Extensive blaschkoid macules and patches since birth

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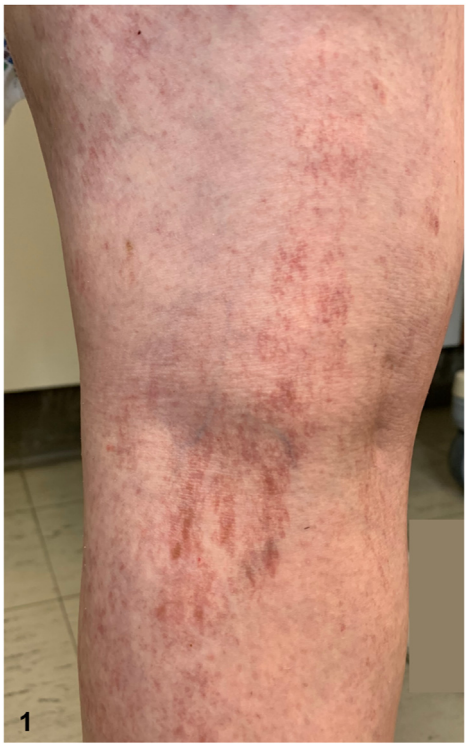

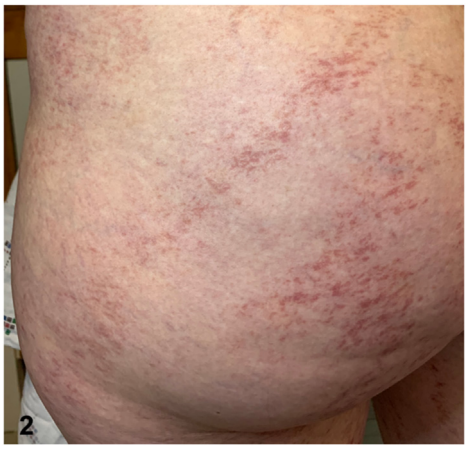

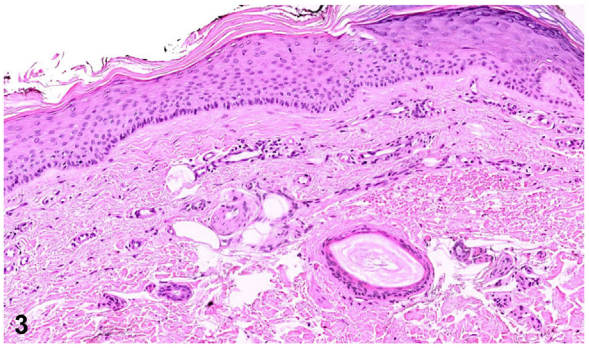

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CASE PRESENTATION

A 35-year-old female presented to clinic for evaluation of a blaschko-linear rash present since birth on her bilateral arms, legs, buttocks, torso, face, and ears (Figs 1 and 2). The lesions were non-blanching, atrophic, and pink-red macules and patches that became more extensive over time. The patient otherwise had no significant medical or relevant family history. She had multiple healthy children. A skin biopsy demonstrated dermal atrophy with adipocytes abnormally located in the superficial dermis, and slightly thickened and dilated blood vessels in the papillary dermis (Fig 3). Whole exome sequencing was performed on the skin biopsy and saliva specimens.

Question 1: Based on the patient's history and histopathologic findings, what is the most likely diagnosis?

A. Blaschkitis

B. Focal dermal hypoplasia (FDH, Goltz syndrome)

C. Incontinentia pigmenti

D. Linear and whorled nevoid hypermelanosis (LWNH)

E. Rothmund-Thomson syndrome (RTS)

Answers:

A. Blaschkitis — Incorrect. Blaschkitis is an acquired inflammatory dermatitis that presents with pruritic papules and vesicles following Blaschko's lines on the trunk and resolves within months.[1] Histology shows features of spongiotic dermatitis. This patient has had these lesions her entire life, making blaschkitis less likely.

B. FDH (Goltz syndrome) — Correct. Skin findings of FDH include pink or red atrophic macules following Blaschko's lines and telangiectasias.[2] Histology reveals reduced dermal thickness and adipocytes interspersed in the upper dermis, as seen in our patient.

C. Incontinentia pigmenti — Incorrect. The skin manifestations of incontinentia pigmenti occur in progressive stages, developing from erythematous and vesicular lesions to verrucous lesions to hyperpigmented plaques to an atrophic, hypopigmented appearance.[2] Skin biopsies during the hyperpigmented stage show dermal melanin incontinence, which was not seen in our patient.[3] During the atrophic stage, there is epidermal hypopigmentation and an absence of eccrine glands.

D. LWNH — Incorrect. While cutaneous findings of FDH are present at birth, the hyperpigmentation of LWNH presents within a few weeks of birth and may progress for 1-2 years.[4] LWNH is not associated with telangiectasias or thinning of the dermis.

E. RTS — Incorrect. The cutaneous manifestations of RTS occur after 3 months of age unlike FDH where lesions are present at birth.[2] Patients with RTS tend to have poikiloderma, a skin condition involving hypopigmentation and hyperpigmentation, atrophy, and telangiectasias.[3] Skin biopsy specimens in RTS show vacuolar interface dermatitis, lymphohistiocytic perivascular inflammation, and dilated vessels.

Question 2: What gene is affected in this disease?

A. Acquired (no known affected gene/multifactorial)

B. *HCCS*

C. *RECQL4*

D. *PORCN*

E. *IKBKG/NEMO*

Answers:

A. Acquired (no known affected gene/multifactorial) — Incorrect. FDH is an X-linked inherited disease, not acquired.[2] Blaschkitis is an acquired inflammatory dermatitis with spontaneous resolution.[1]

B. *HCCS* — Incorrect. While this gene is also located on the X chromosome, mutations in *HCCS* lead to microphthalmia with linear skin defects (MLS) syndrome rather than FDH.[5] Both MLS syndrome and FDH can cause skin defects, but the lesions are restricted to the face and neck in MLS syndrome.

C. *RECQL4* — Incorrect. Mutations in *RECQL4* have been found in patients with RTS.[3]

D. *PORCN* — Correct. FDH is caused by mutations affecting the *PORCN* gene on the X chromosome.[5] The mutation is typically present in a heterozygous or mosaic fashion. The majority of live-born cases are in females, as FDH is associated with male lethality in utero.[2,5] Our patient was found to have a pathogenic mutation in the *PORCN* gene (*PORCN* p.R124X) in both saliva and skin specimens.

E. *IKBKG/NEMO* — Incorrect. Mutations of this gene on the X-chromosome can cause incontinentia pigmenti.[3]

Question 3: What are the most common abnormalities are found in this disease besides skin manifestations?

A. Limb and skeletal malformations

B. Increased cancer risk

C. Cardiac malformations

D. Hematologic abnormalities

E. None, skin manifestations only

Answers:

A. Limb and skeletal malformations — Correct. A variety of limb and skeletal abnormalities can be seen in FDH including syndactyly, split hand/foot malformation, and asymmetry of the face, trunk, or limbs.[2] Other clinical manifestations include ocular anomalies, dental anomalies, craniofacial anomalies, and cognitive impairment.[2,3] Despite having a germline pathogenic mutation, this patient did not exhibit any obvious extracutaneous malformations.

B. Increased cancer risk — Incorrect. FDH is not associated with an increased cancer risk. However, RTS is associated with an increased risk of osteosarcoma, basal cell skin cancer, and squamous cell skin cancer.[3]

C. Cardiac malformations — Incorrect. FDH is not associated with increased cardiac malformations.[2,3]

D. Hematologic abnormalities — Incorrect. FDH is not associated with hematologic abnormalities.[2,3] Fanconi anemia is a hereditary DNA repair disorder that causes bone marrow failure and can cause irregular skin pigmentation.[3]

E. None, skin manifestations only — Incorrect. Although cutaneous abnormalities are the most common manifestation and may be the only feature of the disease present, FDH can also cause defects in the skeletal system, teeth, eyes, and other organs.[2]

Abbreviations used:

FDH: focal dermal hypoplasia
LWNH: linear and whorled nevoid hypermelanosis
MLS: microphthalmia with linear skin defects syndrome
RTS: Rothmund-Thomson syndrome

Conflicts of interest

None disclosed.

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