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Focal Dermal Hypoplasia (Goltz Syndrome): A Case Report Showing a Wide Variety of Systemic and Oral Manifestations

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Focal dermal hypoplasia (FDH), also known as Goltz syndrome, consists of an unusual genodermatosis that affects tissues of ectodermal and mesodermal origin and various organs and systems, especially skin, bones, eyes, and oral cavity. While systemic manifestations of FDH have been well documented, the oral manifestations have not been extensively discussed. We present a 22-year-old female patient with history of FDH that showed a variety of systemic and oral manifestations. FDH was diagnosed at birth based on cutaneous alterations. Extra and intraoral examination showed facial asymmetry, lip and perioral atrophy, upper lip papilloma, malocclusion, enamel hypoplasia, and gingival hyperplasia. Mucosal lesions, periodontal diseases, and malocclusion were treated by oral surgery, periodontal therapy and orthodontic treatment, respectively. Although FDH is an uncommon syndrome, health professionals should be aware of its systemic and oral manifestations to establish an early diagnosis and adequate treatment.

Keywords: Diagnosis, Focal dermal hypoplasia, Genetics, Oral manifestations

INTRODUCTION

Focal dermal hypoplasia (FDH), originally described by Goltz et al.[1] 1962, is an unusual genodermatosis, characterized by abnormalities of ectodermal and mesodermal tissues[2]. It is related to mutations in the porcupine homolog—Drosophila (*PORCN* gene), which is linked to the X chromosome, justifying the predominance of females (9:1 ratio). Complete expression of this mutation is usually lethal in male fetuses, except in cases of genetic mosaicism[3,4].

Clinical characteristics of FDH typically involves several systems and different severity levels, including cutaneous manifestations and ocular, oral, musculoskeletal, and neuropsychiatric abnormalities[5,6]. To date, there are a limited number of case reports and literature reviews on FDH, and few of them focused on oral manifestations[7]. Here, we describe a patient with a variety of systemic and oral manifestations of FDH.

CASE REPORT

A 22-year-old female patient with FDH diagnosed at birth based on skin abnormalities. The patient was born preterm (36 weeks) by cesarean section presenting extensive cutaneous lesions characterized by wrinkled skin and erythematous lesion on the left flank. Since childhood, the patient has received regular dermatological and genetic monitoring. No family history or consanguineous marriage between her parents was reported.

Physical examination showed low nasal bridge. Dermatological examination revealed atrophic lesions following the Blaschko's lines, ranging from hyperchromic, hypochromic and achromic lesions in the upper limbs, trunk, abdomen and lower limbs, papillary lesions on the left thigh, micropapular lesions on the face and hyperconvex nails. In addition, she had syndactyly on the left hand (surgically corrected) and right foot, and anomalous implantation on the right fifth fin-

ger (Fig. 1). Extraoral examination revealed atrophic lesions on the lips and perioral region, microstomia, and papillomatous lesion of 6 mm on the upper lip. Intraoral examination revealed accumulation of biofilm and calculus, generalized gingivitis, multiple areas of gingival growth, delayed tooth eruption, dental enamel hypoplasia and malocclusion (Fig. 2). Biopsy of the lip lesion showed digitiform mucosal epithelial proliferation supported by connective tissue, with areas of hyperkeratosis and koilocytosis. Immunohistochemistry staining of p16 was negative. Histopathological features of gingival lesions were parakeratotic hyperkeratosis of stratified squamous epithelium, acanthosis and spongiosis. The lamina propria and submucosal areas were composed of a dense fibrous connective tissue with severe chronic inflammatory cell infiltrate of lymphocytes and endothelial blood vessels. Final diagnosis was compatible with gingival inflammatory hyperplasia. We received the patient's consent form about publishing all photographic materials.

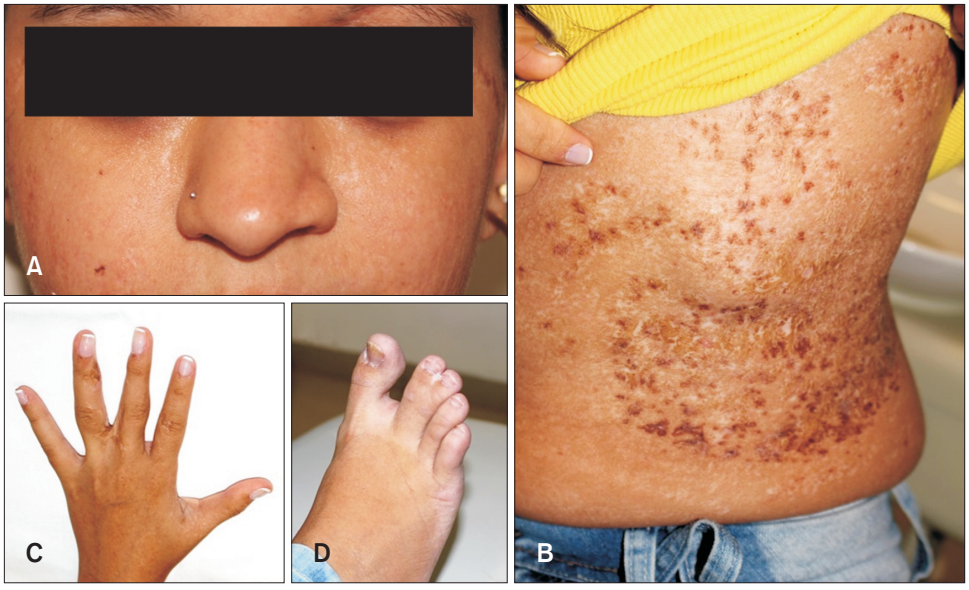

Fig. 1. Focal dermal hypoplasia: facial, limbs, and dermatological findings. (A) Low nasal bridge; (B) atrophic lesions following the Blaschko's lines, ranging from hyperchromic, hypochromic and achromic on the trunk and abdomen; syndactyly on the left hand (surgically corrected) (C), and right foot (D).

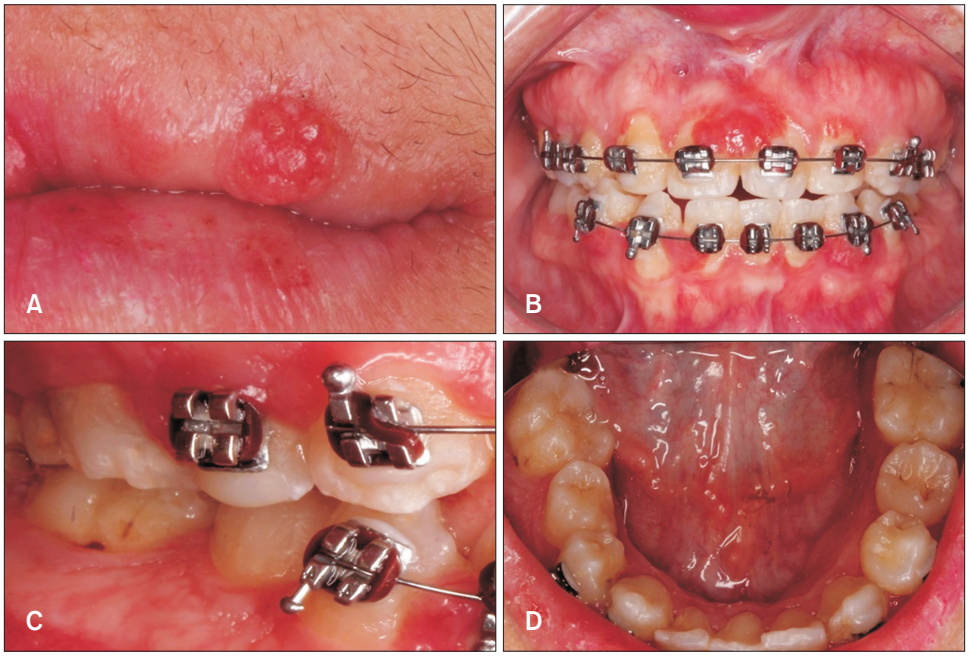

Fig. 2. Focal dermal hypoplasia: oral features. (A) Oral (raspberry-like) squamous papilloma on the upper lip; (B) multiple areas of gingival hyperplasia, mainly between the upper central incisors, and agenesis of the 13th, 22nd ,and 32nd teeth; (C) enamel hypoplasia; and (D) premolars rotation and absence of lingual frenulum.

DISCUSSION

This study describes a case of FDH with typical systemic manifestations, including skin, limb, ocular, as well as oral and dental defects, which are usually variable among patients with FDH and poorly described in the literature. Wang et al.[8], reviewed 159 published cases, of which most were female (140; 88.05%) regardless of ethnicity. Most of the reviewed cases (95%) showed skin abnormalities with multiple papillomas, accompanied by ocular and limb defects. In addition, orofacial manifestations varied widely, from and included facial asymmetry, enamel hypoplasia and malocclusion, as observed in our patient. According to the literature, oral soft tissue abnormalities appear in about 65% to 68% of cases, and hard tissue abnormalities, in 80% to 94%. Among them, the presence of papilloma in mucous membranes and enamel hypoplasia are the most common[9,10].

Vertical transmission of FDH phenotype occurs in heterozygous female, and are lethal in the majority of fetuses[3,4,8]. Although most cases of FDH in female result from mutations in the *PORCN* gene in individuals with no family history of the disorder, genetic counseling is required[9,11]. Even though a genetic analysis was not performed in our case, there was no evidence of inheritance or similar cases in the family.

Bostwick et al.[11], in 2016, proposed clinical diagnosis criteria for FDH, which include three or more skin manifestations and at least one characteristic limb malformation of FDH (Fig. 3). Our case showed typical skin and limb manifestations of FDH since birth, and also other abnormalities described in the literature, such as hyperconvex nails and low nasal bridge[9].

Other manifestations of FDH include ocular involvement (cataract, microphthalmia, colobomas and lacrimal duct abnormalities), growth and developmental defects (short stature, chewing problems, and difficulties in swallowing)[6,8,12,13]. Regarding ocular malformations, our patient had heterochromia and blocked tear duct in the left eye treated with its opening, probing and irrigation in childhood. No strabismus, microphthalmia or coloboma as well as no growth or developmental defect were observed in our case.

Regarding oral manifestations, there are many alterations associated with FDH (Table 1)[2-9,11,12,14-20]. Our patient had atrophy of the lips and perioral region, microstomia, and raspberry-like papilloma in the upper lip (Fig. 2). The occurrence of multiple papillomas on mucosa and skin is a common, especially in the perioral, perivulvar, perianal and periocular regions[8]. In the oral cavity, these lesions may affect gingiva, tongue, palate, buccal mucosa, and have been reported in the pharynx[14]. Surgical excision is the recommended treatment, as performed in our case. In addition, our patient had malocclusion, enamel hypoplasia, tooth rotation, external root resorption, multifocal gingival hyperplasia and absence of lingual frenulum (Fig. 2). The same findings were described by Wright et al.[14], who reviewed the main oral manifestations of FDH and highlighted enamel defects as a distinguishing characteristic of the syndrome that may negatively affect the oral hygiene.

An important finding of our study was the presence of multiple hyperplastic lesions in patient's marginal gingiva. Baxter et al.[7], observed the presence of arborescent hyperplastic lesions in several areas of the gingiva, especially in anterior areas as observed in our case.

In conclusion, this case demonstrates oral manifestations associated with FDH. Identification of these features can contribute to the early diagnosis of this syndrome, genetic counseling, specific treatment and preventive procedures,

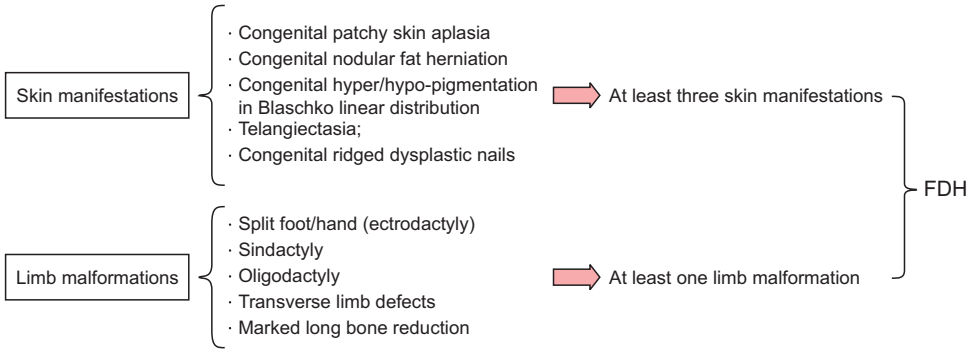

Fig. 3. Focal dermal hypoplasia (FDH): clinical diagnostic criteria proposed by Bostwick et al.[11]

Table 1. Studies reporting orofacial and dental manifestations of focal dermal hypoplasia

Author (year)	Study design	No. of patients	Age (yr)	Sex	Main orofacial manifestation	Country or continent
Hall and Terezhalmy (1983)[5]	Case report and literature review	1	23	Male	Facial asymmetry, hypodontia, spaced teeth, malocclusion, prognathism, supernumerary teeth, odontodysplastic appearance	United States of America
Greer and Reissner (1989)[15]	Case report	1	31	Female	Oral papillomas, papillary gingival lesions, hyperkeratosis of the buccal mucosa	United States of America
Baxter et al (2000)[7]	Case report	2	16 and 19	Female	Enamel hypoplasia, arborescent hyperplastic gingival lesions, hypodontia, microdontia, agenesis, external root resorption	England
Al-Ghamdi and Crawford (2003)[2]	Case report	1	8	Female	Facial asymmetry, papillomas of the base of tongue and tonsils, spaced teeth, hypodontia, enamel hypoplasia, delayed tooth eruption, teeth rotation, agenesis, odontodysplasic appearance	England
Balmer et al. (2004)[16]	Case report	3	10.6*	2 Female, 1 Male	Enamel defects, delayed and ectopic tooth eruption, oral papilloma, germination, taurodontism, teeth with roots and open apices	Australia
Tejani et al. (2005)[3]	Case report	1	5	Female	Facial asymmetry, enamel defects, hypodontia, malocclusion, microdontia, abnormal tooth morphology, delayed tooth eruption, oral papillomas, agenesis, palatal mucosal hyperpigmentation and striae	England
Seoane et al. (2009)[17]	Case report	1	15	Female	Red patch (raspberry-like) on hard palate, enamel defects, absent lingual frenulum	Spain
Murakami et al. (2011)[6]	Case report	1	4	Female	Facial asymmetry, low-set protruding ears, narrow nasal bridge, cleft lip or palate, high-arched palate, micrognathia, pointed chin, delayed or ectopic tooth eruption, extensive dental caries, hypodontia or oligodontia, microdontia, supernumerary teeth, taurodontism, teeth germination or fusion, decreased dentine formation, spaced teeth or malocclusion, external root resorption, abnormal roots, talon cusp, odontodysplastic appearance of unerupted teeth, arborescent papillomas of the oral mucosa, gingival hypertrophy and gingivitis, high/double labial frenum, ability to touch the nose with the tongue, absent lingual frenulum	Brazil
Wang et al. (2014)[8]	Literature review	159	NA	140 Female and 19 Male	Facial asymmetry, notched alae nasi, pointed chin, cleft lip/cleft palate, hypodontia, enamel hypoplasia, abnormal teeth number	South America, North America, Europe, Africa, Oceania, and Asia†
Bostwick et al. (2016)[11]	Case series	18	11.5*	16 Female and 2 Male	Facial asymmetry, nasal asymmetry, pointed chin, hypoplastic alae nasi, perioral skin hypoplasia, enamel defects, oral papillomas	United States of America
DiSalvo et al. (2016)[18]	Case report	1	38	Male	Malocclusion, papillary gingival hyperplasia, papillomatous mass in the oropharynx	United States of America
Fete and Fete (2016)[9]	Case series	19	10.6*	17 Female and 1 Male	Facial asymmetry, notched nasal alae, cleft lip/cleft palate, malocclusion, oral tissue abnormalities, enamel defects, enamel hypoplasia, intra-oral lipoma or papilloma	United States of America

Table 1. Continued

Author (year)	Study design	No. of patients	Age (yr)	Sex	Main orofacial manifestation	Country or continent
Wright et al. (2016)[14]	Case series	19	10	16 Female and 3 Male	Facial asymmetry, cleft lip, cleft palate, malocclusion, delayed tooth eruption, intraoral papillomas, intraoral lipoma, generalized gingivitis, high frenum attachment	United States of America
Alsharif et al. (2018)[12]	Case report	1	16	Female	Facial asymmetry, tooth malformation, hypodontia in upper laterals	Saudi Arabia
Frisk et al. (2018)[4]	Case report	1	3	Male	Facial asymmetry, spaced teeth	Sweden
Jose et al. (2018)[19]	Case report	1	18	Female	Multiple papillomas in tongue, buccal mucosa, lips, left nasal cavity, facial asymmetry, wide nose, low set ears, left corneal opacity, oligodontia, enamel defects	India
Nathwani et al. (2018)[20]	Case report	1	58	Male	Facial asymmetry, intraosseous lipoma, microdontia, hypodontia, multiple intraoral papillomas	United Kingdom
Present case	Case report	1	22	Female	Facial asymmetry, low nasal bridge, malocclusion, delayed tooth eruption, dental enamel hypoplasia, papilloma on the upper lip, tooth rotation, external root resorption, multifocal gingival hyperplasia, absence of lingual frenulum	Brazil

NA: non available, *Mean; †Continents: South America (Argentina, Brazil), North America (Mexico, Puerto Rico, United States of America), Europe (Austria, France, Greece, Ireland, Italy, Netherlands, Norway, Poland, Portugal, Spain, Switzerland, United Kingdom), Africa (Burkina Faso, Ethiopia, Nigeria, South Africa, Togo), Oceania (Australia), and Asia (India, Iran, Japan, Korea, Lebanon, Singapore, Thailand).

which involve many fields of dentistry. More than an aesthetic concern, this syndrome causes functional and psychological problems that require a multidisciplinary team approach to improve the quality of life of these patients.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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