CASE REPORT

Goltz syndrome: a rare case of father-to-daughter transmission

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Accepted 1 August 2016

SUMMARY

An 8-year-old girl presented to us with skin-coloured to yellowish soft compressible papules, intermixed with hypopigmented and hyperpigmented macules in a Blaschkoid pattern, and 'lobster-claw deformity' affecting her bilateral feet. Additional examination findings included short stature, facial asymmetry, low-set ears, hypodontia, enamel hypoplasia, tonsillar enlargement and spina-bifida occulta at S1–3 vertebral level. A diagnosis of Goltz syndrome was suspected clinically, which was confirmed on skin biopsy. Her father also had hypopigmented and hyperpigmented macules in a Blaschkoid distribution, 'lobster-claw' deformity and kyphoscoliosis. None of the other family members were affected.

BACKGROUND

Goltz syndrome, also known as focal dermal hypoplasia, is characterised by focal ectodermal and mesodermal defects. Since majority reports are on females, it is regarded as a X linked-dominant disorder and lethal in utero for males. We report a father and daughter with Goltz syndrome, and discuss the various hypotheses explaining this extremely rare occurrence.

CASE PRESENTATION

An 8-year-old girl from Nepal, a product of non-consanguineous marriage, was referred to us for the evaluation of her skin lesions and bilateral feet deformity present since birth. Her father also had similar skin lesions and feet abnormality. Other family members, including two male siblings, were unaffected. There was no history of abortions in the mother. General physical examination was significant for short stature (124 cm, <50th centile), 'lobster-claw' deformity affecting the right foot, one missing digit and malformed third and fourth digits of the left foot, facial asymmetry with left mandibular hypoplasia, and low-set ears. There were skin-coloured to yellowish soft compressible papules intermixed with atrophic, slightly depressed hypopigmented and hyperpigmented reticulate macules in a Blaschkoid pattern affecting the left side of the face and scalp, trunk, and both upper and lower limbs asymmetrically. Five café-au-lait macules, each measuring about 1.5 cm, were present on the abdomen. Oral cavity examination showed irregular spacing of teeth, enamel hypoplasia, hypodontia and grade 3 tonsillar enlargement (figure 1A–D). Ocular examination and intelligence was within normal limits. The patient's father also had similar Blaschkoid

hypopigmented and hyperpigmented macules over the trunk and extremities, a 'lobster-claw' affecting his left foot, malformed ears and kyphoscoliosis (figure 2). However, there were no lesions suggestive of fat herniation. Eye, oral, mental and radiological examinations were unremarkable.

INVESTIGATIONS

Skin biopsy from a soft compressible papule on the thigh of the patient showed marked reduction in dermal thickness with replacement of mid-dermis with adipocytes, consistent with the diagnosis of focal dermal hypoplasia (figure 1E). Abdominal ultrasonogram and radiological examination of the long bones were normal, while spina bifida occulta was noted at S1–3 vertebral level. The father refused for a skin biopsy.

DIFFERENTIAL DIAGNOSIS

The most striking finding in our patient was the 'lobster-claw' deformity, also known as ectrodactyly. The differential diagnosis for this distinctive skeletal deformity are quite few, and include ectodermal dysplasias-like ectodermal dysplasia-ectrodactyly-clefting syndrome and ectodermal dysplasia-ectrodactyly-macular dystrophy syndrome, apart from Goltz syndrome. Hypomelanosis of Ito, which presents as hypopigmented macules in a Blaschkoid distribution, may also rarely be associated with ectrodactyly. However, the fat herniation, coupled with Blaschkoid hypopigmentation and hyperpigmentation suggested the diagnosis of Goltz syndrome.

DISCUSSION

Goltz syndrome or focal dermal hypoplasia, a rare genodermatosis affecting all the three embryonic layers, was first described by Goltz *et al*¹ in 1962. Cutaneous manifestations typically follow the lines of Blaschko, and include fat herniations, atrophic hypopigmented or hyperpigmented macules, and papillomas. The nails may be dystrophic and hairs sparse. Skeletal abnormalities include syndactyly, polydactyly, hypoplasia of digits, malformed digits and vertebral defects; 'lobster-claw' deformity is quite characteristic. Other hallmark features are dental anomalies, eye abnormalities and 'osteopathia striata', fine parallel radiopaque lines in the metaphysis of long bones. Abdominal wall defects, diaphragmatic hernias and renal abnormalities have also been reported. Histology is characterised by markedly thinned dermis.^{2 3} The genetic defect has been identified as mutation in *PORCN* gene (Xp11.23).⁴ Approximately 95% cases are

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To cite: Gupta V, Saginatham H, Arava S, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2016-216599

Figure 1 (A) Skin-coloured to yellowish papules in a Blaschkoid pattern affecting the left lower limb; (B) irregular spacing of teeth, hypodontia and enamel hypoplasia; (C) 'lobster-claw' deformity affecting the right foot, missing one digit and malformed third and fourth digits in the left foot; (D) enlarged tonsils reaching the uvula; (E) skin biopsy from a papule on the thigh showing reduced dermal thickness, with replacement of mid-dermis with adipose tissue (H&E, 100×).

Figure 2 (A,B) Depressed hypopigmented and hyperpigmented macules in a Blaschkoid pattern over the trunk and extremities; (C) 'lobster-claw' deformity affecting the left foot.

sporadic. With around 90% patients being females, it is considered to be X linked-dominant and thus lethal in utero for males. However, affected males can survive, and very rarely, transmit the disease to their daughters. We could find only four previous reports of father-to-daughter transmission. Fathers have been described as having a milder phenotype.^{5–8} Interestingly, the manifestations in the father can be so mild that the correct diagnosis was made only when the daughter exhibited typical clinical features of Goltz syndrome.^{7–8} In our case, though the father lacked the fat herniated papules, ocular or dental changes, the Blaschkoid pigmentation coupled with the 'lobster-claw' deformity was fairly characteristic to suspect the diagnosis. Mosaicism may explain not only the survival of males affected by X linked-dominant disorders, but also the difference in phenotypic severity between males and females. If only a subset of the X-chromosomes harbours the causative gene mutation, with the rest being normal, the disease may not be fatal in the hemizygous male. A similar mechanism is operational in females too, where random X-chromosome inactivation

(lyonisation) produces functional mosaicism. This theory is further supported by the presence of Blaschkoid cutaneous lesions, a well-known pattern of cutaneous mosaicism, in Goltz syndrome and also in other X linked-dominant diseases.⁹ Incontinentia pigmenti and Conradi-Hunermann-Happle syndrome are classical examples of X linked-dominant disorders typified by skin lesions in a Blaschkoid pattern; vesicular, verrucous, hyperpigmented or hypopigmented lesions depending on the stage of the disease in the former, and ichthyosis and follicular atrophoderma in the latter. *PORCN* mosaicism has been reported in males with Goltz syndrome.^{4–10} This mosaic state may result from either a postzygotic somatic mutation or a gametic half-chromatid mutation. Mutations in the germline can explain the father-to-daughter transmission.^{6–7} Although a Klinefelter genotype (XXY, 47) could also explain the occurrence of a X linked-dominant disorder in a male,¹¹ this is unlikely in our case as these patients are infertile. Unfortunately, we could not confirm any of these hypotheses for lack of facilities for molecular analysis at our institute.

Learning points

- Goltz syndrome or focal dermal hypoplasia is a rare X linked-dominant genodermatosis, characterised by a variety of cutaneous, skeletal, dental and ocular defects.
- Though considered to be lethal in utero for males, genetic mosaicism can rescue males from this lethal phenotype.
- X-chromosome mosaicism in males may result from gametic half-chromatid mutation or postzygotic somatic mutation.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Goltz RW, Peterson WC, Gorlin RJ, et al. Focal dermal hypoplasia. *Arch Dermatol* 1962;86:708–17.

- 2 Moore DJ, Mallory SB. Goltz syndrome. *Pediatr Dermatol* 1989;6:251–3.
- 3 Mianda SB, Delmaestro D, Bertoli R, *et al.* Focal dermal hypoplasia with exuberant fat herniations and skeletal deformities. *Pediatr Dermatol* 2005;22:420–3.
- 4 Wang X, Reid Sutton V, Omar Peraza-Llanes J, *et al.* Mutations in X-linked PORCN, a putative regulator of Wnt signaling, cause focal dermal hypoplasia. *Nat Genet* 2007;39:836–8.
- 5 Larrègue M, Michel Y, Maroteaux J, *et al.* [Focal dermal hypoplasia; considerations on osteopathia striata and on the genetic problem]. *Ann Dermatol Syphiligr (Paris)* 1971;98:491–500.
- 6 Burgdorf WH, Dick GF, Soderberg MD, *et al.* Focal dermal hypoplasia in a father and daughter. *J Am Acad Dermatol* 1981;4:273–7.
- 7 Mahé A, Couturier J, Mathé C, *et al.* Minimal focal dermal hypoplasia in a man: a case of father-to-daughter transmission. *J Am Acad Dermatol* 1991;25:879–81.
- 8 Gorski JL. Father-to-daughter transmission of focal dermal hypoplasia associated with nonrandom X-inactivation: support for X-linked inheritance and paternal X chromosome mosaicism. *Am J Med Genet* 1991;40:332–7.
- 9 Happle R. The categories of cutaneous mosaicism: a proposed classification. *Am J Med Genet A* 2016;170A:452–9.
- 10 Bornholdt D, Oeffner F, König A, *et al.* PORCN mutations in focal dermal hypoplasia: coping with lethality. *Hum Mutat* 2009;30:E618–628.
- 11 Kunze J, Frenzel UH, Hettig E, *et al.* Klinefelter's syndrome and incontinentia pigmenti Block-Sulzberger. *Hum Genet* 1977;35:237–40.

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