Severe Hypophosphatemia: The Hidden Truth

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CASE DESCRIPTION

A 52-year-old woman presented with a 14-year history of progressive proximal muscle weakness and myalgia. She had been wheelchair-bound for the previous 10 years, with a significant loss of height since the onset of symptoms. She was previously healthy, with no family history of metabolic bone disease. Clinical examination revealed a proximal myopathy, short stature with marked kyphoscoliosis and pectus carinatum. Her admission laboratory investigations showed severe hypophosphatemia, with a serum phosphate of 0.87 mg/dL (0.28 mmol/L [reference interval 2.5–4.5 mg/dL; 0.8–1.4 mmol/L]). 25-Hydroxy vitamin D (25-OHD) was reduced with a normal 1,25-dihydroxy vitamin D (1,25-OHD). Laboratory results are summarized in Table 1. Of note, the tubular maximum reabsorption of phosphate for glomerular filtration rate (TmP/GFR) was 0.8 mg/dL (0.22 mmol/L [reference interval 2.0–3.4 mg/dL; 0.80–1.35 mmol/L]), suggestive of renal phosphate wasting. Fibroblast growth factor 23 (FGF-23) was elevated at 9207 pg/mL (reference interval 12–49 pg/mL). Despite phosphate and vitamin D replacement, the hypophosphatemia persisted.

QUESTIONS TO CONSIDER
• What are the causes of urine phosphate wasting?
• What is the most likely cause of persistent hypophosphatemia in the setting of a normal or low plasma calcitriol level (1,25-OHD)?
• What is the most common phosphatonin responsible for diseases characterized by urine phosphate wasting?
• What is the diagnostic localization image of choice in this case?

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Table 1. Biochemical results at the time of admission (all serum unless specified otherwise).

Analyte	Reference interval	Result
Adjusted calcium	8.8–10 mg/dL	8.8
Phosphate	2.5–4.5 mg/dL	0.87
Magnesium	1.5–2.6 mg/dL	1.97
Albumin	3.5–5.2 g/dL	4.4
Parathyroid hormone	14–72 pg/mL	622
25-hydroxy vitamin D	<20 ng/mL—deficient; >30 ng/mL—sufficient	13
1,25-dihydroxy vitamin D	17–65 pg/mL	53
Alkaline phosphatase	42–98 IU/L	460
Bone-specific alkaline phosphatase	14–42 IU/L	305
Creatinine	0.55–1.02 mg/dL	0.43
Estimated glomerular filtration rate	90–120 mL/min/1.73m^2	117
TmP/GFR	2.0–3.4 mg/dL	0.8
Fibroblast growth factor 23	12–49 pg/mL	9207

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the May 2023 issue of *Clinical Chemistry*. To view the case and comments online, go to https://academic.oup.com/clinchem/issue/69/5 and follow the link to the Clinical Case Study and Commentaries.

Educational Centers

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