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Hyperostosis-hyperphosphataemia syndrome – shortening a diagnostic odyssey

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Introduction

Hyperostosis-hyperphosphataemia syndrome (HHS) is a rare autosomal recessive condition caused by inactivating mutations in the *GALNT3* gene, characterised by elevated serum phosphate and 1,25$(OH)_2$ vitamin D, increased urinary tubular reabsorption of phosphate and hyperostosis of long bones. [1,2]

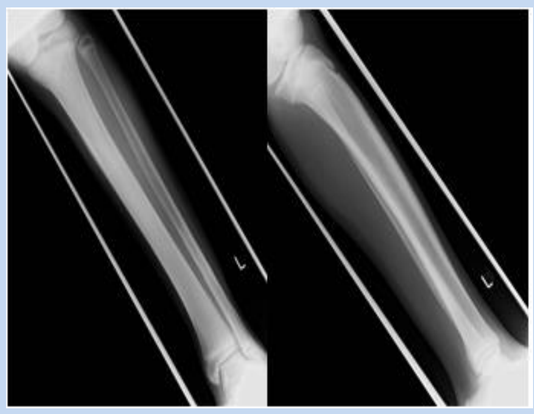
Case report

- A 15 year old boy (weight +1.05 SD; height -0.1 SD) with consanguineous parents of Palestinian descent, presented with a 6 year history of recurrent episodes of flitting pain in his forearms and lower legs.
- Episodes typically lasted 1-4 weeks were associated with erythema of the overlying skin, swelling of the underlying tissue with no obvious triggers.
- Previous investigations had included a biopsy of the ulna which revealed only non-specific findings (ossified material surrounding calcified cartilaginous tissue).
- Diagnoses of osteopetrosis and chronic recurrent multifocal osteomyelitis (CRMO) had been made in the past.
- Treatment with intermittent glucocorticoids and NSAIDS had produced symptomatic benefit.
- General examination was unremarkable apart from thickening and widening of the right ulnar border and anterior border of the right tibia.

Biochemistry

- Revealed a high serum phosphate [2.29 mmol/L (fasted)] with an inappropriately elevated TmP/GFR [3.11 mmol/L].
- Serum 25-hydroxy vitamin D [13nmol/L] was low with a high 1, 25 dihydroxy vitamin D [195pmol/L] and normal parathyroid hormone [6 pmol/L].
- Combined C-terminal and intact FGF23 concentration was high [>1400 HRU/ml (normal <100)] ; intact FGF23 concentration was normal [38 pg/mL].

Figure 1: AP & lateral radiographs of left leg showing the cortical thickening and irregularity on AP and lateral projections.



Radiology

- Radiographs showed a mild degree of periosteal reaction, cortical irregularity and poor cortico-medullary distinction throughout the shafts of the bones in the forearm and lower leg. [fig 1]
- MRI revealed high signal lesions within the medullary cavity of the diaphyses of the left fibula and right tibia on T2-weighted and STIR, corresponding to low signal on T1 sequences.

Diagnosis

The clinical, biochemical and radiological findings are all consistent with the rare diagnosis of HHS. Mutation analysis of the *GALNT3* gene revealed a homozygous *GALNT3* frame shift mutation (c.803dupC), confirming the clinical diagnosis of Hyperostosis-hyperphosphataemia syndrome.

Discussion

This case report illustrates the characteristic clinical, biochemical and radiological features of HHS along with the potential for misdiagnosis. Judicious use of NSAIDS and steroids may be helpful. Surgical decompression has been described for patients with severe pain not amenable to analgesics. Long term monitoring of blood pressure and cardiovascular health would seem prudent.

Conclusion

This case report bespeaks the value of both thorough clinical assessment and targeted genetic screening in the prompt diagnosis of rare disorders.

Reference

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