Focal dermal hypoplasia: oral and dental findings

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Focal Dermal Hypoplasia/Goltz Gorlin syndrome is a rare syndrome characterized by widespread dysplasia affecting tissues of mesodermal and ectodermal origin with cutaneous, osseous, ocular, oral and dental defects. Enamel hypoplasia is the most commonly reported dental manifestation and has recently been described as a possible manifestation of Lyonisation. This article reviews the reported dental findings and reports a new case with typical findings of focal dermal hypoplasia, which has been under review on our department for 10 years. It discusses the differential diagnosis as well as newer concepts of aetiology and pathogenesis in relation to dental anomalies.

Enamel hypoplasia may make plaque control difficult, resulting in generalized gingivitis. Hand anomalies may limit dexterity and exacerbate this. From the dental standpoint we emphasize the implementation of timely preventive and/or therapeutic strategies. Since there are periods of exacerbation during the course of this syndrome, regular surveillance from an early age with the frequency of visits increasing during and after adolescence is indicated. The role of the dentist in improving aesthetics and function can have tremendous psychological impact to enhance self-esteem of such patients.

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INTRODUCTION:

Focal Dermal Hypoplasia (Goltz Gorlin Syndrome/Goltz Syndrome/Congenital Ectodermal and Mesodermal Dysplasia) is a rare syndrome characterized by widespread dysplasia affecting tissues of mesodermal and ectodermal origin with cutaneous, osseous, ocular, oral and dental defects.[1] The earliest report of this condition was published in 1921 by Jessner.[2] The first case, which was histologically confirmed to have what is now known as focal dermal hypoplasia syndrome was reported by Lieberman[3] in 1935. In 1941 Cole et al[4] reported a similar case which presented with a clinical and histological presentation of focal dermal hypoplasia. However the first description of this condition under the title of focal dermal hypoplasia is ascribed to Goltz[5] and co-authors in 1962. This syndrome is seen mainly in females and appears to be spontaneous with no relevant family history. It is suggested that the disorder is X-linked dominant or autosomal dominant with sex linked inheritance caused by a single mutant gene with variable expression. The syndrome, in its full expression, usually proves fatal to the hemizygous male foetus. Only 10% of reported cases occur in males probably due to half chromatid mutations.[6]

Skin abnormalities[7-12] have been reported in all but two of the reported cases and are the most typical defects of Goltz syndrome. Common cutaneous findings include linear areas of hyperpigmentation or hypopigmentation combined with raised red/pink macules, linear deposits of superficial fat causing soft yellow nodules, telangiectasis, and papillomatous or verucous lesions. Raspberry like papillomata may develop

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at any time during life, most frequently at the junction of the skin and mucous membrane (lips and perianal areas) but also at other sites including the ears, fingers and toes. Papillomata also constitute a significant component of the oral manifestations. Hypoplasia or aplasia of hair and nails are also frequently noted. Skeletal defects[8,9,13] are the second most common abnormalities observed. Abnormalities range from shortness to aplasia of metacarpal bones, claw hands or feet, syndactyly, and polydactyly. Other less common bony changes include short stature, asymmetry of the face, trunk or extremities, microcrania, vertebral abnormalities and deformities of long bones. Facial asymmetry may be accompanied by notching or hypoplasia of the nasal alae, protruding ears, auricular appendages, and branchial clefts. Ocular abnormalities[7,9,13,14] include colobomas or congenital defects of the iris, retina, choroids and optic nerve. These lesions may result in blindness. Other abnormalities include strabismus, nystagmus, photophobia, microphthalmus, or a congenitally missing eye. The cornea may be clouded and tear ducts may be blocked. Central nervous system abnormalities may include mild mental retardation, hydrocephalus and hearing loss.[15]

The presence of uveal colobomata suggests an onset of the syndrome 4-5 weeks in utero. Dental development begins at 6-7 weeks in utero, so dental defects are an obvious feature of this syndrome.[16] Oral manifestations[7,9,14,16-23] are variable and are present in over half of all patients. Developmental problems may affect the eruption, position, size and number of teeth. Microdontia, hypodontia, oligodontia, abnormal root morphology, taurodontism, double primary teeth, fusion and gemination, ectopic and delayed eruption and malocclusion have also been described. In addition, external root resorption has been associated with the syndrome. The enamel may be defective, leading to early caries. Enamel hypoplasia is the most commonly reported dental manifestation. Balmer et al[22] believe that the pattern of enamel defects in focal dermal hypoplasia is a manifestation of Lyonisation (inactivation of 1X chromosome in a female cell during terminal differentiation resulting in clones of cells with normal or abnormal phenotype) similar to the pattern seen in females with X-linked amelogenesis imperfecta. Cleft lip and/or palate (including a case[23] of combined Tessier number 3 and 4 cleft), cleft tongue, or high arched palate may be present. Multiple frenulae, high frenal attachments, an absent/small uvula and velopharyngeal incompetence secondary to submucous cleft palate have been reported. Other oral anomalies include notching of the alveolus and mandibular hypoplasia. Oral soft tissue lesions may also be present including gingival hyperplasia, hemihypoplasia of the tongue, hyperkeratosis of the buccal mucosa, absence of the labial sulcus and intraoral papillomas of the gingivae, papillomas of the oral mucosa even extending to the oesophageal region, palatal mucosa, lips and cheeks.

Radiographic findings reflect focal dermal hypoplasia related skeletal defects. In addition osteopathia striate seen on radiographs may suggest the presence of focal dermal hypoplasia.[24] These striations are linear densities parallel to the long axis of metaphyseal sections of long bones. Oral and maxillofacial imaging may reveal abnormal crown and root morphology, with overall delayed dental development. Some cases have demonstrated taurodontism and external resorption of teeth. There may be large pulp chambers and decreased dentinal structure. Hypoplasia of the maxillary sinus, cysts of the jaw, bifid teeth, odontodysplastic appearance of unerupted teeth and impacted teeth reported multiple central giant cell tumors of the maxilla and mandible have been reported. Also noted are facial and cranial asymmetries, hydrocephalus and intracranial calcifications.[24]

This paper presents a case of focal dermal hypoplasia and discusses the dental findings as well as management strategies during the 10 years of follow-up in our department.

CASE REPORT:

A 5-year old girl was referred for a routine dental examination. She was a previously diagnosed case of Goltz syndrome. Clinically she presented with extensive skin abnormalities and linear defects of the epidermis, fat herniation affecting her arms and legs and areas of hyperpigmentation. She presented with syndactyly of the 3rd and 4th toes of her right foot. In addition nail defects were noted. She had localized alopecia

Figure 1a. Facial view showing coloboma of the right eye, deviation of the nasal tip and skin defects (6.8 years old)

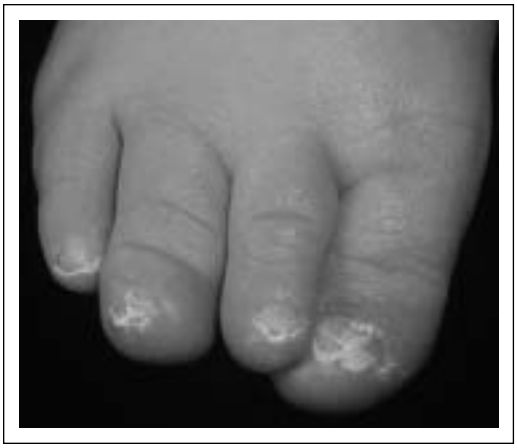

Figure 1b. Right foot with syndactyl of 3rd and 4th toe and nail defects

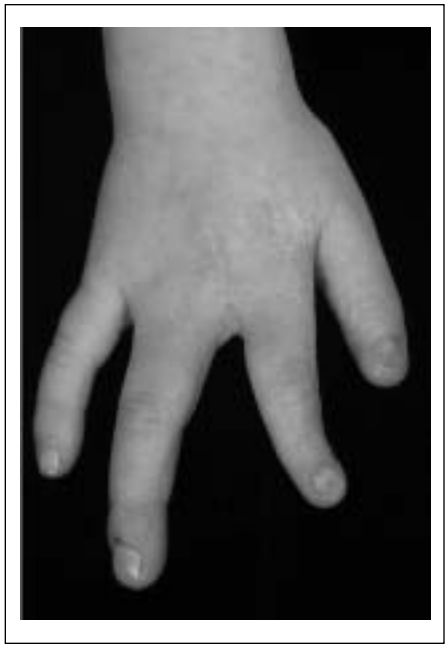

Figure 1c. Right hand missing third finger

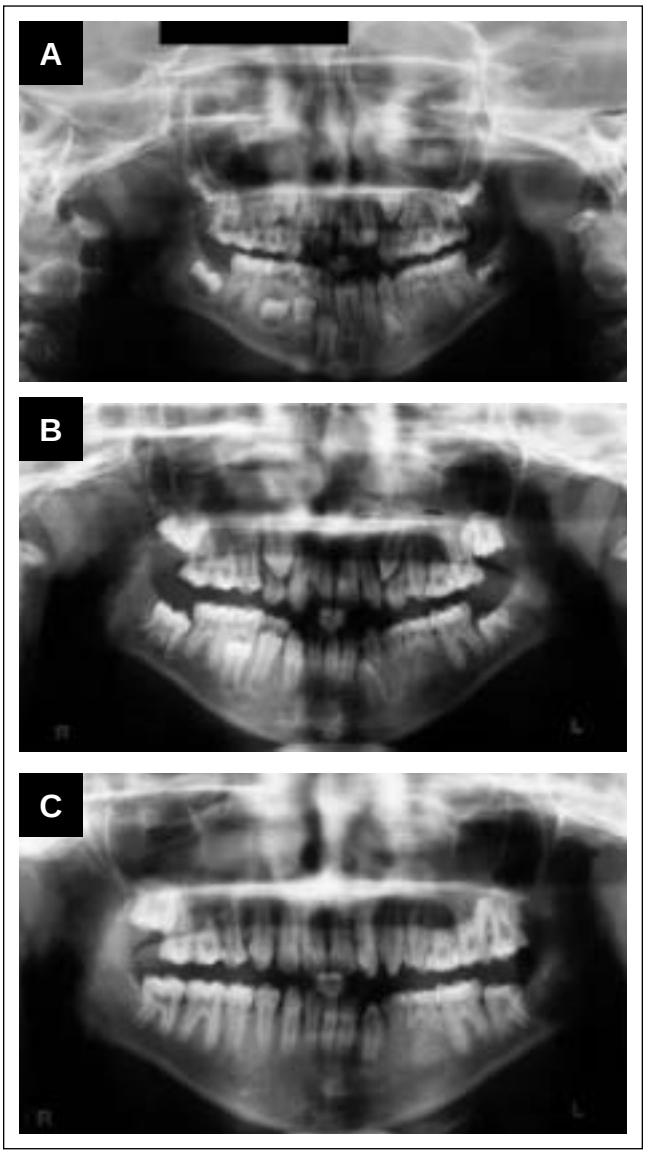

Figure 2. Dental Panoramic Tomographs at **a)** 8.7 years old; **b)**12.9 years old; **c)** 14.0 years old

and sparse hair growth on the scalp. Her right hand showed a missing 3rd finger. She had congenital nystagmus and astigmatism with a coloboma of her right eye. Although she did not have a cleft palate, the soft palate function was abnormal, resulting in velopharyngeal incompetence. The right ear was much larger in size compared to the left ear. There was mild facial assymetry and the nasal tip appeared to be deviated to the right (Figs. 1a, b, and c).

Generalized enamel pits were seen in the primary dentition and radiographic examination confirmed hypodontia. The crown root ratio appeared to be abnormal. Oral hygiene as well as dietary instructions were given to the patient. The patient was kept under regular follow-up and her dental development was closely monitored as she grew.

The patient's dental anomalies included hypodontia, microdontia, abnormal tooth morphology and delayed dental development. There were generalized enamel pits noted in both the primary and the permanent dentition and the roots of the permanent teeth were short. Papillomas of the oral mucosa were present and the palatal mucosa presented with zones of hyperpigmentation and striae as on the skin. Dental panoramic tomographs showed that all the permanent third molars were missing. The second premolars were absent in the upper left, upper right and lower left quadrants; the second primary molars were retained in the corresponding quadrants. The first premolar was missing on the lower left quadrant; the lower left primary first molar was retained. The lower right lateral incisor was also missing (Figs 2a, b and c). The lower facial and chin region showed fatty herniation of dermal tissue through linear defects of the facial epider-

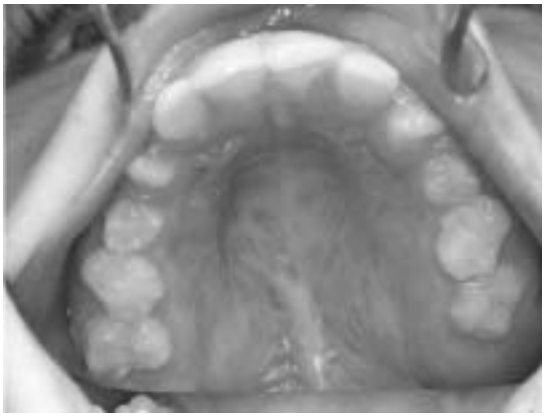

Figure 3a. Fig Maxilla with microdont premolars; posterior teeth displaying hypoplasia and abnormal morphology; palatal mucosal hyperpigmentation and striae

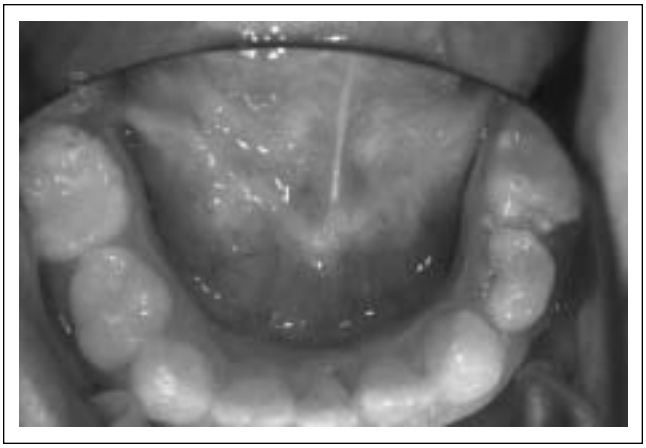

Figure 3b. Mandible with posterior teeth displaying hypoplasia and abnormal morphology

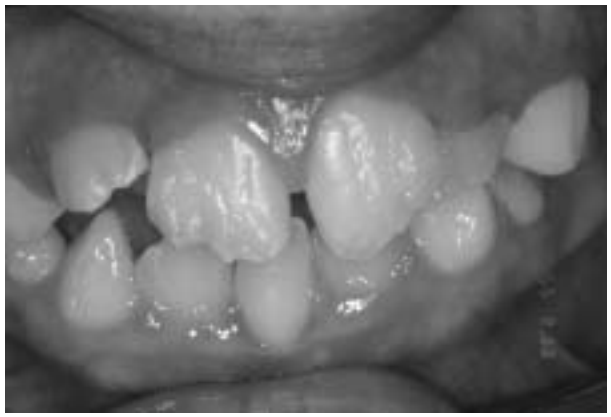

Figure 3c. Upper and lower incisors showing ridging and pits; caniniform 22

mis. The upper and lower central incisors as well as the upper right lateral incisor showed vertical ridging while the upper left lateral incisor was caniniform. The premolars, first permanent molars and primary molars were very hypoplastic and presented with atypical morphology; the upper premolars were microdonts (Fig. 3a, b and c). The patient continued to maintain good oral hygiene and was caries-free.

Treatment was mainly preventive, with constant reinforcement of oral hygiene and fissure sealants of all four first molar teeth. As the patient was unhappy with the appearance of her front teeth at the age of 14-years old, direct composite veneers were placed on 12, 11, 21 and 22, along with a composite build-up of 41. Light-cured composite was used for the facings along with light-cured compomer for the tips to reduce the translucency. This produced veneers of acceptable aesthetics and the patient was very pleased (Figs. 4a and b).

The patient subsequently moved to Spain and is being followed-up by a general dental practitioner there.

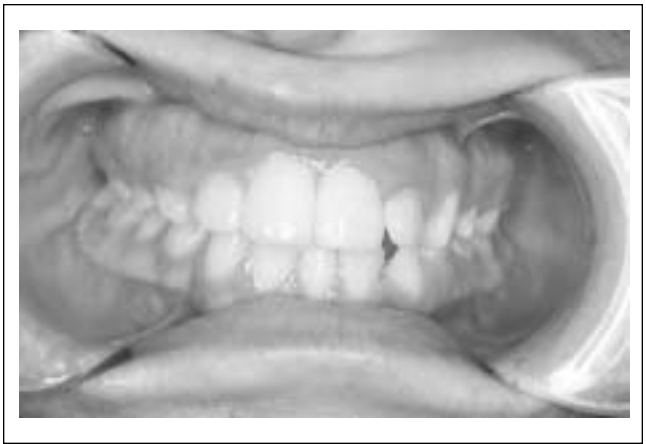

Figure 4a. After placement of composite veneers

Figure 4b. Patient at the end of treatment (14.11 years old)

DISCUSSION:

According to McNamara T et al,[19] the two syndromes Goltz Gorlin and Gorlin Goltz are very distinct yet confusion exists in literature from the similarities in nomenclature. To avoid errors in diagnosis because of the similarity of names, the authors caution that preferred names for both the syndromes should be focal dermal hypoplasia syndrome for Goltz Gorlin syndrome and Nevoid Basal Cell Carcinoma Syndrome for Gorlin Goltz syndrome.

The clinical signs are distinctive. The syndrome can be diagnosed with relative certainty on the basis of clinical examination or a fully documented description. In the differential diagnosis consider incontinentia pigmenti, aplasia cutis congenital, Rothmund-Thompson syndrome and tuberous sclerosis.[7,25] The atrophic macules in focal dermal hypoplasia are sometimes linear, as can be seen in incontinentia pigmenti, but there is no actual dermal atrophy in incontenentia pigmenti. Aplasia cutis congenital, unlike focal dermal hypoplasia, is not a generalized disorder and does not have associated anomalies. Rothmund-Thompson syndrome (congenital poikiloderma) is usually not visible at birth and lacks the characteristic fat herniations and periorificial papillomas seen in focal dermal hypoplasia. Cutaneous findings in tuberous sclerosis are distinctive and may be the earliest markers of this syndrome. These comprise of pink to reddish-brown, smooth, dome shaped papules, 1-4mm sometimes associated with telangiectasia; they occur in a symmetrical butterfly distribution over the nose, nasolabial folds and cheeks from ages 2-8 years. In our patient the palatal mucosa is remarkable for a striated character, which is similar in appearance to the linear streaking of the hypoplastic areas of the skin.

Lyonisation[26] takes place early in somatic development when one of the X chromosomes in females is inactivated. The process of X inactivation is controlled by a region of the X chromosome termed the X inactivation center, located at Xq13. The XIST (X-inactivation specific transcript) gene is transcribed exclusively from the inactive X and is both necessary and sufficient for the initiation and propagation of X inactivation. Inactivation is permanent and clonal and occurs randomly. This produces specific phenotypic patterns in certain tissues. In the teeth vertical grooving defects reflect columns of normal or defective ameloblasts. This type of enamel grooving is a distinctive feature of heterozygous females in families with X-linked amelogenesis imperfecta and is a striking example of Lyonisation.[27,28] The pattern of dental defects secondary to this process is also consistent with the pattern of abnormalities in the bone and skin. Skin lesions correspond to the lines of Blaschko and may reflect outgrowth of cell populations, a proportion of which carry the mutated gene. Striations in bone coincide with zones of osteogenesis secondary to parallel columns of chondroblasts forming cartilage. If some of these chondroblasts carry the defective gene then the typical pattern of linear hypocalcification is seen.[22]

Although the gene responsible for focal dermal hypoplasia has not been identified, there is evidence suggesting that the location is in the region of Xp22.31.[29] The locus of the amelogenin (AMELX) gene has been mapped to Xp22.31-p22.1, mutations of which result in amelogenesis imperfecta. The vertical pattern of enamel hypoplasia seems to be similar in both these disorders.

The goals of treatment include improving function and cosmetic appearance through orthopaedic and plastic surgery. The parents and when appropriate the patient should receive genetic counseling so that informed decisions can be made about future childbearing. Differential diagnosis of facial swellings should include infections of both dental origin and facial dermal lesions. Early detection of dental defects and oral soft tissue lesions could facilitate the implementation of timely preventive and/or therapeutic strategies consistent with clinical findings. The restorability of the teeth is dependent on tooth morphology and the extent of pulpal involvement. Prevention should be emphasized through dietary control, fluoride supplementation, and special consideration in plaque control. There are periods of exacerbation during the course of this syndrome. Regular surveillance from an early age with the frequency of visits increasing during and after adolescence is indicated. The gingival papillomas in focal dermal hypoplasia are frequently recurrent and excision could compromise the periodontal condition of the patient. The morphological abnormalities in the size and shape of the dentition with limited dexterity of patients due to hand anomalies makes plaque control difficult, resulting in generalized gingivitis and potentially high caries rates. Further consideration in dental treatment should emphasize space maintenance and/or replacement of missing teeth for aesthetics and guidance of the developing occlusion. Multidisciplinary care may be required. The role of the dentist in intervention and improvement of aesthetics and function can have a tremendous psychological impact and enhance the self-esteem of such patients.[7,9,14-22]

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