Delayed diagnosis of a scaling genodermatosis

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Accepted 25 April 2023

DESCRIPTION

A man in his early 60s presented to the dermatology clinic with a lifelong history of dry, scaling skin. He had congenital deafness but no other medical problems. He had received a diagnosis of ichthyosis vulgaris several years ago and was treating the condition with topical emollients. Further questioning confirmed a positive family history; his maternal grandfather had been affected with the same skin changes, whilst his mother was reported to have had a milder presentation, with scale only affecting the shins. He has no brothers and one unaffected sister. He has no offspring.

On examination, there was polygonal brown scaling affecting all four limbs; with involvement of the trunk including the neck. Palms were not affected with no hyperlinearity of the palmer creases. The flexures were spared and hair and nail examination were unremarkable (figure 1A–C).

Given the family history and clinical findings, X-linked ichthyosis (XLI) was suspected, and a steroid sulfatase (STS) level requested. This was markedly low at 2.5 pmol/mg/hour consistent with a biochemical diagnosis of XLI. Subsequently genetic testing involving targeted microarray analysis demonstrated a 1.6 Mb interstitial deletion of the short arm of the X chromosome within band p22.31. This loss included the STS gene confirming the diagnosis of XLI.

He was referred to ophthalmology to assess for associated ophthalmic complications and was noted to have corneal guttata. There had been no history of cryptorchidism. He had no neurological disability or psychiatric issues. He was subsequently commenced on acitretin 10 mg daily and achieved an excellent response to treatment.

XLI was identified as a unique entity affecting only males in 1965 by Wells and Kerr.[1] It affects approximately 1:6000 males[2] and represents an inborn error of metabolism associated with a deficiency of the enzyme STS. Ninety per cent have a complete STS gene deletion, while 10% have a partial deletion or point mutation. Contiguous defects can occur when there are deletions of neighbouring genes. STS deficiency results in impaired hydrolysis of cholesterol sulfate and dehydroepiandrosterone sulfate, with resultant accumulation of cholesterol 3-sulfate in the epidermis. High levels of this metabolite can inhibit transglutaminase-1, which explains the partial overlap with lamellar ichthyosis.[3]

Typical presentation is with desquamation and erythema in the first year of life. There may be failure of progression of labour due to low or absent placental oestrogen. Later in childhood a symmetrical polygonal brownish scale becomes apparent on the limbs, neck and trunk. Flexures are usually spared. Scaling typically continues into later life. Palms are not hyperlinear distinguishing XLI from ichthyosis vulgaris. Infants do not present with a collodian membrane unlike lamellar ichthyosis.

Associations include cryptorchidism in up to 20%, asymptomatic corneal opacites and attention deficit hyperactivity disorder.[4] Rodrigo-Nicolás *et al* reviewed 30 patients with XLI and observed that 13% had epilepsy and 30% had an ADHD diagnosis.[5] There is also emerging evidence of an association between XLI and development of atrial fibrillation/flutter in middle age,[6] as well as Dupuytren's contracture. Post operative bleeding complications are reported to occur in 3.5% of those carrying the deletion verses 0.5% of non-carriers.[7]

Distinguishing the clinical variant of ichthyosis can be challenging, particularly when the patient presents later in life such as in this case. It highlights the importance of eliciting family history in reaching the correct diagnosis. Differential diagnoses of XLI include ichthyosis vulgaris, lamellar ichthyosis and even asteatotic eczema but careful history and examination can provide vital clues, prompting appropriate investigations.

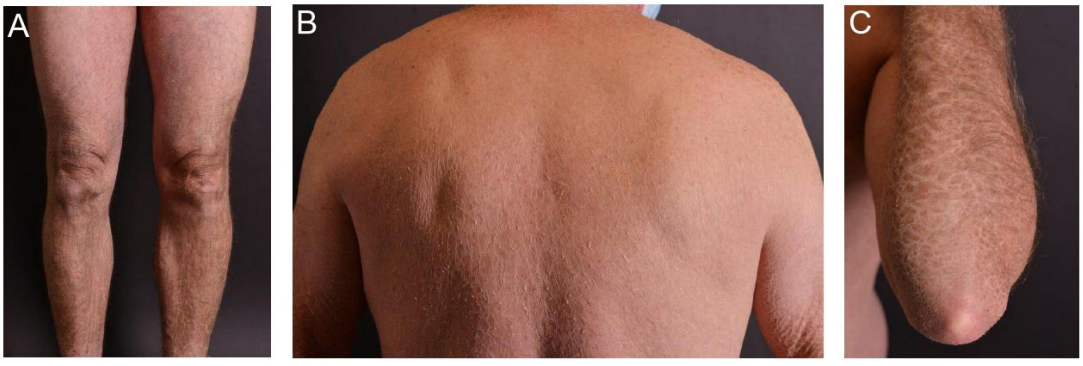

Figure 1 (A) Polygonal scale on the lower legs. (B) Scale on the back. (C) Scale on the extensor aspect of the arms.

To cite: Harnett C, Al-Jubouri M, Meah N. *BMJ Case Rep* 2023;**16**:e253838. doi:10.1136/bcr-2022-253838

Learning points

- X-linked ichthyosis is caused by deficiency of the enzyme steroid sulfatase (STS). There is either a complete or partial deletion of the STS gene, which is located on the X-chromosome on genetic analysis.
- This case highlights the importance of taking a family history when assessing a patient presenting with ichthyosis due to the potential extracutaneous health consequences for the patient and their offspring.

Contributors This report was written by the corresponding author CH. The report writing was supervised and then edited by NM. The case/diagnosis was discussed with MA-J and the subsequent written report reviewed by this contributor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Consent obtained directly from patient(s).

Provenance and peer review Not commissioned; externally peer reviewed.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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REFERENCES

1 Wells RS, Kerr CB. Genetic classification of ichthyosis. *Arch Dermatol* 1965;92:1–6.
2 Hernández-Martín A, González-Sarmiento R, De Unamuno P. X-Linked ichthyosis: an update. *Br J Dermatol* 1999;141:617–27.
3 Richard G, Ringpfeil F. Ichthyoses, erythrokeratodermas and related disorders. In: Bolognia JL, Schaffer JV, Cerroni L, eds. *Dermatology*. Philadelphia: Elsevier, 2017: 894–7.
4 Traupe H, Fischer J, Oji V. Nonsyndromic types of ichthyoses-an update. *JDDG: Journal Der Deutschen Dermatologischen Gesellschaft* 2014;12:109–21. 10.1111/ddg.12229 Available: http://doi.wiley.com/10.1111/ddg.2014.12.issue-2
5 Rodrigo-Nicolás B, Bueno-Martínez E, Martín-Santiago A, *et al*. Evidence of the high prevalence of neurological disorders in nonsyndromic X-linked recessive ichthyosis: a retrospective case series. *Br J Dermatol* 2018;179:933–9.
6 Brcic L, Underwood JF, Kendall KM, *et al*. Medical and neurobehavioural phenotypes in carriers of X-linked ichthyosis-associated genetic deletions in the UK Biobank. *J Med Genet* 2020;57:692–8.
7 Brcic L, Wren GH, Underwood JFG, *et al*. Comorbid medical issues in X-linked ichthyosis. *JID Innov* 2022;2:100109.