Hong Kong J. Dermatol. Venereol. (2013) **21**, 197-200

Paediatric Dermatology Column: Case Report

Focal dermal hypoplasia (Goltz-Gorlin syndrome): a Chinese case report and review of literature

局灶性真皮發育不良（戈爾茨—格林綜合症）：中國人病例一則及文獻回顧

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A 14-year-old Chinese girl presented with multiple congenital deformities, including linear and whorled hypo/hyperpigmented macules with pink/yellow nodules and plaques which generally followed the Blaschko lines. Asymmetry of the cranium, anonychia and dystrophic nails were also present. Systemic investigation revealed a persistent left superior vena cava and minor degree of pulmonary artery stenosis. The clinical picture and pathologic findings were consistent with focal dermal hypoplasia (FDH). Clinical features, histological features and the research progress of FDH will be discussed.

一名十四歲華裔女孩自幼出現多種先天畸形，包括線狀或旋渦狀沿 Blaschko 線排列的色素減退或色素加深交替的斑片以及粉紅色或黃色結節和斑塊。並有顱骨不對稱，無甲及甲發育異常。系統檢查發現左上腔靜脈殘存及輕度肺動脈狹窄。其臨床表現及病理檢查結果符合局灶眞皮發育不良。本文將討論局灶性眞皮發育不良的臨床表現、組織學特徵及研究的進展。

Keywords: Focal dermal hypoplasia, Goltz-Gorlin syndrome, Blaschko lines

關鍵詞：局灶眞皮發育不良、戈爾茨—格林綜合症、 Blaschko 線

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Introduction

Focal dermal hypoplasia (FDH; OMIM 305600) is a rare X-linked dominant ectomesodermal dysplasia syndrome first described by Goltz et al in 1962,[1] later summarised and reviewed by Gorlin et al. in 1963,[2] is now also known as Goltz-Gorlin syndrome. It is a disease with multi-system symptoms and characterised by patchy dermal hypoplasia along the lines of Blaschko with

deposition or even herniation of subcutaneous fat into the dermis. Other abnormalities include papillomas around the mucocutaneous junction, dystrophic nails, sparse brittle hair and various developmental anomalies of bones, teeth, eyes and head. Management is therefore multidisciplinary. However, patients are frequently undiagnosed or misdiagnosed for a long period resulting in avoidable life-long defects. Two hundred to 300 cases have been previously reported in the literatures with no ethnic or racial predilection.[3] Few Chinese cases in the Chinese or English literature have been reported. We hereby report a case of FDH in a Chinese patient with typical clinical and pathological findings.

Case history

A 14-year-old Chinese girl was born full-term after a normal pregnancy with a birth weight of 2.25 kg. The mother was a dye factory worker who reported no medications taken during pregnancy and there was no history of previous miscarriages. Her parents were non-consanguineous and she had a healthy younger brother. Erythematous, atrophic patches were present at birth with a tendency to break down with weeping. Asymmetry of the cranium, anonychia and dystrophy of the toe nails were also present. Systemic investigations revealed a persistent left superior vena cava and minor degree of pulmonary artery stenosis. The infant was otherwise normal and intellectual development progressed normally with the child's age. With time, some of the easily eroded weeping lesions healed with atrophic scars with new papules erupting in the perioral skin, vestibulum oris and tongue at five years of age. These were confirmed by biopsy to be papillomas. Repeated laser ablations and electric coagulations were performed but the lesions continued to appear.

On examination, there were linear and whorled hypo/hyperpigmented macules with pink/yellow nodules and plaques which generally followed the Blaschko line (Figure 1). Teeth were mal-occluded, malformed and there were linear enamel hypoplasia (Figure 2a). Multiple papillomas were seen on the tongue surface becoming confluent to give a "geographic tongue" appearance (Figure 2b). The skin adnexa, especially nails, were dystrophic or missing (Figure 2c). Biopsy of the pink/yellow nodules revealed decreased thickness of the dermis and extensive replacement by fat tissue (Figure 2d).

Discussion

Focal dermal hypoplasia is a rare syndrome with distinct clinical and pathological features. Similar histopathological changes can only be found in naevus lipomatosus cutaneous superficialis. Diagnosis is made by clinico-pathological correlation. For mild cases, aplasia cutis congenita should be considered in the differential diagnosis because scraping or biopsy may be contraindicated. In contrast to the diversity of FDH, aplasia cutis congenita is often an isolated finding in which the lesions are usually found in the head and are monomorphous. The epidermis, dermis, and fat may all be missing; a single absence of the dermis theoretically exists but is different from "hypoplasia". Linear and whorled nevoid hypermelanosis is another monomorphous disease, although some patients may present with systemic involvement. Denuded hypopigmented lesions, fat herniation and papillomas are absent. In comparison to the evolving lesions of incontinentia pigmenti, the linear and whorled macules of FDH are relatively static. For severe cases with prominent limb deformity, a series of syndromes should be considered in the differential diagnosis. The lobster-claw deformity is present in several autosomal dominant syndromes, but fat herniation is never a feature.[4]

The only gene recognised to cause FDH is *PORCN*, located at Xp11.23 and the inheritance is thought to be X-linked dominant with early intrauterine mortality in males as supported by reports of affected families, in which female-to-female transmission, an increased rate of pregnancy wastage and a decreased male-female ratio have been observed.[5,6] However, the fertility of female patients is markedly reduced.[7] It was estimated that more than 95% of all cases and 100% of all male patients appear de novo as evidenced by the fact that reported male cases have always been the first affected members of their families.[6,8] Father-daughter transmission has occasionally been reported.[7] The affected females are either heterozygous or have somatic mosaicism for a *PORCN* mutation, whereas all affected males have somatic mosaicism for *PORCN* mutations.[6,9]

According to the Lyon hypothesis, one of the two X chromosomes in each embryonic cell is randomly and permanently inactivated (lyonisation) and gives rise to two functionally different cell populations. Rarely there are examples of varying expressions of FDH in as many as four sisters and in at least three generations of female subjects. This is because lyonisation may give rise to three patterns of

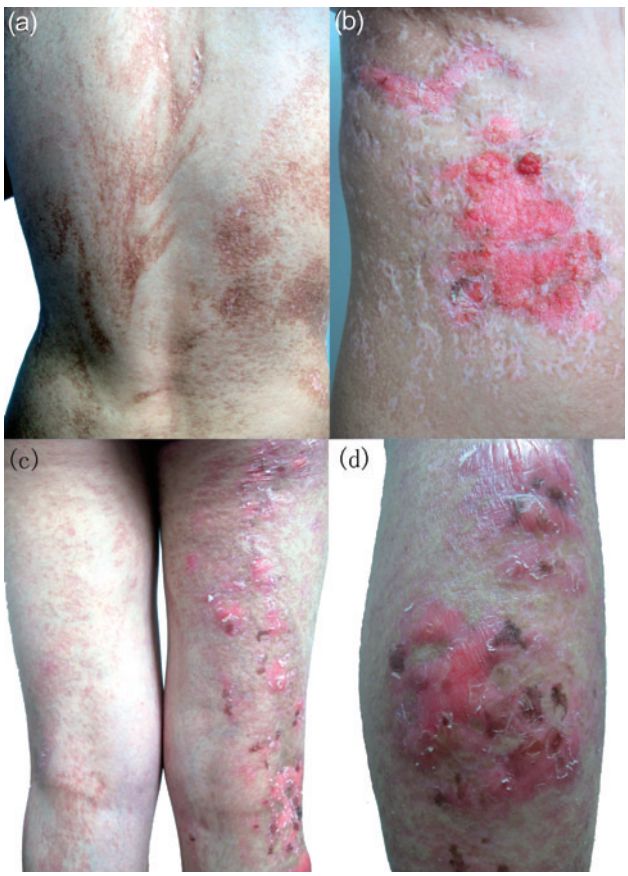

Figure 1. (a) Linear and whorled hypo- or hyper-pigmented macules on the back; (b) pink/yellow nodules and plaques on the right side of the chest; (c) similar lesions on the lower limbs, it is more severe on the right side; (d) a close-up view of the lesions on the right calf.

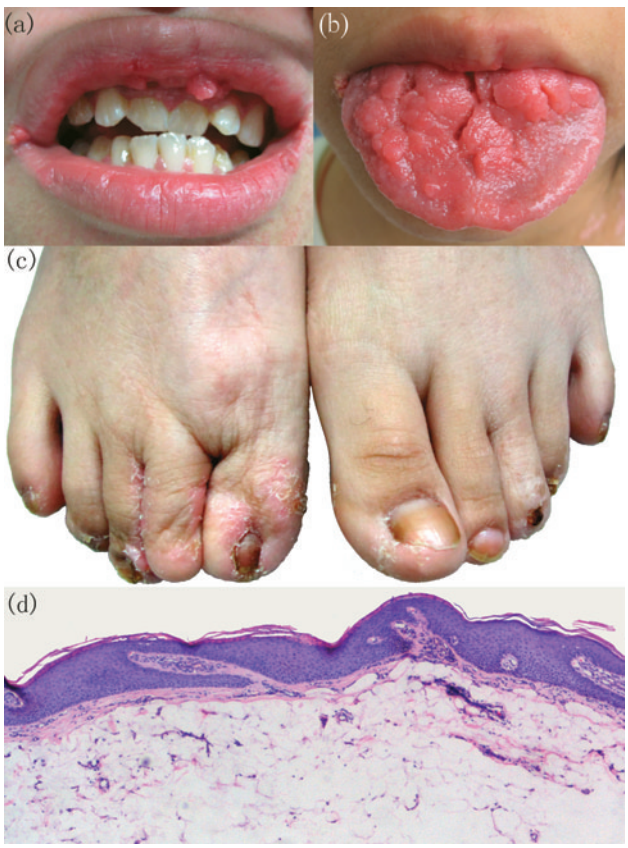

Figure 2. (a) Multiple papillomas in the perioral skin and vestibulum oris; (b) confluence of papillomas on the tongue surface resulting in a 'geographic tongue' appearance; (c) anonychia and toenail dystrophy; (d) diminished thickness of the dermis resulting in fat tissue replacement (haematoxylin and eosin, original magnification x 40).

functional mosaicism: following the Blaschko lines, in a lateralisation pattern or in a checkerboard pattern.[10,11]

Our patient is a sporadic and most probably somatic mosaic case who manifests typical but relatively mild mucocutaneous lesions, dystrophic nails, limb malformations, teeth defects and cardiac involvement. The anomalies were bilateral but more prominent on one side.

The histopathological findings were consistent with FDH. We did not perform amplification and sequence analysis of *PORCN* gene from the peripheral white blood cells because when a *PORCN* mutation occurs post-zygotically in early embryos, the cells with mutated *PORCN* allele may not be present in the blood cells in all cases and we believed that taking fresh tissue from the lesional skin for further confirmation was not necessary.[9]

There is no cure for FDH but appropriate aesthetics, especially dental treatment, is advocated. Some authors have suggested that children should attend their first dental visit as early as possible to prevent the occurrence of dental caries as enamel hypoplasia may make plaque control difficult and skeletal hand anomalies may limit the dexterity needed to conduct proper oral hygiene. During dental procedures, antibiotic prophylaxis against infectious endocarditis should be implemented depending on the type of cardiac septal or valvular defects presented. Uncontrolled observation found that weekly topical application of fluoride varnish might prevent oral papillomas as well as dental caries.[3]

In conclusion, although FDH is not curable, with early diagnosis, proper treatment and consultation, patients' quality of life may be greatly improved.

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