

Severe Hypophosphatemia: The Hidden Truth

Farzahna Mohamed ^{a,*} and Frederick J. Raal ^a

^aDepartment of Internal Medicine, Division of Endocrinology and Metabolism, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.

*Address correspondence to this author at: University of the Witwatersrand, 7 York Rd, Parktown, Johannesburg, South Africa, 2193. E-mail Farzahna.mohamed@wits.ac.za.

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?

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

If you are associated with an educational center and would like to receive the cases and questions 1 month in advance of publication, please email clinchemed@aacc.org.

All previous Clinical Case Studies can be accessed and downloaded online at <https://www.aacc.org/science-and-research/clinical-chemistry/clinical-case-studies>

AACC is pleased to allow free reproduction and distribution of this Clinical Case Study for personal or classroom discussion use. When photocopying, please make sure the DOI and copyright notice appear on each copy.

AACC is a leading professional society dedicated to improving healthcare through laboratory medicine. Its nearly 10,000 members are clinical laboratory professionals, physicians, research scientists, and others involved in developing tests and directing laboratory operations. AACC brings this community together with programs that advance knowledge, expertise, and innovation. AACC is best known for the respected scientific journal *Clinical Chemistry* and the world's largest conference on laboratory medicine and technology. Through these and other programs, AACC advances laboratory medicine and the quality of patient care.