


Genodermatoses with teeth abnormalities

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Abstract

Many genodermatoses exhibit abnormal teeth findings. Studies examining these entities are scarce and narrow in their scope. This paper reviews the evolution, development, and structure of the tooth and provides a summary of genodermatoses with aberrant dental findings. The latter are classified according to the abnormal dental findings: periodontal disease, anodontia/oligodontia/hypodontia, polyodontia, enamel hypoplasia, natal teeth, dental pits, and others. Finally, we provide an algorithm that dermatologists and dentists can follow to better recognize genodermatoses with dental involvement.

KEYWORDS

dental, dermatology, genetics, genodermatoses, teeth

1 | INTRODUCTION

Teeth have played a major part in the evolution of vertebrates. Their preservation across the geologic timescale lends itself to the durability of enamel and dentine. Fossil records credit the jawless fish, or agnathans, with the first appearance of tooth-like structures on the posterior pharynx approximately 500 million years ago. Subsequently, the evolution of jaws with superimposed teeth helped the gnathostomes, or the jawed vertebrates, achieve evolutionary success (Smith & Coates, 1998).

The dentition of most fish, reptiles, and amphibians contains a vast number of teeth (polyodonty) of similar morphology (homodonty) that are continuously replaced (polyphodonty). Furthermore, those teeth lack a dental root canal and are directly attached to bone via fibrous tissue. Moving up the evolutionary pathway from fish to reptiles to mammals, a decrease in number (oligodonty) and generations (e.g., diphyodonty in humans; monophyodonty in rats) of teeth is observed. Moreover, an ever-increasing change in mammalian dietary habits necessitated an increase in the morphological complexity of teeth (heterodonty). Some organisms, most notably turtles, birds, and anteaters, have lost their dentition (anodontia) altogether despite developmental studies highlighting the presence

of embryonal tooth germs that undergo apoptosis prior to birth (Koussoulakou, Margaritis, & Koussoulakos, 2009).

2 | EMBRYOLOGY OF THE TOOTH

Odontogenesis is the process by which the teeth form. Humans are diphyodonts, meaning that they develop two sets of teeth. The first set is composed of 20 baby teeth (also called primary, deciduous, or milk teeth) and begins to form between the sixth and eighth week of prenatal development. The second set is made up of 32 permanent teeth (also called adult or succedaneous teeth) which begin development at the twentieth week. Each tooth is derived from the ectoderm of the first pharyngeal arch and the ectomesenchyme of the neural crest (Zohrabian, Poon, & Abrahams, 2015). Initiation of tooth development begins with thickening of the oral epithelium. This is followed by the bud stage where the thickened cells proliferate forming a dental lamina that invaginates into the mesenchyme. Meanwhile, mesenchymal cells underneath the epithelial bud give rise to the dental papilla. During the cap stage, the epithelial bud grows surrounding the dental papilla, the primary enamel knot (which regulates the shape of the teeth) forms, and mesenchymal

cells give rise to the dental follicle. The latter later forms the cementum, periodontal ligament, and alveolar bone which are responsible for tooth anchoring. During the bell stage, secondary enamel knots form and determine the location of the tooth cusps. Tooth-specific cell types, such as the ameloblasts and odontoblasts, begin to differentiate. Ameloblasts secrete the enamel matrix which later mineralizes. Odontoblasts produce dentin matrix (Jheon, Seidel, Biehs, & Klein, 2013).

3 | STRUCTURE OF THE TOOTH

The adult tooth possesses two major anatomical parts: the crown and the root. The crown is the visible part and is covered by a hard outer layer called enamel. The latter is the hardest substance in the body and consists mainly of hydroxyapatite. Dentin is found underneath the enamel and is not as resilient. The dental pulp is the soft tissue containing the blood and nerve supply of the tooth. Cementum is the outer layer covering the root and is not as hard as enamel (Figure 1; Jheon et al., 2013).

4 | MOLECULAR PATHWAYS IN TOOTH DEVELOPMENT

Pathways involving bone morphogenetic protein (BMP), fibroblast growth factor (FGF), sonic hedgehog protein (Shh), and Wnt ligands and their receptors are the major determinants of tooth development and will be discussed in this section. Mutations involving these pathways and other pathways result in syndromic and non-syndromic hereditary teeth disorders. Table 1 and Figure 2 provide a summary of selected genodermatoses with dental abnormalities.

4.1 | Bone morphogenetic protein

Bone Morphogenetic Proteins are proteins that belong to the transforming growth factor- β (TGF- β) superfamily of proteins. They were initially discovered for their ability to induce bone and cartilage formation, but they also play major roles during embryonic development and regulate several functions in the adult, including the maintenance of joint integrity, the initiation of fracture repair, and vascular remodeling. There are two BMP signaling pathways: the canonical and non-canonical pathways. In the canonical pathway, BMPs bind to a dimer of type I receptors and a dimer of type II receptors forming a heterotetrameric complex. Type II receptors then phosphorylate type I receptors. The latter become activated and phosphorylate downstream proteins known as the receptor-regulated Smads (R-Smads) which translocate to the nucleus to initiate the transcription of target genes. There are various non-canonical pathways which are Smad-independent (Wang et al., 2014).

Bone Morphogenetic Proteins, in particular BMP4, are crucial during several steps of odontogenesis. During the initiation stage,

epithelial BMP antagonizes FGF signaling to determine the site of teeth formation. The transition from the bud to the cap stage and induction of the enamel knot depend on the regulation of Shh expression by mesenchymal BMP4. BMP is therefore an important regulator of tooth shape. It is also involved in the formation of the root and of the tooth-specific cell types (Jheon et al., 2013).

4.2 | Fibroblast growth factor

Fibroblast growth factors are a family of proteins that regulate the development of both vertebrates and invertebrates. Therefore, any disruption in their function leads to a range of developmental defects. FGFs also control several cellular processes in the adult including tissue repair and regeneration, and aberrant signaling results in metabolic disorders and cancer. FGFs bind to the fibroblast growth factor receptors (FGFRs), leading to receptor dimerization. The receptors then phosphorylate each other via their kinase domains and interact with adaptor proteins. This results in the activation of four key downstream pathways: Ras/Raf/MAPK, PI3K-AKT/mTOR, signal transducer and activator of transcription (STAT), and phospholipase C γ (PLC γ ; Ornitz & Itoh, 2015).

FGF8 and FGF9 are expressed early during odontogenesis. FGF8 is required for cell survival and patterning of the first branchial arch. The inactivation of this molecule leads to defects in several structures including the teeth and the jaw. Mice lacking the IIIb isoform of FGFR2 had defective tooth development that failed to progress beyond the bud stage. FGFs 3, 4, 9, and 10 are also thought to be involved in odontogenesis, and the inactivation of certain FGF inhibitors leads to supernumerary teeth or ectopic enamel formation (Jheon et al., 2013).

4.3 | Sonic hedgehog protein

The hedgehog (hh) signaling pathway is crucial during vertebrate development, organogenesis, and regeneration. It also plays a major role in several types of tumors. There are three mammalian Hh proteins: Shh, Indian hedgehog (Ihh), and desert hedgehog (Dhh). The Shh pathway can be activated through the canonical and non-canonical pathways. In the canonical pathway, Shh binds to the 12-transmembrane protein patched (Ptch), leading to its inactivation. This will relieve the inhibition that Ptch exerts on the 7-transmembrane protein smoothened (Smo). The latter will then accumulate and initiate a signaling cascade that leads to the activation of Gli family proteins. Gli will then translocate into the nucleus and initiate the transcription of target genes. The "non-canonical Shh signaling" is independent of Gli and regulates cell proliferation, survival, and migration (Carballo, Honorato, Lopes, & Spohr, 2018).

The expression of Shh is upregulated during the initiation stage of tooth formation, downregulated at the end of the bud stage, and then increases again in the enamel knot and throughout ameloblast differentiation. Shh is thought to stimulate the proliferation

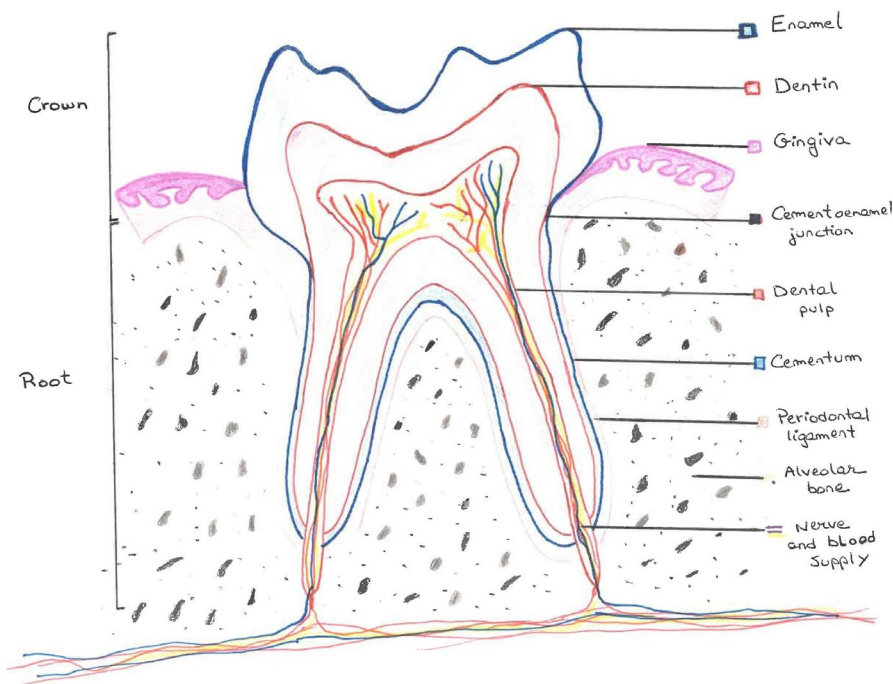


FIGURE 1 Structure of the tooth. The tooth possesses two major parts: the crown and the root. The crown is covered by enamel. Below the enamel is dentin. The dental pulp is the soft tissue containing the blood and nerve supply. Cementum is the outer layer covering the root [Colour figure can be viewed at wileyonlinelibrary.com]

of epithelial and mesenchymal tissues during odontogenesis. It also regulates tooth separation, size, morphology, and cellular organization (Jheon et al., 2013). Mutations in *PTCH1* gene result in Gorlin syndrome which is characterized by multiple basal cell carcinomas as well as several dental anomalies (Table 1; Manfredi, Vescovi, Bonanini, & Porter, 2004).

4.4 | Wnt

The Wnt pathway is a highly conserved pathways that regulates several crucial cellular processes including cell proliferation, differentiation, and migration. It involves at least nineteen proteins and is divided into the canonical (β -catenin-dependent) and non-canonical (β -catenin-independent) pathways. For signal transduction, Wnt proteins bind to the receptor Frizzled (Fz) and its coreceptors, such as the low-density lipoprotein-related protein 5/6 (LRP5/6), leading to the activation of the cytoplasmic protein disheveled (Dsh). The signaling cascade then branches into the canonical and non-canonical pathways. The non-canonical pathway can be divided into the planar cell polarity pathway and Wnt/Ca²⁺ pathway. The canonical pathway involves the cytoplasmic protein β -catenin. The latter is usually degraded by the β -catenin destruction complex which several proteins like axin, adenomatous polyposis coli (APC), and protein phosphatase 2A (PP2A). Binding of Wnt to Fzd and LRP 5/6 leads to the dissociation of the β -catenin destruction complex, allowing β -catenin to translocate to the nucleus and regulate gene transcription (Komiya & Habas, 2008).

The Wnt pathway plays a role during all stages of tooth development with multiple ligands, receptors, inhibitors, and key signal transducers being expressed throughout the dental tissue. The exact mechanism of action is still unknown. Over-activation leads to

misshapen and ectopic teeth, while under-activation results in an arrest in tooth development (Liu et al., 2008). Schöpf-Schulz-Passarge is due to mutations in the *Wnt10A* gene and is characterized by hypodontia, palmoplantar keratoderma, and eyelid hidrocystomas among other features (Table 1; Manchanda, Anthonappa, Al-Mulla, & King, 2017).

5 | TOOTH REGENERATION

Teeth generation is triggered by the epithelial-mesenchymal interactions that occur during embryogenesis. Central to this process are several stem cell populations that form niches in the tooth. The epithelial stem cell niche, also known as the cervical loop, is recognized as the most morphologically distinctive. These cells are derived from Sox2+ cells of the competent dental epithelium and are themselves the precursors of ameloblasts (Balic, 2018). The FAK-YAP-mTOR signaling pathway was found to coordinate stem cell expansion and their differentiation toward the ameloblast lineage (Hu et al., 2017). Root formation and subsequent tooth eruption signal the loss of the epithelial stem cells followed by the demise of the epithelial compartment including the ameloblasts. Animal models have implicated the loss of *Fgf10* as the molecular switch responsible for the loss of the tooth epithelial stem cell and the initiation of root formation (Yokohama-Tamaki et al., 2006).

While enamel destruction is irreversible due to the loss of ameloblasts prenatally, dentin owes its continuous physiologic and reactive deposition in human teeth to the presence of mesenchymal stem cells in the postnatal tooth. Unlike epithelial stem cells, tooth mesenchymal stem cells are derived from neural crest cells and form niches that are not morphologically distinguishable (Balic, 2018).



TABLE 1 Genodermatoses with teeth abnormalities

Disease	Gene	Mode of inheritance	Clinical findings	Phenotype MIM number	Reference
Periodontal disease					
Papillon-Lefevre	Cathepsin C	AR	Destructive periodontitis (primary and permanent dentition), palmoplantar erythema and hyperkeratosis, calcification of dura and choroid plexus, pyogenic infections	245000	Fantasia (2014)
Haim-Munk	Cathepsin C	AR	Papillon-Lefevre with atrophic nail changes, and finger findings of acro-osteolysis and claw-like volar curves	245010	Fantasia (2014)
Ehlers-Danlos	Variable	Variable	Periodontitis, enamel hypoplasia, high cusps and deep fissures on the crowns of teeth, pulp stones, short and deformed roots, temporomandibular dysfunction and hypermobility, skin hyperextensibility, joint hypermobility	Variable	Mitakides and Tinkle (2017)
Leukocyte adhesion deficiency type I	Integrin beta-2	AR	Progressive periodontitis, hypoplasia of cementum adjacent to the dentogingival junction, blood neutrophilia, recurrent infections, impaired wound healing, delayed separation of the umbilical chord	116920	Hajishengallis and Moutsopoulos (2014)
Palmoplantar keratoderma with sex reversal and squamous cell carcinoma	RSPO1	AR	Periodontal disease with early loss of teeth, palmoplantar keratoderma, sex reversal, or ambiguous genitalia	610644	Micali et al. (2005)
Anodontia/oligodontia ^a /hypodontia ^b					
Ectodermal dysplasias	Variable	Variable	Hypodontia, peg-shaped/conical teeth, hypoplastic alveolar bone, sparse to absent hair, nail dystrophy, variably decreased sweating (the teeth are normal in hidrotic ectodermal dysplasia)	Variable	Hekmatfar et al. (2012)
Witkop syndrome	Msh homeobox 1	AD	Hypodontia, thin brittle nails, koilonychia	189500	Subramaniam and Neeraja (2008)
Hypomelanosis of Ito	Uncertain	—	Hypodontia, anodontia, hamartomatous cusps, talon cusps, enamel defects, irregularly spaced teeth, hypopigmented whorls of skin along the lines of Blaschko	300337	Happle and Vakilzadeh (1982)

(Continues)



TABLE 1 (Continued)

Disease	Gene	Mode of inheritance	Clinical findings	Phenotype MIM number	Reference
Incontinentia pigmenti	Nuclear factor KB essential modulator (NEMO)	XLD	Hypodontia, retention of deciduous molars, delayed eruption, crown malformation, peg-shaped teeth, 4 stages of skin lesions: vesicular, verrucous, hyperpigmented, and hypopigmented	308300	Chen and Chen (2017)
Odonto-onycho-dermal dysplasia	WNT10A	AR	Hypodontia, smooth tongue, barrel-shaped mandibular incisors, nail dysplasia, palmoplantar hyperkeratosis and hyperhidrosis, hypotrichosis, slow-growing hair	257980	Kantaputra, Kaewgahya, Jotikasthira, and Kantaputra (2014)
Johanson-Blizzard syndrome	Ubiquitin-protein ligase	AR	Small and malformed deciduous teeth, missshapen or absent permanent teeth, aplastic/hypoplastic nasal alae, hearing disorder, microcephaly, hypothyroidism, dwarfism, malabsorption, mental retardation	243800	Santhosh and Jethmalani (2013)
Schöpf-Schulz-Passarge	Wnt10A	AR	Hypodontia, palmoplantar keratoderma, eyelid hydrocystomas, nail dystrophy	224750	Manchanda et al. (2017)
Werner syndrome	RECQL2 (DNA helicase)	AR	Hypodontia, protuberant teeth, periodontal disease, premature aging, scleroderma-like skin, cutaneous ulcers, "bird-like" facies, high pitch voice, early-onset diabetes and ischemic heart disease, hypogonadism, malignancies	277700	Sá Fernandes et al. (2012)
Dyskeratosis congenita	Dyskerin gene (DKC), telomerase catalytic reverse transcriptase (TERT), telomerase RNA component (TERC)	XLR AD AR	Tooth decay, hypodontia, thin enamel, dental caries, taurodontism, blunted roots, periodontitis, premalignant oral leukoplakia, poikiloderma, dystrophic nails, pancytopenia, malignancies	Variable	Serindere (2018)
Monilethrix	Keratins 81, 83, 86	AD	Anodontia, conical and missing teeth, short beaded hair, keratosis pilaris, mental retardation, syndactyly, cataract, nail abnormalities	158000	Vora et al. (2014)
Scalp-ear-nipple syndrome (Finlay-Marks syndrome)	Potassium-channel tetramerization domain-containing 1 (KCTD1)	AD	Oligodontia, widely spaced teeth, nipple and/or breast hypo- or aplasia, aplasia cutis congenital of the scalp, nail dystrophy, abnormal ears, syndactyly	181270	Morales-Peralta, Andres, and Campillo Betancourt (2014)

Polyodontia

(Continues)



TABLE 1 (Continued)

Disease	Gene	Mode of inheritance	Clinical findings	Phenotype MIM number	Reference
Gardner syndrome	Adenomatous polyposis coli (APC)	AD	Unruptured teeth, polydontia, odontomas, impacted teeth, dental cysts, fused or unusually long roots, osteomas, colon polyps and cancer, epidermoid cysts, congenital hypertrophy of the retinal pigment epithelium, desmoid tumors	175100	Pereira et al. (2016)
Enamel hypoplasia					
Oculodentodigital dysplasia	GJA1	AD; rarely AR	Enamel hypoplasia, anodontia, microdontia, dental caries, early tooth loss, brittle nails, sparse hair, microphthalmia, microcornea, thin nose, syndactyly, variable neurologic manifestations	164200	Doshi, Limdi, Parekh, and Gohil (2016)
Epidermolysis bullosa (junctional and dystrophic)	Variable	Variable	Enamel defects (thin/hypoplastic/pitted), dental caries, skin fragility, cutaneous and mucosal blistering and ulceration	Variable	Wright (2010)
Sjögren-Larsson	Fatty aldehyde dehydrogenase	AR	Caries, periodontitis, gingivitis, enamel hypoplasia, ichthyosis, spastic diplegia, mental retardation	270200	Forsberg, Jagell, and Reuterving (1983)
Tricho-dento-osseous syndrome	DLX3 homeobox protein	AD	Yellow-brown tooth discoloration, hypocalcification or hypomaturation enamel defects with enamel hypoplasia, dental abscesses, taurodontism, curly/kinky/wavy hair, radiodense bones, nail defects	190320	Al-Batayneh (2012)
Natal teeth					
Pachyonychia congenita	Keratin 6b, 17	AD	Natal teeth, palmoplantar keratoderma, dystrophic nails, steatocystoma multiplex	167210	Eliason et al. (2012)
Steatocystoma multiplex	Keratin 17	AD	Natal teeth, steatocystomas	184510	King and Lee (1987)
Restrictive dermopathy	Lamin A/zinc metalloproteinase (ZMPSTE24)	AR	Natal teeth, rigid and tense skin, abnormal facies, joint contractures, restrictive lung disease, early death	275210	Smitt et al. (1998)
Dental pits					
Tuberous sclerosis	TSC1 (type 1); TSC2 (type 2)	AD	Dental enamel pit, oral fibromas, hypomelanotic macules, angiofibromas, shagreen patch, retinal hamartomas, renal angiomyolipoma, cardiac rhabdomyoma, lymphangiomyomatosis of lungs	191100 (type 1); 613254 (type 2)	Sparling et al. (2007)

(Continues)



TABLE 1 (Continued)

Disease	Gene	Mode of inheritance	Clinical findings	Phenotype MIM number	Reference
Ichthyosis-hypotrichosis syndrome	Suppression of tumorigenicity 14 (ST14)	AR	Pitted teeth, conical teeth, ichthyosis, curly sparse hair, pili torti and bifurcate, corneal opacities	602400	Basel-Vanagaite, Attia, Ishida-Yamamoto, Rainshtein, & Ben Amitai, Lurie, Pasmanik-Chor, Indelman, Zvulunov, Saban, Magal, Sprecher, and Shohat (2007)
Others					
Nevoid basal cell carcinoma syndrome (Gorlin syndrome)	Protein patched homolog 1 (PTCH 1)	AD	Tooth impaction, tooth agenesis, ectopic position of tooth, unerupted teeth, root resorption, multiple basal cell carcinomas, palmar/plantar pits, rib deformities, odontogenic keratocysts	109400	Manfredi et al. (2004)
Job syndrome	STAT3	AD	Retention of primary teeth (delayed resorption of roots), lack of eruption of secondary teeth, ectopic position of tooth, eczema, recurrent infections, elevated IgE levels	147060	Esposito et al. (2012)
Congenital erythropoietic porphyria (Gunther disease)	Uroporphyrinogen-III synthase	AR	Erythrodontia, red fluorescence of teeth under wood's lamp, skin photosensitivity with blistering and scarring, hypertrichosis, red urine	263,700	Bhavasari, Santoshkumar, and Prakash (2011); Ramanujam and Anderson (2015)
Hepatoerythropoietic Porphyria	Uroporphyrinogen decarboxylase	AR	Erythrodontia, red fluorescence of teeth under wood's lamp, skin photosensitivity with blistering and scarring, hypertrichosis, red urine	176100	Ramanujam and Anderson (2015)
Osteogenesis imperfecta	Type I collagen	Variable	Dentine dysplasia (dentinogenesis imperfecta), bulbous crowns, constricted cemento-enamel junctions, short roots, obliteration of the pulp chambers, periapical radiolucencies in the root canals, easy skin bruising, hearing loss, blue sclerae, multiple fractures, mitral valve prolapse	Variable	Abukabbos and Al-Sineedi (2013)
Keratitichthyosis-deafness syndrome	Connexin 26	AD	Small or absent teeth, delayed eruption, dental caries, ichthyosis, keratitis, hearing loss	148210	Caceres-Rios, Tamayo-Sanchez, Duran-Mckinster, and de la Luz Orozco, and Ruiz-Maldonado, (1996)
Rubinstein-Taybi syndrome	CREB-binding protein	AD	Talon cusps, dental caries, unerupted supernumerary teeth, broad thumbs and toes, pilomatricomas, hypertrichosis, tendency to form keloids, distinctive facies, mental retardation	180849	Tirali, Sar, and Cehreli (2014); Zaouak, Magdoud, Jouini, Hammami, and Fenniche (2019)
Naegeli-Franceschetti-Jadassohn syndrome	Keratin 14	AD	Yellow discoloration of the teeth, dental caries, early tooth loss, hypohidrosis, palmar/plantar hyperkeratosis, reticular hyperpigmentation, adermatoglyphia	161000	Sanodia, Hulmani, and Kumar (2019)

(Continues)



TABLE 1 (Continued)

Disease	Gene	Mode of inheritance	Clinical findings	Phenotype MIM number	Reference
Lipoid proteinosis	Extracellular matrix protein 1 (ECM1)	AR	Hyperplasia or aplasia of teeth, carious teeth, early loss of teeth, enlarged tongue with restricted movement, yellow papules over oral mucosa, recurrent vesiculobullous eruptions, facial papulonodules and scars, verrucous plaques over extremities, beaded papules over eyelids, hoarse voice	247100	Ravi Prakash et al. (2013); Zaouak et al. (2015)
Mandibuloacral dysplasia with lipodystrophy	Lamin A/C (type A lipodystrophy), ZMPSTE24 metalloproteinase (type B lipodystrophy)	AR	Variable dental anomalies (premature loss of teeth, poorly implanted teeth, hypoplastic teeth, overlapping teeth) growth retardation, mandibular and clavicular hypoplasia, acro-osteolysis, atrophy of the skin over hands and feet, alopecia	248370, 608612	Garavelli et al. (2009)
Ulnar-mammary syndrome	T-Box 3	AD	Abnormal canine teeth, ulnar ray defects, apocrine/mammary gland hypoplasia or dysfunction, genital abnormalities	181450	Bamshad et al. (1997)

Abbreviations: AD, autosomal dominant; AR, autosomal recessive; XLD, X-linked dominant; XLR, X-linked recessive.

^aAgnesis of 6 or more permanent teeth.

^bAgnesis of less than 6 teeth (Fantasia, 2014).

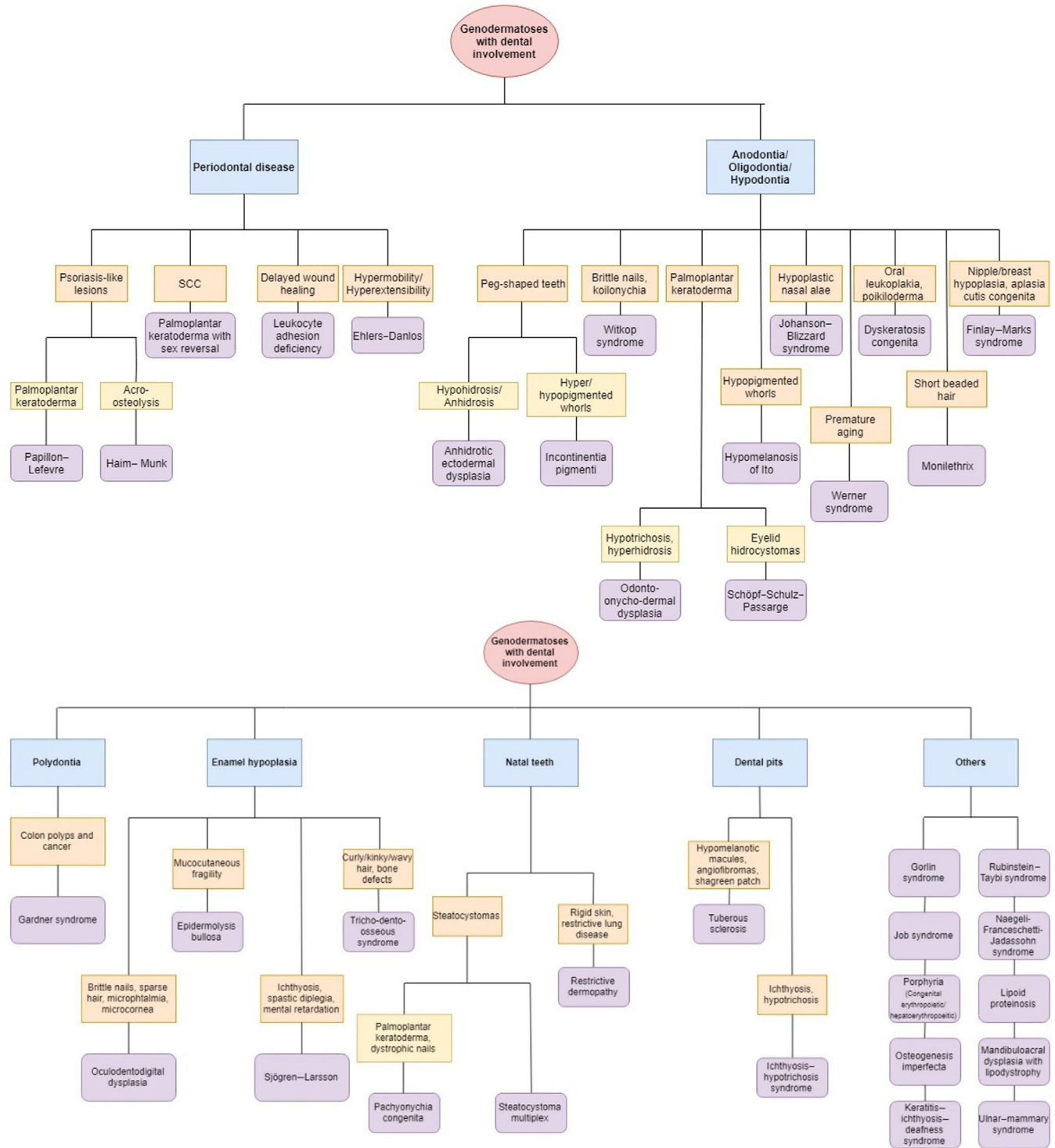


FIGURE 2 Clinical diagnostic approach to genodermatoses with dental involvement [Colour figure can be viewed at wileyonlinelibrary.com]

By recombining epithelial and mesenchymal cells and transplanting the resultant tooth germ into the jaw of a postnatal mouse, Nakao et al. (2007) managed to generate a fully developed tooth. While the Nakao method led to a breakthrough in the field, its translation into humans is not applicable due to practical, ethical, and legal considerations regarding the cultivation of cells from human embryonic tooth

germs (Balic, 2018). Despite successful creation of dental mesenchyme from mouse-induced pluripotent stem cells (iPSCs; Otsu et al., 2011), competent dental epithelium production has not yet been achieved. As the cellular and molecular interactions involved in *in vivo* tooth development become elucidated with further research, iPSCs can become a potential application for future dental regenerative efforts.



FIGURE 3 Papillon–leFevre. This patient presented with (a) periodontitis, (b) psoriasis-like plaques on her elbows, and (c) palmoplantar keratoderma [Colour figure can be viewed at wileyonlinelibrary.com]

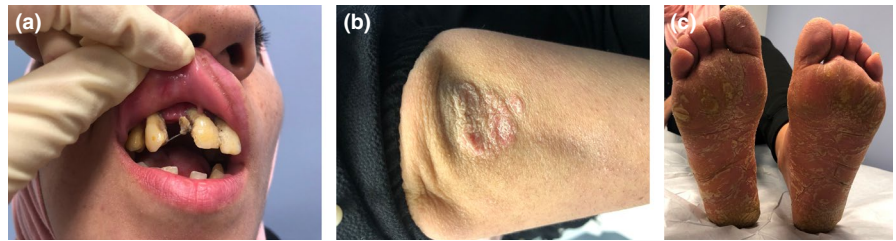
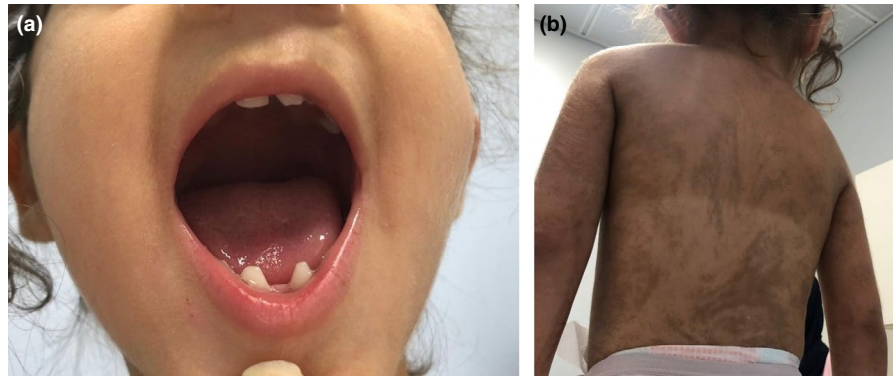


FIGURE 4 Incontinentia pigmenti. This patient presented with (a) hypodontia, peg-shaped teeth, and (b) hyperpigmented patches following the lines of Blaschko [Colour figure can be viewed at wileyonlinelibrary.com]



6 | DISCUSSION AND CONCLUSION

In this review, we have summarized several genodermatoses affecting the teeth. In Figure 2, we provide an algorithm each dentist and dermatologist can refer to when evaluating patients with skin and teeth findings and a suspected hereditary disorder. First, the medical specialist needs to assess the type of dental abnormality: periodontal disease, anodontia/oligodontia/hypodontia, polydontia, enamel hypoplasia, natal teeth, dental pits, or others. Then, the associated cutaneous and systemic features are evaluated to aid in making the final diagnosis. For instance, a patient presenting with periodontitis, psoriasis-like lesions, and palmoplantar keratoderma is likely to have Papillon–Lefevre (Figure 3; Fantasia, 2014). Haim–Munk disease is similar to Papillon–Lefevre with the additional features of atrophic nail changes and acro-osteolysis (Fantasia, 2014). Ehlers–Danlos is also characterized by periodontitis with the additional features of skin hyperextensibility and joint hypermobility. Hypodontia, peg-shaped teeth, and skin lesions following the lines of Blaschko are seen in incontinentia pigmenti (Figure 4; Mitakides & Tinkle, 2017). Hypodontia and peg-shaped teeth are also a feature of anhidrotic ectodermal dysplasia which is also characterized by hypo/anhidrosis (Figure 5; Hekmatfar, Jafari, Meshki, & Badakhsh, 2012). Anodontia, conical and missing teeth, and short beaded hair are features of monilethrix (Vora, Anjaneyan, & Mehta, 2014). On the other hand, Gardner syndrome is characterized by polydontia, colon polyps, and an increased risk of colon cancer (Pereira et al., 2016). Enamel hypoplasia and dental caries are common in epidermolysis bullosa patients who also suffer from easy blistering of the skin and mucous membranes following minor trauma (Figure 6; Wright, 2010). Natal teeth are seen in pachyonychia congenita. This disease also features steatocystomas, palmoplantar keratoderma, and dystrophic nails (Eliason, Leachman, Feng, Schwartz, & Hansen, 2012). Tuberosus



FIGURE 5 Hypohidrotic ectodermal dysplasia. This patient presented with hypodontia and peg-shaped teeth in addition to hypo/anhidrosis [Colour figure can be viewed at wileyonlinelibrary.com]

sclerosis is characterized by dental enamel pits and various cutaneous lesions such as hypomelanotic macules, angiofibromas, and the shagreen patch. Patients might also suffer from retinal hamartomas, renal angiomyolipoma, cardiac rhabdomyoma, and lymphangiomyomatosis of the lungs (Sparling, Hong, Brahim, Moss, & Darling, 2007). Oral manifestations of lipid proteinosis include hyperplasia or aplasia of the teeth, early loss of teeth, an enlarged tongue with restricted movement, and yellow papules over oral mucosa. In addition, carious teeth may result from dryness of the mouth due to the infiltration of the parotid duct by the hyaline material normally deposited in this disease. Other features include facial papulonodules which resolve with scarring, verrucous plaques over the extremities, beaded papules over the eyelids, and a hoarse voice (Figure 7; Ravi

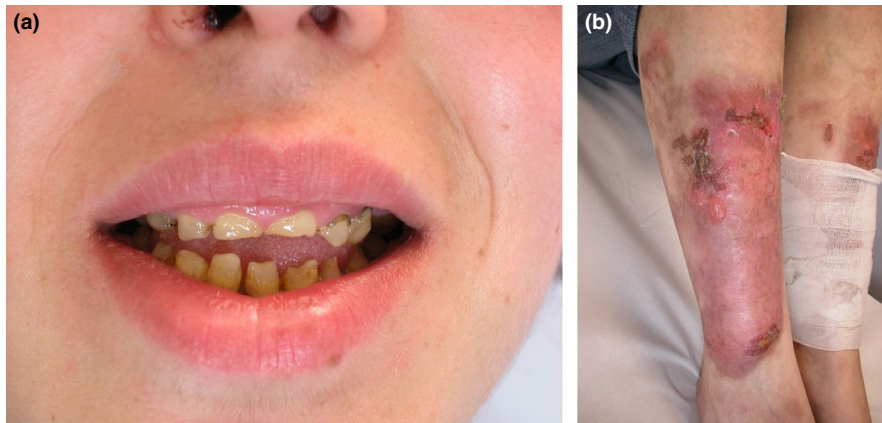


FIGURE 6 Junctional epidermolysis bullosa. This patient presented with (a) enamel hypoplasia and dental caries and (b) mucocutaneous blistering and ulceration [Colour figure can be viewed at wileyonlinelibrary.com]

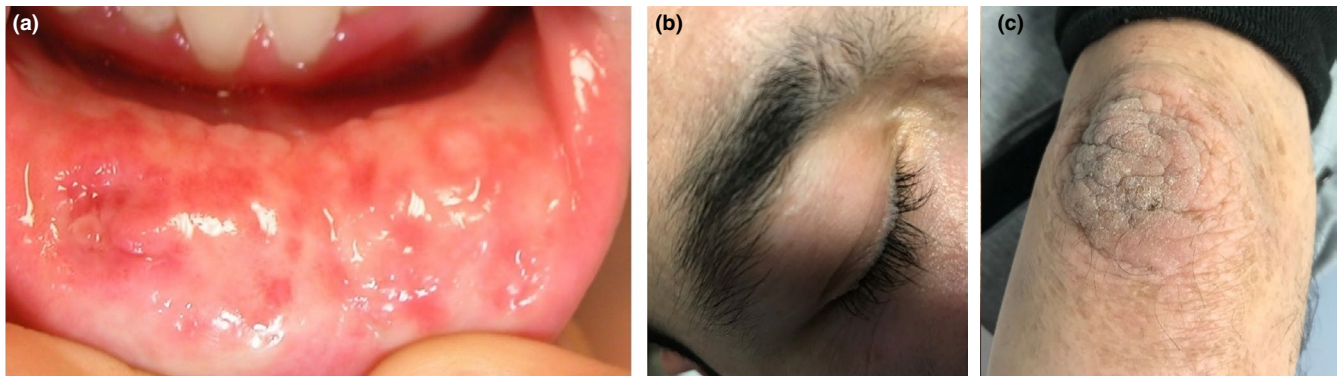


FIGURE 7 Lipoid proteinosis. This patient presented with (a) yellow papules over oral mucosa, (b) beaded papules over the eyelids, and (c) verrucous plaques over the elbows [Colour figure can be viewed at wileyonlinelibrary.com]

Prakash, Verma, Sumalatha, & Chattopadhyay, 2013; Zaouak, Zribi, Eleuch, & Mokni, 2015). The characteristic features of the other genodermatoses with dental involvement are highlighted in Table 1 and Figure 2.

6.1 | Why is this paper important to pediatric dentists

- Many genodermatoses affect the teeth.
- Early recognition is critical to test for and detect other systemic findings of these diseases.

This paper provides an algorithm that dentists and dermatologists can follow to better recognize genodermatoses with dental involvement.

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CONFLICT OF INTEREST

None to declare.

AUTHOR CONTRIBUTION

Samar Khalil, Edward Eid, Tara Bardawil and Lamiaa Hamieh: wrote the main article. Mazen Kurban, Ossama Abbas, Ziad Moujaes and Wael Khalil: proposed the main outline of the paper, wrote some parts and edited the final manuscript.

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