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X-Linked Ichthyosis

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A 78-year-old man with a history of multiple nonmelanoma skin cancers presented for a skin examination. In addition to his skin cancer concerns, the patient reported mild diffuse “scaling” of the bilateral forearms, bilateral legs, and back with associated pruritus that has been present “since as long as [he] can remember.” He noted that his condition improves greatly when exposed to sunlight and after bouts of sweating following athletic activity, and that it worsens during the winter. There was a family history of a similar rash in many male family members (**Figure 1**).

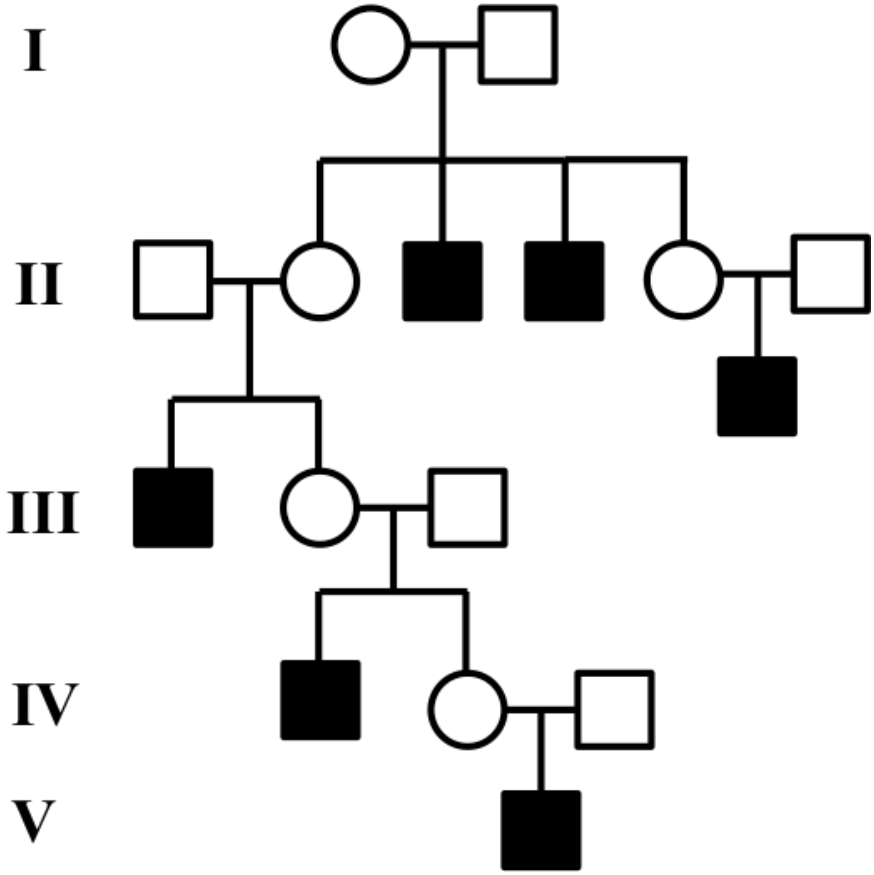

Figure 1. *Pedigree showing inheritance of possible cases of X-linked ichthyosis in the patient's family. Of note, these are not genetically confirmed cases, but rather the shading indicates individuals with presentations similar to the patient's own condition, per his report. The patient described in this case report can be found at III.1.*

In 1961, at age 21, with consideration of his clinical presentation and his remarkable family history, he was given a provisional diagnosis of "ichthyosis," not otherwise specified. Currently, he uses ammonium lactate cream, 12%, daily on affected areas, and he has noticed mild improvement of his condition and symptoms.

Physical examination revealed areas of an eczematous rash with overlying wafer-like, slightly hyperpigmented scale covering the entire surface of the back (**Figures 2 and 3**). There was a similar but milder appearing rash involving the arms and legs, and there was notable sparing of the antecubital fossae, popliteal fossae, face, palms, and soles.

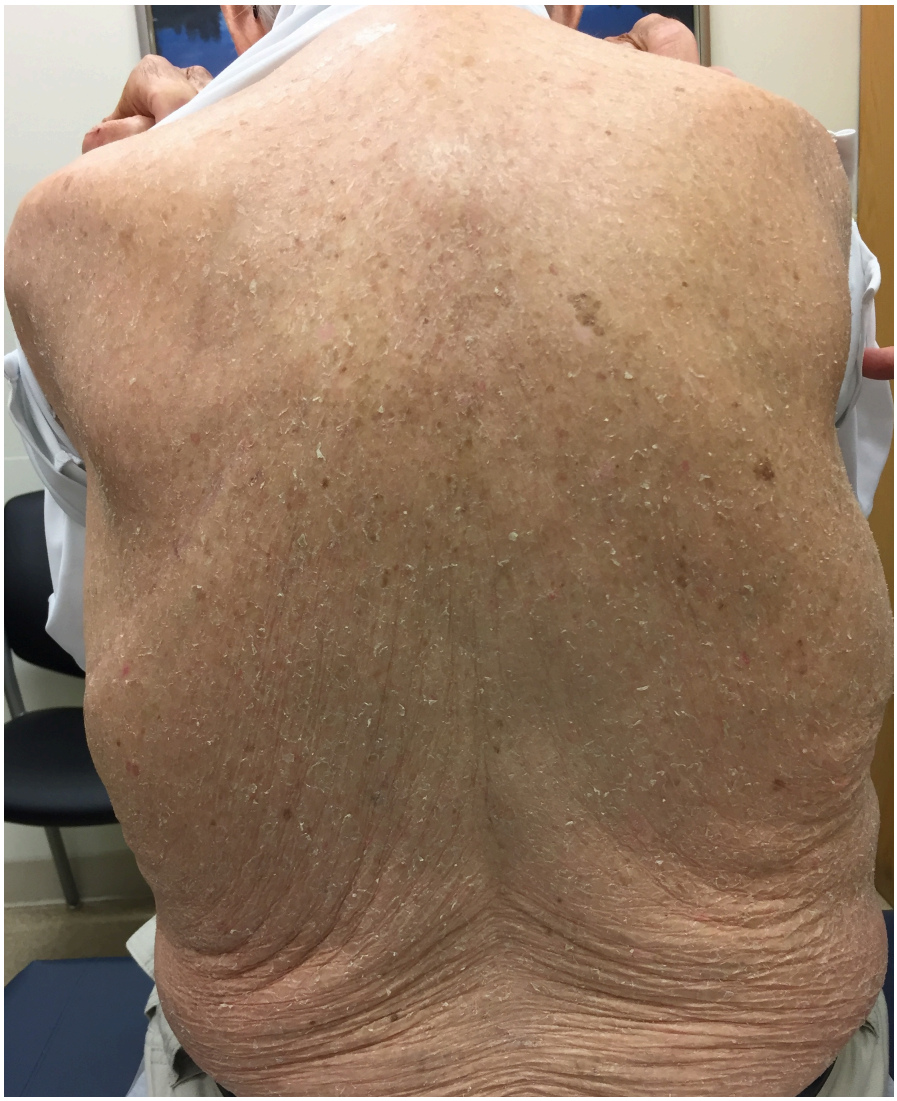

Figure 2. *The patient's back demonstrating copious superficial scaling.*

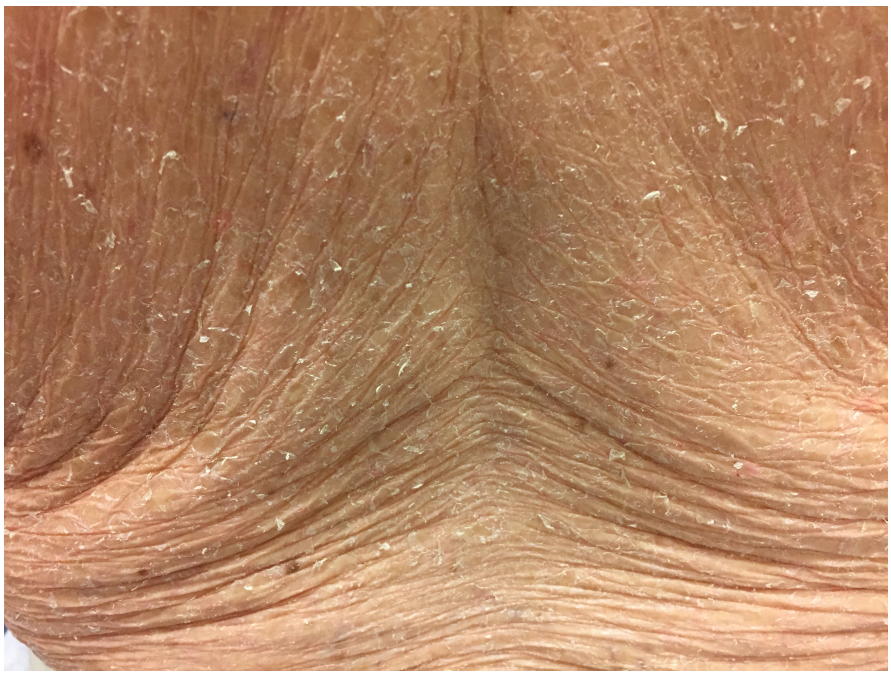

Figure 3. *Higher-detail image of the patient's back demonstrating the characteristic wafer scale of X-linked ichthyosis.*

This patient's history and physical examination findings were consistent with a diagnosis of X-linked ichthyosis (XLI). He was instructed to continue using ammonium lactate cream, 12%, as needed in order to reduce the scaling.

DISCUSSION

First recognized in 1966, XLI describes an inherited disorder affecting up to 1 in 2000 males with a characteristic darkened, polygonal scale present primarily on the trunk and extremities.1

XLI is caused by a deficiency in the protein steroid sulfatase (STS), which stems from deletion or mutation of the steroid sulfatase gene.2,3 STS is highly active in the stratum granulosum and corneum of the epidermis, where it plays a role in desquamation and regulation of permeability. Deficiency of STS results in increased corneocyte adhesion with subsequent thickening of the stratum corneum and decreased permeability.4

XLI begins to manifest in the first weeks of life with mild, diffuse scaling. As the child ages, the characteristic signs of XLI become more apparent with larger brown or even gray scaling on the trunk, extremities, and neck with distinct sparing of flexural regions such as the antecubital and popliteal fossae. Often telling is the presence of exclusively male family members, which might suggest the X-linked inheritance of XLI.1 Known historical associations with XLI include maternal failure to progress during labor and cryptorchid testes, noted in 36% and 28% of patients, respectively, in one study.5

XLI may be confused clinically with other underlying conditions, including the most common type of ichthyosis, autosomal dominant ichthyosis vulgaris, as well as atopic dermatitis (AD). However, the patterning and quality of scale of affected areas, combined with the patient's history and physical examination findings, aid in differentiating these entities. Marked sparing of the flexural areas, such as the antecubital and popliteal fossae in our patient, can suggest XLI over the typical lichenified, scaling plaques often seen in this location in patients with AD.1

Atopic dermatitis in infancy can look similar to XLI with diffuse scale, however atopic dermatitis has been shown to clear in 74% of children by age 16.2 Our patient's report of only male members of his family having similar conditions would make autosomal dominant ichthyosis vulgaris unlikely due to its established autosomal dominant inheritance.1 With regard to scale quality, our patient presented with classic wafer scale, which is seen in approximately 70% of persons with XLI.3-7

Topical therapies include daily use of emollients, such as petrolatum, and keratolytic agents, such as urea-containing products or lactic acid. In patients aged 1 to 16 with moderate disease, twice daily application of 10% urea lotion over an 8-week treatment course achieved a 65% response rate at 4 weeks and 78% response at 8 weeks. Interestingly, urea-free lotion achieved

similar response rates of 50% and 72% at 4 and 8 weeks, respectively.8

Other topical alternatives include lactic acid for mild disease and even short 3-day courses of topical salicylic acid, 2%, applied to limited areas can aid in severe disease flares.9 Salicylic acid aids in thinning the thickened stratum corneum, thereby eliminating scale and allowing further penetration of emollients and humectants. Oral retinoids, such as acitretin, through their antikeratinizing properties and modulation of keratinocyte proliferation and differentiation can aid in this disease, although long-term management is limited due to adverse effects such as hyperlipidemia, elevated liver enzymes, and hyperostosis.9

References

1. Richard G, Ringpfeil F. Ichthyoses, erythrokeratodermas and related disorders. In: Bolognia JL, Jorizzo JL, Schaffer JV, eds. *Dermatology.* Vol 3rd ed. Philadelphia, PA: Elsevier Saunders; 2012:chap 57.
2. Williams HC, Strachan DP. The natural history of childhood eczema: observations from the British 1958 birth cohort study. *Br J Dermatol.* 1998;139(5):834-839.
3. Cañueto J, Ciria S, Hernández-Martín A, Unamuno P, González-Sarmiento R. Analysis of the *STS* gene in 40 patients with recessive X-linked ichthyosis: a high frequency of partial deletions in a Spanish population. *J Eur Acad Dermatol Venereol.* 2010;24(10):1226-1229.
4. Alperin ES, Shapiro LJ. Characterization of point mutations in patients with X-linked ichthyosis: effects on the structure and function of the steroid sulfatase protein. *J Biol Chem.* 1997;272(33):20756-20763.
5. Traupe H, Happle R. Clinical spectrum of steroid sulfatase deficiency: X-linked recessive ichthyosis, birth complications and cryptorchidism. *Eur J Pediatr.* 1983;140(1):19-21.
6. Elias PM, Williams ML, Maloney ME, et al. Stratum corneum lipids in disorders of cornification. Steroid sulfatase and cholesterol sulfate in normal desquamation and the pathogenesis of recessive X-linked ichthyosis. *J Clin Invest.* 1984;74(4):1414-1421.
7. Hand JL, Runke CK, Hodge JC. The phenotype spectrum of X-linked ichthyosis identified by chromosomal microarray. *J Am Acad Dermatol.* 2015;72(4):617-62
8. Küster W, Bohnsack K, Rippke F, Upmeyer H-J, Groll S, Traupe H. Efficacy of urea therapy in children with ichthyosis: a multicenter randomized, placebo-controlled, double-blind, semilateral study. *Dermatology.* 1998;196(2):217-222.
9. Oji V, Traupe H. Ichthyosis: clinical manifestations and practical treatment options. *Am J Clin Dermatol.* 2009;10(6):351-364.