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Annular Plaques With Skin Atrophy in a Young Patient

Eray Yihui Zhou, MD; Yi Zhao, MD; Zhimiao Lin, MD

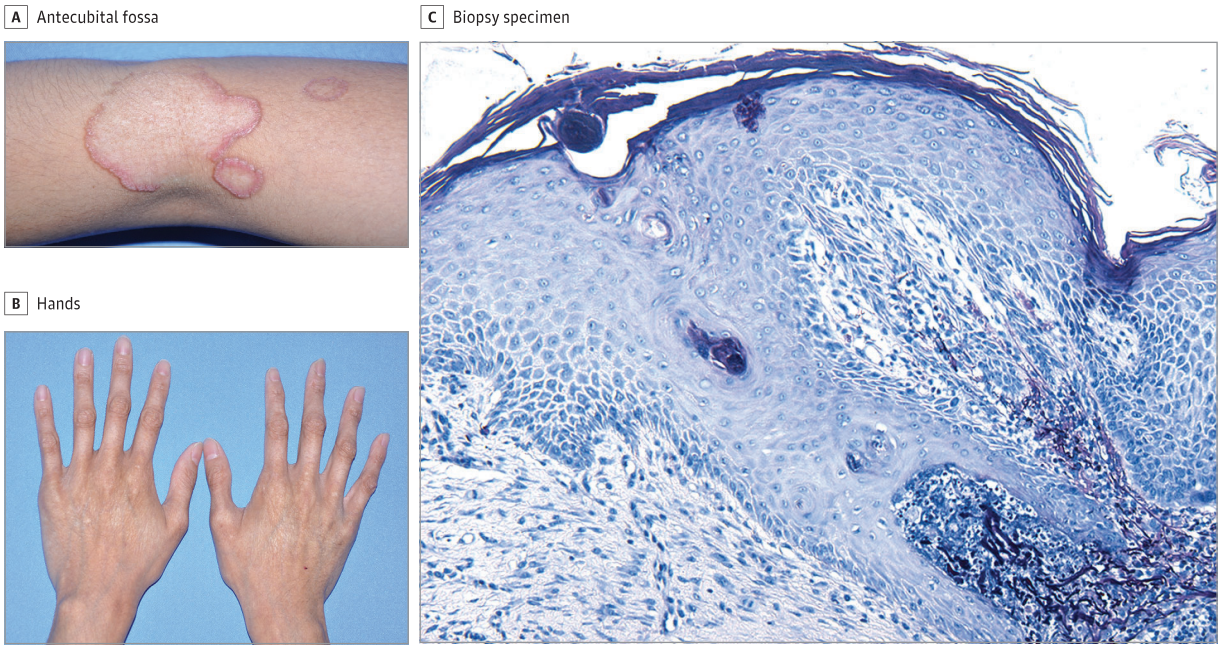

Figure. Clinically, arciform to annular plaques surround white atrophic patches on the left antecubital fossa (A), and skin atrophy is apparent on the dorsal aspects of the hands (B). C, Histopathologically, a punch biopsy specimen from a papule on the left arm was analyzed with Verhoeff–van Gieson stain (original magnification ×100).

A young woman presented with multiple arciform to annular plaques on her extremities, favoring the antecubital and popliteal fossae (**Figure**, A). The patient reported that these asymptomatic lesions had been present since her adolescence, and she was easily bruised with minimal trauma since birth. There was no family history of similar cutaneous findings.

On close inspection, the plaques were found to be composed of individual 2- to 4-mm keratotic papules surrounding white atrophic patches. Physical examination also revealed remarkable skin atrophy on the dorsal aspects of her hands (Figure, B) and feet. The patient's skin was generally pale and translucent with visible veins, especially on the chest and abdomen. The face appeared to be emaciated, with a pinched nose, thin lips, sunken cheeks, and prominent eyes. A punch biopsy specimen from an individual papule from the left arm was obtained and analyzed under Verhoeff–van Gieson stain (Figure, C).

WHAT IS YOUR DIAGNOSIS?

A. Annular elastolytic giant cell granuloma

B. Granuloma annulare

C. Porokeratosis

D. Vascular Ehlers-Danlos syndrome with elastosis perforans serpiginosa

Diagnosis

D. Vascular Ehlers-Danlos syndrome (vEDS) with elastosis perforans serpiginosa

Microscopic Findings and Clinical Course

Histological examination under Verhoeff–van Gieson staining revealed accumulation and transepidermal elimination of elastic fibers, characteristic pathologically of elastosis perforans serpiginosa (EPS). Given the medical history, cutaneous findings, and characteristic facial appearance, a suspicion of vEDS (OMIM 130050) was raised, which was confirmed by detection of a pathogenic missense mutation c.3535G>C (p.G1179R) in the *COL3A1* gene by Sanger sequencing. This mutation was de novo; it was not detected in her parents, which was in accordance with the negative family history. The patient was monitored regularly in local facilities for any vascular and organ complications, and she was advised to avoid collision sports and elective surgery in favor of more conservative management.

Discussion

vEDS (OMIM 130050) is a rare autosomal dominant disorder caused by mutations in the *COL3A1* gene that leads to synthesis of abnormal collagen type III.[1] Collagen type III is widely distributed in skin, blood vessels, pleuroperitoneal linings, and ligaments.[1] In addition to prominent arterial and gastrointestinal complications, patients with vEDS demonstrate characteristic cutaneous findings and facial features, including thin, translucent skin, acrogeria, easy bruising, early-onset varicose veins, thin vermillion of the lips, narrow nose, and prominent eyes.[2] Furthermore, vEDS is associated with other dermatologic disorders, including piezogenic papules and EPS.[3,4]

EPS is a rare skin condition of unknown cause characterized histologically by transepidermal elimination of abnormal elastic fibers. EPS has been reported to be induced by drugs, especially penicillamine. In approximately 25% of cases, an underlying systemic disorder can be detected, particularly connective tissue disorders, including EDS, Marfan syndrome, osteogenesis imperfecta, Down syndrome, and pseudoxanthoma elasticum.[4] In this case, the skin findings and facial features coexistent with typical EPS manifestations suggested the diagnosis of vEDS, which was confirmed by genetic testing.

The clinical severity of vEDS is associated with the types and locations of variants in *COL3A1*. A variant that results in a substitution for a triple helical glycine residue by a larger residue is more likely to cause a severe vEDS phenotype than variants resulting in haplo insufficiency or nonglycine missense variants located in the C- or N-terminal regions of the protein.[5,6] The G1179R glycine substitution mutation detected in our patient was predicted to result in a severe vEDS phenotype, consistent with a previous report of this mutation elsewhere.[7]

The diagnosis of vEDS carries with it the life-threatening risks of vascular and organ rupture leading to sudden death. In a French cohort of 215 individuals with vEDS, the median age at the first major vascular, digestive, or obstetrical complication was 29 years.[5] Therefore, a close surveillance of major complications is encouraged in patients with vEDS. The patient described herein was advised to undertake blood pressure monitoring and periodic noninvasive imaging of the arterial vasculature.

ARTICLE INFORMATION

Author Affiliations: Department of Dermatology, Peking University First Hospital, Beijing, China (Zhou, Lin); Department of Dermatology, Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China (Zhou, Zhao).

Corresponding Author: Zhimiao Lin, MD, Department of Dermatology, Peking University First Hospital, 8 Xishiku St, Beijing 100034, China (zhimiaolin@bjmu.edu.cn).

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