# An Amish boy with recurrent ulcerations of the lower extremities, telangiectases of the hands, and chronic lung disease

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## CASE SUMMARY

### History

A 6-year-old white boy of Amish ancestry with chronic lower extremity ulcers was seen in the dermatology clinic at the National Institutes of Health (NIH) Clinical Center in Bethesda, MD. Since the age of 2 years, the patient had experienced numerous deep ulcers on the thighs, legs, and feet that developed without preceding trauma. His wounds typically healed slowly leaving depressed atrophic scars. At the time of presentation, the patient had ulcers limited to the soles of both feet and difficulty ambulating because of associated pain. The ulcers on the left sole had been present for 9 months. His parents reported frequent epistaxis and easy bruising. At age 4 years, the patient underwent splenectomy for thrombocytopenia and was found to have esophageal varices and cirrhosis. He also had pulmonary hypertension, recurrent pneumonias with bronchiectasis, recurrent otitis media, and chronic sinusitis. At the time of evaluation, the patient required 3 L/min of continuous oxygen via nasal canula.

*Abbreviations used:*

HIES: hyper-IgE syndrome
NIH: National Institutes of Health
*PEPD*: peptidase D

The patient's parents were second cousins. Several family members had experienced similar medical problems: his older brother died at 13 months of age of respiratory failure with history of leg ulcers and recurrent infections; a paternal cousin also died at 13 months of age with recurrent infections, chronic lung disease, and pulmonary hypertension; and a living maternal cousin had leg ulcers and recurrent infections. The patient had 3 healthy siblings. He shared a common ancestry with an Amish kindred several generations earlier who exhibited similar physical findings.

### Physical examination

The patient was a white boy appearing smaller than stated age with hypertelorism and a depressed nasal root. On the left foot there were two deep ulcers with irregular borders and yellow adherent material on the heel and side mid aspect of sole (Fig 1). The plantar surface of the right foot had multiple smaller ulcers. The ulcerated areas were tender to palpation and prevented normal ambulation. Multiple well-healed depressed scars were present on both soles. Numerous 1- to 3-cm ovoid depressed, atrophic scars were observed on the side and front aspects of the thighs (Fig 2). A few scattered telangiectatic vessels were noted on the back of the feet and front of thighs. More pronounced densities of telangiectatic vessels were present on the palmar

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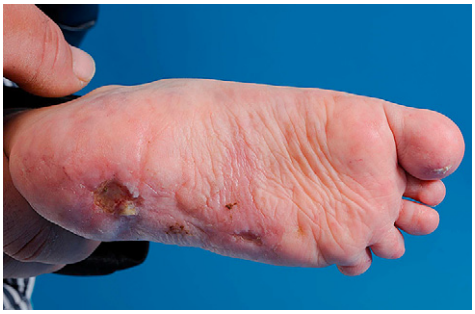

**Fig 1.** Irregularly shaped ulcers with necrotic debris in variable stages of healing on plantar foot with atrophic depressed scars and telangiectatic vessels.

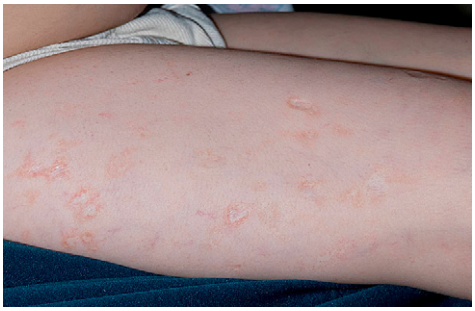

**Fig 2.** Multiple atrophic, depressed, porcelain-white scars on front and side of right thigh.

and back surfaces of both hands (Fig 3). There was marked clubbing of all fingers. Oral examination revealed normal mucosa with absence of multiple teeth. The abdomen was distended with a large well-healed surgical scar on the right upper quadrant.

### Significant diagnostic studies

Notable laboratory results performed at the time of the patient's admission to the NIH included increased white blood cells (41.83 K/$\mu$L) with neutrophilia (87.6%) and increased platelet count (810 K/$\mu$L). These hematologic abnormalities were related to his prior splenectomy. He had elevated IgA (306 mg/dL), IgG (2320 mg/dL), and IgE (3065 IU/mL) levels but a normal IgM level (138 mg/dL). Prothrombin time/partial thromboplastin time and routine urinalysis revealed unremarkable findings.

DNA mutation analysis from cord blood at birth indicated a single nucleotide nonsense mutation of the peptidase D* (*PEPD*) gene resulting in a premature stop codon.

*The nonsense mutation of *PEPD* in this Amish patient with prolidase deficiency and his kindred was previously reported by Wang et al.[8]

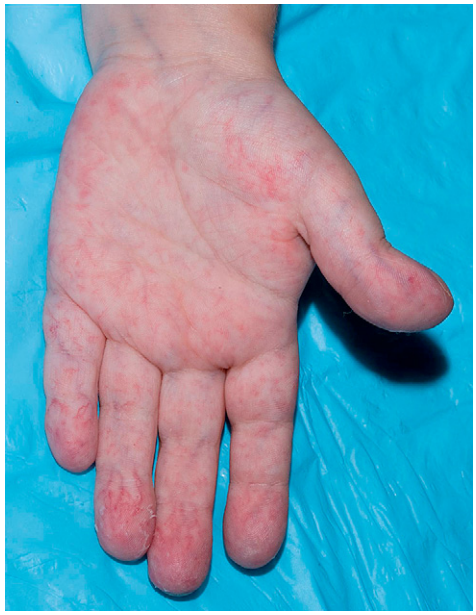

**Fig 3.** Numerous telangiectatic vessels on ventral aspect of palms and fingers with clubbing of distal fingers. Similar telangiectases were present on back aspect of fingers.

### Diagnosis

Prolidase deficiency.

## DISCUSSION

Prolidase deficiency is a rare autosomal-recessive inborn error of amino acid metabolism that results from mutation of the human prolidase gene *PEPD* on chromosome 19q12-q13.2. To date, at least 13 mutations of *PEPD* have been described.[1] Prolidase is a ubiquitous metalloenzyme involved in the catabolism of dietary and endogenous proteins, especially imino acid–rich proteins such as collagen. Prolidase is important for supplying and recycling proline for protein synthesis and cellular growth through hydrolysis of iminopeptides with C-terminal proline or hydroxyproline.[2,3]

Patients with prolidase deficiency have high circulating levels of iminopeptides containing a C-terminal proline with resultant urinary excretion of these iminopeptides. The first description of prolidase deficiency was by Goodman et al[2] in 1968. The clinical characteristics were further defined by Powell et al[4] in 1974 with the report of absent prolidase in association with the characteristic clinical features of prolidase deficiency. Approximately 60 cases have now been described in the literature.[5]

The range in clinical features observed with prolidase deficiency varies from no obvious clinical abnormalities to a constellation of recurrent infections, chronic leg ulcers, characteristic facies, mental