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Multiple Xanthoma Tuberosum in a Case of Familial Homozygous Hypercholesterolemia

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Key words: xanthoma, familial, hypercholesterolemia, LDL

A 15-year-old, Indian, female child of a second-degree consanguineous marriage, presented with polymorphic yellowish-brown nodular cutaneous lesions over the dorsal aspect of both elbows, knees (Figure 1A) and buttocks (Figure 1B). These were suggestive of xanthoma tuberosum and were first noted at 4 years old. There were no spots over the eyelids, acanthosis, skin tags or tendon xanthomas. Arcus juvenilis was not noted. A bilateral carotid bruit was appreciated. Her father and mother also have hypercholesterolemia and were receiving atorvastatin.

Her lipid profile showed total cholesterol: 790 mg/dL, LDL-C: 736 mg/dL, HDL-C: 34 mg/dL, VLDL-C: 124 mg/dL and triglyceride: 102 mg/dL. There was also increased carotid intima media thickness on doppler and severe aortic stenosis and normal Ejection fraction of 62% on echocardiogram.

Genomic studies revealed homozygous mutation in both alleles of the LDL-R gene, associated with autosomal dominant Familial Hypercholesterolemia. The 737-position arginine (R) was also changed. This change, previously reported by Mozas et al., in a Spanish patient,[1] was not present in genomic databases reviewed as of writing.

The patient was subsequently diagnosed with Homozygous Familial Hypercholesterolemia using the Simon Broome Register criteria.[2] Diet modification, atorvastatin and ezetimibe were started, followed by subcutaneous evolocumab. After 6-8 weeks of therapy with atorvastatin, ezetimibe and evolocumab, her cholesterol levels were markedly reduced by 82 and 89%, respectively. However, the patient discontinued the use of evolocumab due to financial constraints.

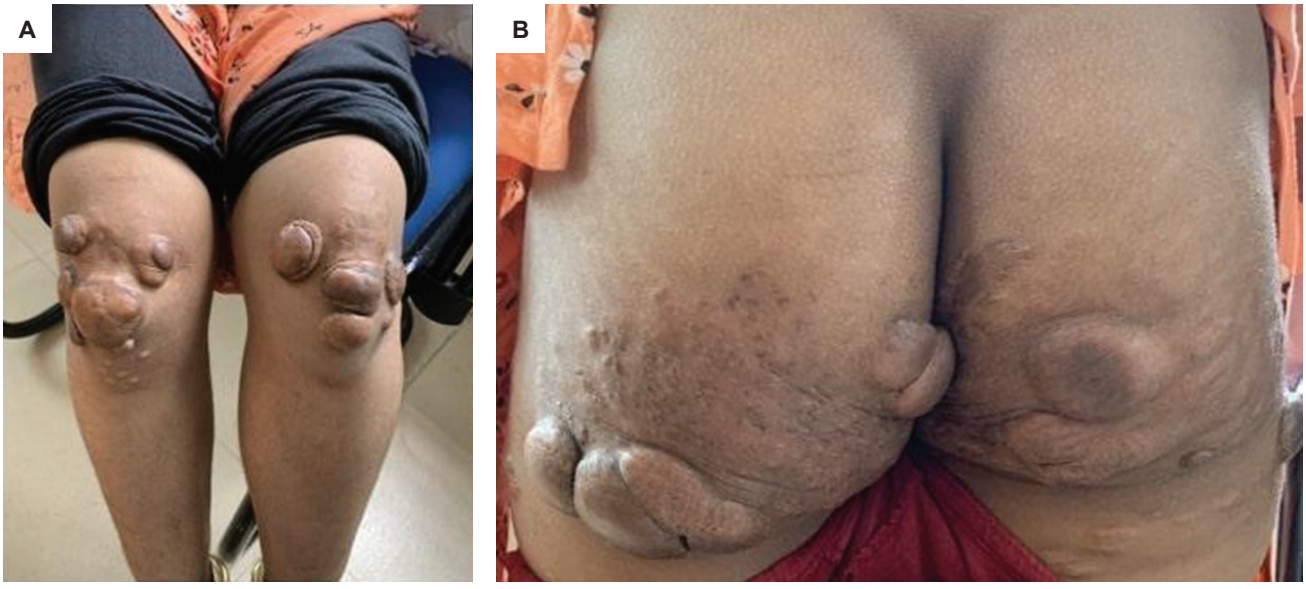

Figure 1. Large tuberous xanthomas on both knees **(A)** and buttocks **(B)**.

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Homozygous familial hypercholesterolemia is a disorder of lipoprotein metabolism from mutations in the low-density lipoprotein receptor (LDLR) gene,[3] which manifests as xanthomas.[4]

Guidelines for dyslipidaemia recommend high intensity statin treatment at 6-10 years of age, with healthy lifestyle measures and use of PCSK-9 inhibitors for children with homozygous familial hypercholesterolemia. Goals for children >10 years of age are LDL-C <3.5 mmol/l (135 mg/dL) or at least a 50% reduction from the baseline.[5, 6]

Ethical Consideration
Patient consent was obtained before submission of the manuscript.

Statement of Authorship
The authors certified fulfilment of ICMJE authorship criteria.

CRediT Author Statement
PS: Conceptualization, Methodology, Software, Validation, Investigation, Resources, Writing – review and editing, Visualization, Supervision, Funding acquisition. **PB:** Conceptualization, Formal analysis, Data curation, Writing – original draft preparation, Visualization, Project administration. **AD:** Conceptualization, Formal analysis, Resources, Writing – original draft preparation, Visualization, Funding acquisition.

Author Disclosure
The authors declared no conflict of interest.

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