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Single Case

Unilateral Focal Dermal Hypoplasia (Goltz Syndrome): Case Report and Literature Review

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Keywords
Focal dermal hypoplasia · Goltz syndrome · X-linked dominant condition

Abstract
Focal dermal hypoplasia (FDH) or Goltz syndrome is a rare X-linked dominant multisystemic disease involving the ectoderm, mesoderm, and endoderm. About 95% of the cases appear de novo, and 90% of them are females. Recently, the studies revealed that FDH is caused by a mutation in the PORCN gene. We report a case of unilateral FDH or Goltz syndrome in a 16-year-old girl presenting with hypopigmented-reticulated atrophic macules and patches in a linear pattern distributed along the lines of Blaschko over the right side of the face and the right arm. Also she is having hypoplasia of the right breast with dental enamel abnormality and partial anodontia in the lower jaw. Sparse hair and partial alopecia on the right side (scalp, eyebrows, and eyelashes) were also observed.

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Introduction

Focal dermal hypoplasia (FDH) or Goltz syndrome is an exceedingly rare disorder. It was first described by Liebermann in 1935 as "atrophodermia linearis maculosa et papillomatosis congenitalis." Goltz, in 1962, mentioned the term "FDH."

It is an X-linked dominant condition caused by mutations in the PORCN gene, which encodes a protein that regulates Wnt signaling. It is characterized by vermiculate dermal atrophy, outpouchings of fat, telangiectasias, and hypopigmentation. Additional features include periorificial raspberry-like papillomas, dystrophic nails, sparse hair, abnormal teeth, split hand/foot ("lobster claw") malformations, ocular abnormalities (e.g., microphthalmia), and the radiographic finding of osteopathia striata in long bones.

We report in this paper a rare case of Goltz syndrome, who presented with congenital unilateral FDH of the right side of the body.

Case Report

A 16-year-old girl presented to the dermatology clinic with asymptomatic lesions that had affected the right side of her body since childhood with no improvement.

Also, the patient complained of alopecia on the right side (scalp, eyebrow, and eyelashes). A systemic review was unremarkable. All her milestones of development were normal. No family members have similar lesions. There was no consanguinity in her parents. Her brother and sister as well as her parents have no abnormal development, i.e., there is no current or previous similar case in this family apart from the patient.

On examination, her height was 135 cm and her weight was 45 kg. Both parameters are within the normal range. Her IQ was 86, which is normal as well. Her teeth were malformed and she had hypodontia with missing upper laterals (Fig. 1, 2).

Cutaneous examination showed hypopigmented atrophic macules and patches in a linear pattern distributed along the lines of Blaschko over the right side of the face, trunk, and the right arm. She had facial asymmetry. She had multiple skin color papules over the right side of the nose (Fig. 3). She also had hypoplasia of the right breast (Fig. 4). Multiple patchy areas of cicatricial alopecia were seen over the right side of the scalp (Fig. 5).

Systemic examination was normal. Skin biopsy showed marked dermal atrophy with thin collagen fibers consistent with FDH.

Her complete blood count, electrolytes, liver and renal function tests were within the normal limits. Urine analysis was normal. Ophthalmological examination, X-rays of long bones, and ultrasound scan of the abdomen did not reveal any abnormality.

The combination of clinical presentation and histopathological findings led to the diagnosis of unilateral FDH (Goltz syndrome).

A molecular genetic test was not available in our hospital. At the 6-month follow-up visit, the patient was in good health; she underwent breast augmentation surgery. She was satisfied with the result of augmentation and the success of surgery met her expectations (Fig. 6).

Discussion

FDH, also known as Goltz syndrome, is a rare but serious multisystem disorder that affects tissues of ectomesodermal origin [1]. It was first described in 1962 by Goltz who reported 3 females presenting with congenital linear areas of thinning of the skin and herniations of adipose tissue in the form of yellowish papules [2]. Then he identified 2 similar cases with additional features including cleft palate, syndactyly, polydactyly, nail and tooth deformities, ocular anomalies, and sparse hair [3]. Although it is usually inherited as an X-linked dominant condition with male lethality in utero, there is a small number of male patients reported in the literature. A possible explanation for this might be due to X-chromosome mosaicism in males that result from gametic half-chromatid mutation or postzygotic somatic mutation [4]. In reviewing the literature, we found only 6 reports of father-to-daughter transmission. In all of them, the fathers have been described as having a milder phenotype [4–9]. In 2016, Prof. Happle [10] demonstrated that Goltz syndrome represents a developmental defect with mosaic distribution of affected tissues, due to a block of Wnt signal transmission from cells carrying a detrimental PORCN mutation on their active X-chromosome.

Cutaneous manifestations of FDH include congenital patchy skin aplasia (95%) evidenced by atrophic and hypoplastic areas of the skin that often follow the lines of Blaschko and appear as depressed regions of pink or white color, often with a fibrous texture. Congenital skin hypo- or hyperpigmentation (90–100%) often follow a Blaschko linear distribution. Congenital nodular fat herniation (60–70%) evidenced by soft, yellow-pink nodules on the skin (which represent fat nodules in the dermis) are typically seen on the trunk and extremities. Telangiectasias (~80%) may be seen on the face, trunk, and extremities, verrucoid papillomas (65%) of the skin and mucous membranes, pebbled skin texture (58%) and photosensitivity (40%). Hair presentations of FDH include patchy alopecia of the scalp (80%) and hair shaft abnormalities on scanning electron microscopy (80–90%). Nail abnormalities of FDH include congenital ridged, dysplastic, or hypoplastic nails (80–90%) [11]. The cutaneous manifestations of our patient were hypopigmented-reticulated atrophic macules and patches in a linear pattern distributed along the lines of Blaschko over the right side of the face and the right arm. Also, she had sparse hair and partial alopecia on the right side (scalp, eyebrows, and eyelashes). Interestingly, in our case, the manifestation of unilateral breast hypoplasia is not mentioned in the previous reports.

Skeletal abnormalities of FDH include syndactyly (70–90%), ectrodactyly (75%), long bone reduction defect (50–80%), oligodactyly (20–40%), which more frequently involved central digits, and transverse limb defect (15%) [11]. In our case, there was not much skeletal involvement. Dental manifestations are seen in more than half of affected individuals. Enamel hypoplasia that predisposes to dental caries is the most common problem. Other findings include: hypodontia, oligodontia, supernumerary teeth, and dental crowding leading to malocclusion of both primary and secondary dentition; vertical grooving of the teeth; microdontia, taurodontia, and abnormal root morphology [12–14]. In our case, dental enamel abnormality and partial anodontia in the lower jaw were observed. In 2010, Dias et al. [15] described a case of severe FDH who presented with an unexpected feature that is natal teeth.

Ocular manifestations of FDH include chorioretinal colobomas (60%), iris colobomas (50%), microphthalmia (45%), nystagmus (30%), strabismus (20%), cataracts (10%), and

anophthalmos (5–10%) [11]. In our case, neither one of the previous ocular manifestations was observed. Occasional anomalies of FDH include hearing defects, microcephaly, horseshoe kidneys, umbilical, inguinal, epigastric, or diaphragmatic hernias, cardiac tumors, and congenital heart diseases like truncus arteriosus. Approximately 15% of affected individuals have mild intellectual disability.

In reviewing the literature, there are over 250 cases of FDH that have been reported worldwide [16]. From all of these reports, only 9 cases presented with unilateral or almost unilateral FDH [16–24] (Table 1). Our case was one of the rare cases of FDH that presented with unilateral manifestations. While FDH is an X-linked disease, as expected, 9 of 10 of the unilateral FDH patients were female. However, only 1 male patient was reported with unilateral FDH. The right side of the body was involved predominantly in 70% of the patients. All patients showed the classic presentation of atrophic skin that follows the lines of Blaschko. However, half of the patients (including our case) did not show any fat herniation represented by fat nodules in the dermis. Also, in half of the patients (including our case), scalp and dental involvement has been reported. Although musculoskeletal abnormalities were involved in 70% of the reported cases, our case did not have any musculoskeletal signs or symptoms. Ocular and nail involvement was described in around 30% of the patients. It is somewhat surprising that internal organ involvement was mentioned in only one case report that was published in 1984. A unique finding in our case was unilateral breast hypoplasia.

FDH was usually diagnosed based on clinical presentations of the classic ectodermal findings and associated symptoms. However, molecular genetic testing can be used to confirm the diagnosis in some cases in whom the clinical findings are inconclusive. Molecular genetic testing approaches can include a combination of single gene testing (either sequence analysis or gene-targeted deletion/duplication analysis), chromosomal microarray analysis, the use of a multi-gene panel, and more comprehensive genomic testing.

Tiered molecular testing approaches can include a combination of single-gene testing (either sequence analysis or gene-targeted deletion/duplication analysis), chromosomal microarray analysis, the use of a multi-gene panel, and more comprehensive genomic testing.

Conclusion

In conclusion, Goltz syndrome is a rare congenital skin disorder characterized by a unique clinical presentation which is FDH. Looking for other associated features is important. Close examination of the extremities is recommended. Recognition of these characteristic features will permit early appropriate genetic counseling and treatment. In our patient, hypoplasia of the right breast was one of the noncommon manifestations found in the literature. She underwent breast augmentation surgery with a satisfying result.

Statement of Ethics

Informed consent has been obtained and the work was done according to the declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest that are directly relevant to the content of this case report. No sources of funding were used to assist in the preparation of the manuscript.

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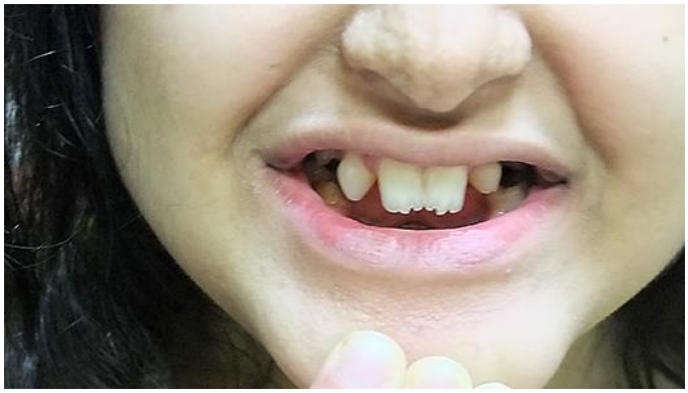

Fig. 1. Malformed teeth with notched and missing upper laterals.

Fig. 2. Hypodontia.

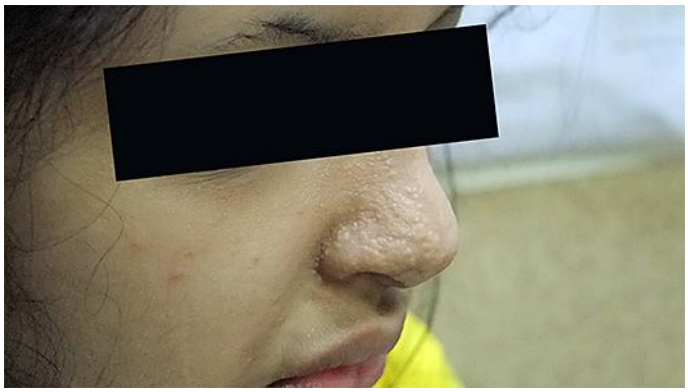

Fig. 3. Multiple skin color papules over the right side of the nose.

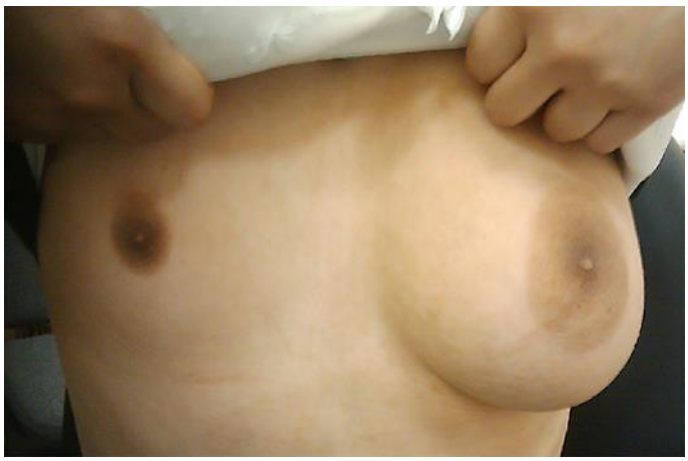

Fig. 4. Hypoplasia of the right breast.

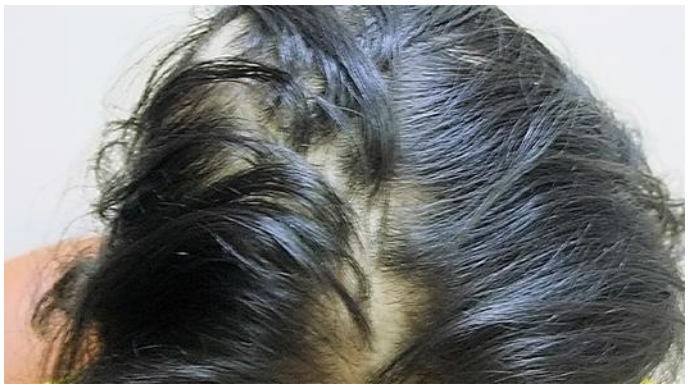

Fig. 5. Multiple patchy areas of cicatricial alopecia were seen over the right side of the scalp.

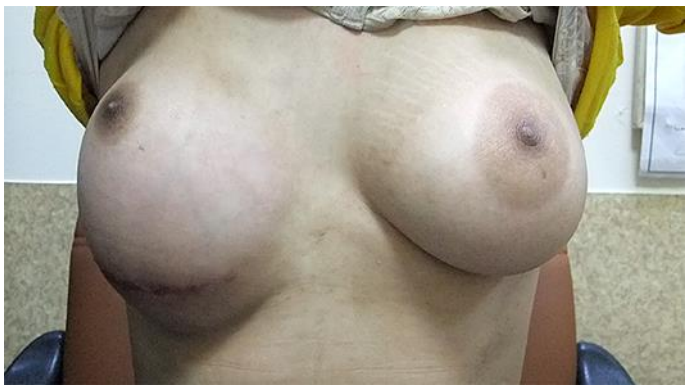

Fig. 6. Breast augmentation surgery.

Table 1. Clinical features of the patients with unilateral or almost unilateral focal dermal hypoplasia

First author	Gender	Involved site	Atrophic skin following the lines of Blaschko	Fat herniation	Scalp lesion	Nail involved	Musculoskeletal involvement	Dental involvement	Ocular involvement	Internal organs involved
Stalder [17]	Male	Right	+	+	–	–	+	–	–	+
Denis-Thely [18]	Female	Right	+	–	+	+	+	+	–	–
Aoyama [19]	Female	Right	+	+	+	–	+	+	+	–
Fernández-Torres [20]	Female	Left	+	+	–	+	–	–	+	–
Tenkir [21]	Female	Left	+	–	+	+	+	+	+	–
Maalouf [22]	Female	Left	+	+	–	–	+	+	–	–
Nakanishi [23]	Female	Right	+	–	–	–	–	–	–	–
Asano [24]	Female	Right	+	–	–	–	+	–	–	–
Lee [16]	Female	Right	+	+	+	–	+	–	–	–
This case	Female	Right	+	–	+	–	–	+	–	–