Coalescing Hyperkeratotic Plaques and Papules

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A 67-year-old man with a history of congestive heart failure, type 2 diabetes mellitus, hypertension, and schizophrenia was admitted to the hospital for subarachnoid hemorrhage and was noted to have heavy scaling on the bilateral legs. Given recent medical events, the patient was nonconversant at the time of consultation, but his daughter provided his medical history at bedside. The patient usually wore long-sleeved clothing and pants, thus no one had seen his skin in many years, and it was unclear how long the scaling had been present. His family history was notable for eczema in distant relatives but negative for comparable conditions. Physical examination revealed thick lichenified skin with many large, exophytic, brown papules (largest measured 1.5×1×1 cm) and platelike scaling on the anterior chest, abdomen, lateral arms, and forearms. Extensive coalescing hyperkeratotic plaques and papules (up to 1 cm in thickness) were present on the anterior legs and feet, and scattered verrucous brown papules were noted on the plantar aspects of the bilateral feet. A punch biopsy of the left foot revealed extensive, dense, compact, orthokeratotic hyperkeratosis with a preserved granular layer with no epidermolysis.

WHAT'S THE **DIAGNOSIS?**

a. ichthyosis bullosa of Siemens
b. ichthyosis vulgaris
c. lamellar ichthyosis
d. rupioid psoriasis
e. X-linked ichthyosis

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The authors report no conflict of interest.

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THE **DIAGNOSIS:** X-Linked Ichthyosis

Immunohistochemical staining of a punch biopsy specimen from the left foot with cytokeratin markers AE1/3, 5/6, and 19 showed normal positive uptake. Further workup was recommended, and the patient was referred to genetics for an ichthyosis gene panel. DNA sequencing revealed a c.1121G>A transition in exon 10 of the steroid sulfatase gene, *STS*, consistent with X-linked ichthyosis (XLI).

X-linked ichthyosis, also known as steroid sulfatase deficiency and X-linked recessive ichthyosis, is a congenital skin disorder classified in 1965 by Wells and Kerr.[1] Ichthyoses are a heterogenous group of acquired and congenital disorders of keratinization that manifest with xerosis, hyperkeratosis, and scaling.[2] Of more than 20 ichthyoses, XLI is the second most common ichthyosis, with a prevalence of 1 in 6000 males.[3] X-linked ichthyosis occurs almost exclusively in males, and although females can be carriers, they rarely exhibit skin manifestations.[4]

X-linked ichthyosis is caused by either a partial or full deletion or mutation in the *STS* gene on the X chromosome.[2] The absence of *STS* activity results in the accumulation of cholesterol sulfate in the stratum corneum, leading to corneocyte cohesion, hyperkeratosis, and impaired skin permeability. The most common clinical phenotype is characterized by polygonal scales concentrated on the upper and lower extremities as well as the trunk (Figure), consistent with our patient's clinical presentation.[5]

X-linked ichthyosis typically presents in the first 6 months of life as generalized desquamation and xerosis that progresses to fine scaling on the trunk and extremities, more commonly and heavily involving the legs; however, the extensor surfaces of the arms also may be affected.[6] After the neonatal period, fine scaling persists on the trunk and extremities, but scales often become coarser and darker over time. Although scaling is generalized, it typically spares the antecubital and popliteal fossae, palms, soles, and midface. The lateral face, axillae, and neck always remain involved.[4] The most common extracutaneous manifestations of XLI affect the ocular, genitourinary, and cognitive/behavioral systems. Patients can develop corneal comma-shaped opacities, hypogonadism, cryptorchidism, and an increased risk for testicular cancer. Female carriers may have prolonged delivery of affected neonates.[2,5,7-9] Given the unrelated debilitating neurologic consequences of our patient's presenting subarachnoid hemorrhage, further workup was not pursued into these associations.

Although XLI is most commonly diagnosed in early childhood, it also must be considered in adult patients presenting with severe scaling of the trunk, arms, and legs who have not had prior dermatologic workup.

X-linked ichthyosis with platelike scaling and lichenified skin over the anterior knees (A) as well as large exophytic papules on the upper chest and neck (B).

Given the similarity of XLI presentation to other ichthyoses, particularly ichthyosis vulgaris, lamellar ichthyosis, and ichthyosis bullosa of Siemens, genetic analysis is the most accurate diagnostic tool and should be considered in patients with an atypical presentation. Rupioid psoriasis also may be considered and can be confirmed on biopsy. Diagnosis of XLI should prompt symptomatic treatment, genetic counseling, and workup for extracutaneous manifestations.

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