

Unveiling the Mystery: A Cryptic Case Study of a Hyperphosphatemic Patient with Puzzling Clinical Presentations

Mehdi Mirzazadeh,^{a,*} Nadia Dehghan,^a and Thomas G. Morris^a

^aDepartment of Chemical Pathology, St Helier Hospital, Epsom and St Helier University Hospitals NHS Trust, Carshalton, Surrey, United Kingdom.

* Department of Chemical Pathology, St Helier Hospital, Epsom and St Helier University Hospitals NHS Trust, Wrythe Lane, Carshalton, Surrey SM5 1AA, United Kingdom. E-mail mehdi.mirzazadeh@nhs.net.

CASE DESCRIPTION

A 37-year-old male patient was referred by his family physician due to consistently high serum phosphate levels of 6.5 mg/dL (reference interval: 2.5 to 4.7 mg/dL, conversion factor to mmol/L: divide by 3.1) in the presence of normal renal function, for some years. No musculoskeletal pain or mobility issues were reported, and he had no history of cardiovascular, rheumatological, respiratory, renal (including nephrolithiasis), or psychiatric disorders. He was a nonsmoker, consumed little alcohol, and had a balanced diet but with low calcium intake. Past medical history revealed the presence of a calcified lesion in his right elbow at age 11, which required several surgical resections. He reported calcium deposition on his knee and calcification in his right shoulder a few years prior. He was the only child and had no children. His parents lived abroad and both had some history of shoulder calcification. Physical examination of his spine was unremarkable. However, when assessing his joints, right shoulder limitation in movements were observed. A lump of 1 cm was noticed on his right lateral heel. His blood pressure and examination of his heart, abdomen, and chest were normal.

Biochemical investigations were performed in house using the Abbott architect platform, which revealed elevated serum phosphate at 5.3 mg/dL, and low parathyroid hormone (PTH) 20.9 pg/mL (reference interval: 24 to 133 pg/mL, conversion factor to pmol/L: divide by 9.5). Total calcium, albumin adjusted calcium, alkaline phosphatase (ALP), albumin, globulins, thyroid stimulating hormone (TSH), thyroxine, luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone and 25-hydroxyvitamin D (25(OH)D) were all within normal range. The analysis of a random urine sample revealed a creatinine concentration of 73.45 mg/dL (conversion factor to mmol/L: divide by 11.3) and a phosphate concentration of 178 mg/dL. These findings correspond to a tubular reabsorption of phosphate (TRP) of 96% and a ratio of the maximum tubular phosphate reabsorption to the glomerular filtration rate (TmP/GFR) of 5.1 mg/dL (ref<3.8).

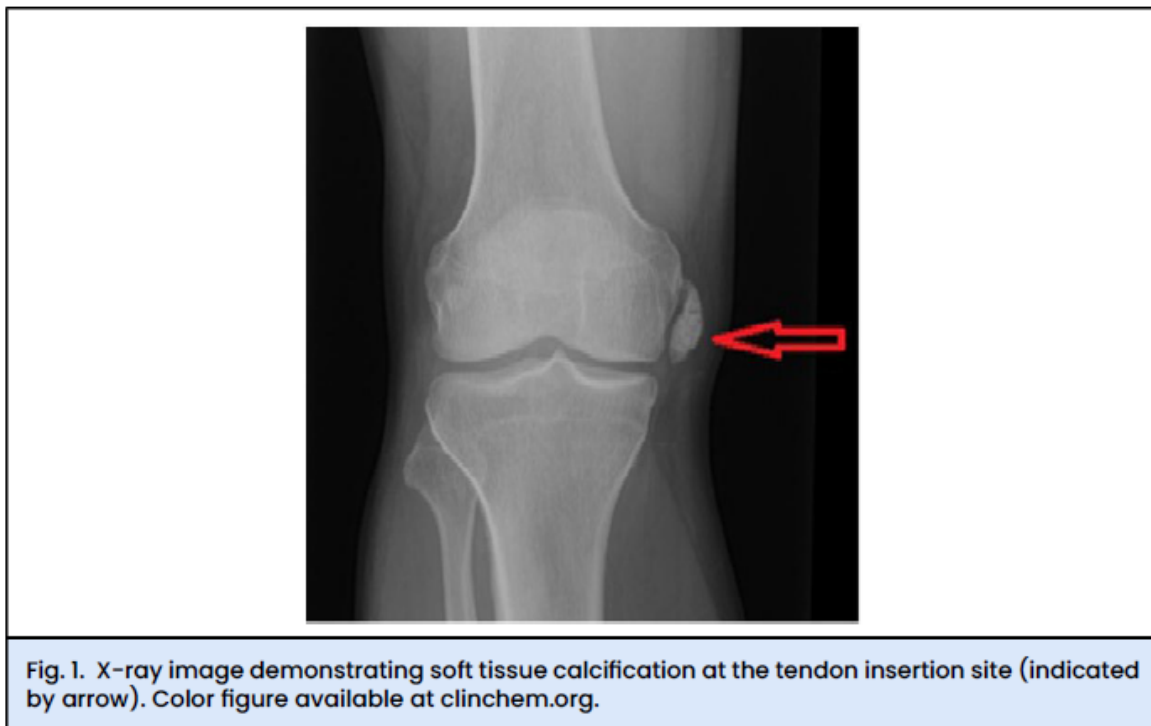
1,25-Dihydroxyvitamin D (1,25(OH)₂D) was measured in the country's Supra-Regional Assay Service for Calcium and Bone Metabolism Service at Norwich University and showed a serum level of 57.7 pg/mL (reference interval: <55.7 pg/dL, conversion factor to pmol/L: multiply by 2.496).

PATIENT FOLLOW-UP

A diagnosis of tumoral calcinosis was considered, and patient serum C-terminal fibroblast growth factor 23 (FGF23) analysis was carried out at the Supra-Regional Assay Service for Calcium and Bone Metabolism at Norwich University using a Quidel-Immutopics assay, the results of which were markedly elevated at 4176 pg/mL (reference interval: <200) with intact FGF23 of 64.6 pg/mL (reference interval 30 to 110). The lump on his right heel noticed during examination had grown rapidly in a month to 4 × 4 cm in width and approximately 16 to 20 mm prominence.

The patient was referred for imaging studies to assess the presence of other ectopic calcifications. His coronary artery calcium score was zero. The skeletal survey report noted multiple foci of soft tissue calcifications at the tendon's insertions (Fig. 1).

QUESTIONS TO CONSIDER
1. What are the causes of hyperphosphatemia?
2. How is pseudohyperphosphatemia excluded?
3. What is the differential diagnosis in light of calcinosis?
4. What is the most likely cause of persistent hyperphosphatemia in the setting of elevated 1,25 dihydroxyvitamin D?



Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the November 2026 issue of *Clinical Chemistry*. To view the case and comments online, go to <https://academic.oup.com/clinchem/issue/72/11> and follow the link to the Clinical Case Study and Commentaries.

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