutations OFDI gene (CXORF5) [12]. This syndrome is characterized by numerous hyperplastic fibrous bands traversing the gingivolabial and gingivobuccal folds. Also gingivitis or gingival recession is noted in these patients. Other findings include thickened alveolar ridges and abnormal dentition, cleft palate, lingual hemartomas and ankyloglossia [12] Patients might also show learning disabilities and polycystic kidneys.

h. Goltz syndrome

Goltz syndrome is associated with mutations in PORCN gene [13]. Intraoral findings include papillomas of gingiva, oral mucosa, skin and nails. Papillary gingival hyperplasia is noted. Few patients present with abnormalities of the extremities, telangiectasia and pigmentation of skin.

i. Prune-belly syndrome

This syndrome is characterized by microdeletion in relationship to hepatocyte nuclear factor-1-beta gene at 17q12 [14]. Gingival fibromatosis along with absence of abdominal muscles, abnormalities of urinary tract, cryptorchidism and facial dimorphism is noted.

j. Sweet syndrome

Intraoral features include gingival fibromatosis and hyperplasia along with necrotizing ulcerative periodontitis. Some of these patients show edematous and aphthous lesions of the upper aero-digestive tract in the mouth and pharynx [15]. Other symptoms, which include fever, myositis, neutrophilia, along with tender erythematous skin is noted. Köbner Phenomenon-'specific' skin lesions at sites of minor cutaneous trauma are also seen in such patients.

k. Bourneville–Pringle syndrome/Tuberous sclerosis

This syndrome is characterized by mutations of the TSC1 (also called hamartin) and / or the mutations of TSC2 (also called tuberin) genes [16] Papular fibrous enlargement of gingiva, especially in the anterior region and cheek mucosa, dental enamel pits, intraoral fibromas are findings in such patients.

l. Cantu syndrome/ Osteochondrodysplasia with hypertrichosis

This syndrome is represented by gain-of-function (GoF) of pathogenic variants in ABCC9 [17]. Intraoral findings include gingival enlargement/hypertrophy, macroglossia, prominent mouth, generalized hypertrichosis and thick lips. Other relevant extra oral findings include skeletal abnormalities, osteoporosis, cardiomegaly, coarse facial features and epicanthal folds.

m. Patterson–Davis syndrome

This syndrome is associated with mutations in the insulin receptor gene (INSR; 19p13.3–p13.2) [18]. Gingival hypertrophy along with thick lips is noted in these patients. Marked facial hirsutism with unusual facies and insulin resistance is noted in this syndromic patient.

n. Apert syndrome/ Acrocephalosyndactyly

Apert syndrome is associated with mutation of fibroblast growth factor recptor-2 (FGFR-2) on chromosome 10q [19]. Intraoral findings include lateral palatal swellings, which gives appearance of apparent increase in size of gingiva with sagittal narrow palate, lateral palatal swellings with prominent central fissure, maxillary arch is V shaped, severe dental crowding and delayed tooth eruption and posterior slanting maxilla giving rise to class III malocclusion [19]

o. Syndrome of hemimaxillary enlargement, asymmetry of the face, tooth abnormalities, and skin findings (HATS)

This syndrome is associated with gingival thickening of the affected side along with delayed eruption of the teeth and unilateral abnormalities of the face involving the bones, teeth, gums, and skin [20].

2. Gingival fibromatosis

Gingival fibromatosis (GF) is characterized by abnormal, localized, or diffuse development of the gingiva. The illness can manifest as a non-syndromic hereditary gingival fibromatosis (HGF) or as a symptom of a syndrome, and it may be caused by hereditary causes. The clinical presentation of GF appears to be influenced by an excessive buildup of extracellular matrix (ECM) components, although the underlying molecular pathways are yet unknown. The syndromes associated with GF are described as follows: (Table 1)

3. Syndromes associated with gingival bleeding

Gingival bleeding (GB) is a common sign of gingival inflammation, which indicates the presence of periodontal diseases. GB is a reversible gingival inflammation brought on by the buildup of dental plaque. Various syndromes associated with gingival bleeding are tabulated in table 2. (Table 2)

Management

Because different gingival findings may be the first observable symptom of an undiagnosed genetic disorder and/or a sign of how that disorder is progressing, oral health professionals need to gain the necessary knowledge and be aware of the uncommon situations in which these diseases may occur.

The examination of gingival enlargement in patients with syndromes mostly shows two components of the overgrown tissues which are either fibrotic or inflammatory [32].

The clinician should give biofilm control priority while treating gingival enlargement since it is a necessary step. Evidence suggests that proper oral hygiene, chemotherapeutic drugs, and routine professional biofilm removal reduce the degree of gingival enlargement and enhance overall gingival

health, even though the precise role played by bacterial biofilm is not entirely know [33, 34].

The development of pseudo-pockets and an abundance of biofilm are linked to the existence of enlarged gingival tissue, which may cause periodontitis. Therefore, careful biofilm management supports the maintenance of attachment levels. In addition, in cases where gingival enlargement was surgically addressed, proper biofilm control may aid in preventing its recurrence. Even after careful evaluation of the first two methods, gingival enlargement still occurs in many people. In these cases, surgical gingival expansion excision must be taken into consideration [35].

Before beginning periodontal therapy in patients who have a higher tendency to bleed from the gingiva, the patient's blood profile, including bleeding and clotting times and platelet count, should be reviewed. The hematologist should also be consulted. Leukemic gingival hypertrophy is frequently linked to spontaneous gingival bleeding. After the acute symptoms have subsided, the gingival expansion needs to be corrected. Controlling the inflammatory component of the enlargement is made easier by eliminating local irritants. To do it, scaling and root planning are used. The patient is given oral hygiene instructions for preventing biofilm as part of the initial therapy procedures, which also include conducting superficial scaling and gently removing all loose debris with cotton pellets. Chlorhexidine mouthrinses should be used every day as part of this hygiene. For these people, oral hygiene practices are crucial. At future visits, definitive scaling and root planing are performed under local anesthetic (if necessary). If hemostasis is difficult to achieve, treatment sessions are limited to a small portion of the mouth. To lower the chance of infection, antibiotics are given systemically the evening before and for a week following each treatment [35].

In cases where gingival hypertrophy was surgically addressed, recurrence is a possibility. The difficulties with postsurgical dental care are the main reason for the return of gingival expansion. Careful home care is recommended, including use of a soft postoperative brush and chlorhexidine gluconate rinses. Additionally, regular expert cleanings might lessen the frequency of recurrence [36].

Table 1: Syndromes associated with gingival fibromatosis

Syndromes	Inheritance pattern	Extra oral findings
Jones syndrome, Jones–Hartsfield syndrome	Autosomal Dominant [21]	-Hearing loss -Deafness
Ramon syndrome	Autosomal dominant [22]	-Cherubism -Mental deficiency
Cornelia de Lange syndrome		-Primordial growth deficiency -Facial dysmorphism -Distinct craniofacial features [23]
Cross syndrome	Autosomal Recessive	-Hypopigmentation -Microphthalmia
Gingival fibromatosis with Murray syndrome (Murray–Puretic–Drescher syndrome, juvenile hyaline fibromatosis)	Mutations in capillary morphogenesis protein-2 (CMG-2 gene)	Nodular, papular skin lesions
Ambras syndrome		-Extreme hypertrichosis involving the shoulders, face, nose, and ears [24]
Rutherford syndrome		-Delayed tooth eruption -Mental retardation -Aggressive behavior [25]

Table 2: Syndromes associated with gingival bleeding

Syndromes	Genetics
Shwachman–Diamond syndrome	SBDS gene is located at chromosome 7q11 [26]
Myelodysplastic syndrome (MDS)	
Hemorrhagic lupus anticoagulant syndrome	
Craniofacial arteriovenous metameric (CAMS) syndrome	
Epstein syndrome	Mutations affecting the myosin heavy chain (MYH-9) gene [28].
Osler–Rendu–Weber Syndrome (Hereditary hemorrhagic telangiectasia)	
Asthenia–polyarthritis. Edema, fever and hemorrhagic syndrome	
Bernard–Soulier syndrome	Genetic abnormalities in the function of the GPIb-V-IX complex, which is required to bind von-Willebrand factor IX [29]
Von Willibrand-like syndrome	Defect of Von Willebrand Factor (VWF) at chromosome 12p13.2 [30]
Sheehan's syndrome (Post-partum pituitary necrosis) [31]	

Conclusion

The patient's main worry is gingival enlargement because it compromises both function and aesthetics. In cases of excessive enlargement, an appropriately scheduled surgical treatment to reduce the tissue to a normal contour will offer the greatest benefit to the patient, minimizing the number of clinical visits required and enhancing the quality of life for the patient.

References

1. Dorlands Illustrated Medical Dictionary, 31st edn. Philadelphia: Saunders Elsevier; c2007. p. 1846.
2. Cohen MM Jr, Kreiborg S. Perspectives on craniofacial syndromes. Acta Odontol Scand. 1998;56:315-320.
3. Haritha A, Jayakumar A. Syndromes as they relate to periodontal disease. Periodontol. 2000-2011;56(1):65-86.
4. Sébastien Molière, Carole Mathelin. The Cowden Syndrome, N Engl J Med. 2020;382:e29.
5. Marshall M, Otero D, Niklander S, Martínez-Flores R. Cowden's syndrome diagnosed through oral lesions: A case report. J Clin Exp Dent. 2021;13(11):e1162-e1166.
6. Yadav V, Chakraborty S, Tewari S, *et al*. Cryotherapy as

a conservative treatment modality for gingival enlargement in a patient with Sturge-Weber Syndrome. Intracta Rare Dis Res. 2017;6(2):145-147.
7. Mapara PN, Taur SM, Hadakar SG, *et al*. Sturge–Weber Syndrome: Roots to a Cure a Nightmare in Pediatric Dentistry. Int J Clin Pediatr Dent. 2021;14(1):145-148.
8. Ebrahim Fakir, Tina Roberts, Lawrence Stephen, *et al*. Klippel-Trenaunay-Weber syndrome: orodental manifestations and management considerations, Oral Surg Oral Med Oral Pathol Oral Radiol Endod, 2009;107(6):754-758.
9. Guven G, Cehreli ZC, Altun C, Sençimen M, Ide S, Bayari SH, *et al*. Mucopolysaccharidosis type I (Hurler syndrome): oral and radiographic findings and ultrastructural/chemical features of enamel and dentin. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008;105(1):72-78.
10. Kamal R, Dahiya P, Kaur S, Bhardwaj R, Chaudhary K. Ellis-van Creveld syndrome: A rare clinical entity. J Oral Maxillofac Pathol. 2013;17(1):132-135.
11. Patton MA, Afzal AR. Robinow syndrome. Journal of Medical Genetics. 2002;39:305-310
12. Syed S, Sawant PR, Spadigam A, Dhupar A. Oro-facial-digital syndrome type I: a case report with novel features. Autops Case Rep [Internet]. 2021;11:e2021315.
13. Ghosh SK, Dutta A, Sarkar S, Nag SS, Biswas SK, Mandal P. Focal Dermal Hypoplasia (Goltz Syndrome): A Cross-sectional Study from Eastern India. Indian J Dermatol. 2017;62(5):498-504.
14. Samal SK, Rathod S. Prune Belly syndrome: A rare case report. J Nat Sci Biol Med. 2015;6(1):255-257.
15. Alexandros Makis, Stavros Stavrou, *et al*. Acute febrile neutrophilic dermatosis (Sweet's syndrome) in a child, associated with a rotavirus infection: a case report, Journal of Medical Case Reports. 2010;4:281.
16. Kinga Mate, *et al*. Bourneville-Pringle disease (Tuberous Sclerosis Complex - TSC) with bilateral renal angiomyolipoma and an epitheloid monomorf angiomyolipoma (EMAML) in a 43-year- old female, a case report, Research Square, February 18th; c2022. p. 1-9.
17. Grange DK, Roessler HI, McClenaghan C, Duran K, Shields K, Remedi MS, *et al*. Cantú syndrome: Findings from 74 patients in the International Cantú Syndrome Registry. Am J Med Genet C Semin Med Genet. 2019;181(4):658-681.
18. Nijim Y, Awni Y, Adawi A, Bowirrat A. Classic Case Report of Donohue Syndrome (Leprechaunism; OMIM *246200): The Impact of Consanguineous Mating. Medicine (Baltimore). 2016;95(6):e2710.
19. Khan S, Chatra L, Shenai P, Veena KM. Apert Syndrome: A Case Report. Int J Clin Pediatr Dent. 2012;5(3):203-206.
20. Alshaiji JM, Handler MZ, Huo R, Freedman A, Schachner LA. HATS syndrome: hemimaxillary enlargement, asymmetry of the face, tooth abnormalities, and skin findings. Cutis. 2014;94(4):E18-21.
21. Rahikkala E, Julku J, Koskinen S, Keski-Filppula T, Weissgraeber S, Bertoli-Avella AM, *et al*. Pathogenic REST variant causing Jones syndrome and a review of the literature. Eur J Hum Genet. 2023;31(4):469-473. Doi: 10.1038/s41431-022-01258-9. Epub 2022 Dec 13.
22. Surej Kumar LK, Deepa DS, Dilna S. Ramon Syndrome-A Rare Form of Cherubism. Ann Maxillofac Surg. 2019;9(2):415-418. Doi: 10.4103/ams.ams_12_19.
23. Mehta DN, Bhatia R. Cornelia de-lange syndrome: a case report. Int J Clin Pediatr Dent. 2013;6(2):115-8. Doi: 10.5005/jp-journals-10005-1201. Epub 2013 Aug 26.
24. Malwade S, Gupta M, Agarkhedkar SR. Ambras syndrome. Med J DY Patil Univ. 2015;8:271-273.
25. Raja TA, Albadri S, Hood C. Case report: Rutherfurd syndrome associated with Marfan syndrome. Eur Arch Paediatr Dent. 2008;9(3):138-141.
26. Lee JH, Bae SH, Yu JJ, Lee R, Yun YM, Song EY. A case of Shwachman-Diamond syndrome confirmed with genetic analysis in a Korean child. J Korean Med Sci. 2008;23(1):142-5. Doi: 10.3346/jkms.2008.23.1.142.
27. Bizymi N, Pitsidianakis G, Ierodiakonou D, Stathakis G, Vasarmidi E, Hiraki S, *et al*. Case Report: Diagnosis of Myelodysplastic Syndrome in a 72-Year-Old Female With Interstitial Lung Disease. Front Med (Lausanne). 2021;8:673573.
28. Desmond Yat Hin Yap, Kai Chung Tse, Tak Mao Chan, Albert Kwok Wai Lie. Epstein Syndrome Presenting as Renal Failure in Young Patients, Renal Failure. 2009;31(7):582-585.
29. Effendi I, Nadeem A, Sarfraz S, Shahid M, Farooq M, Anand A. Bernard Soulier syndrome: A case report from Pakistan. Clin Case Rep. 2023;11(8):e7767.
30. Echahdi H, El Hasbaoui B, El Khorassani M, Agadr A, Khattab M. Von Willebrand's disease: case report and review of literature. Pan Afr Med J. 2017;27:147.
31. Errarhay S, Kamaoui I, Bouchikhi C, Châara H, Bouguern H, Tizniti S, *et al*. Sheehan's Syndrome A Case Report and Literature Review. Libyan J Med. 2009;4(2):81-2.
32. Bhatnagar S. Treatment of Gingival Enlargement [Internet]. Gingival Disease - A Professional Approach for Treatment and Prevention. IntechOpen; c2019.
33. Hall WB. Dilantin hyperplasia: A preventable lesion. Journal of Periodontal Research. Supplement. 1969;4:36-37.
34. Seymour RA, Jacobs DJ. Cyclosporin and the gingival tissues. Journal of Clinical Periodontology. 1992;19:1-11.
35. Newman MG, Takei HH, Klokkevold PR, Carranza FA. In: Carranza, editor. Clinical Periodontology. 10th ed. St. Louis: Elsevier; c2006.
36. Dongari A, McDonnell HT, Langlais RP. Drug-induced gingival overgrowth. Oral Surgery, Oral Medicine, and Oral Pathology. 1993;76:543-548.

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