Case Report

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Spurious Hyperphosphatemia in a Patient with Multiple Myeloma: A Case Report

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Abstract:

Spurious hyperphosphatemia has been reported periodically in multiple myeloma (MM) patients with paraproteinemia. It is important for clinicians to recognize this phenomenon in order to avoid misdiagnosis and unnecessary treatment for true hyperphosphatemia. This case report demonstrates a case of spurious hyperphosphatemia in an MM patient whose serum phosphate could be normalized by deproteinization of a blood sample, a simple and widely available correction technique.

Keywords: hyperphosphatemia, multiple myeloma, paraprotein, pseudohyperphosphatemia, spurious

Introduction

Hyperphosphatemia is not an uncommon condition in clinical practice. A reduced glomerular filtration rate in both acute and chronic renal insufficiency leading to insufficient renal excretion of phosphate is the most common cause. Lack of parathyroid hormone (PTH) action from either hypoparathyroidism or resistance to PTH can also reduce renal phosphate excretion and cause hyperphosphatemia, in such cases generally accompanied by hypocalcemia. The clinical importance of acute severe hyperphosphatemia is related to symptomatic hypocalcemia, with symptoms such as perioral numbness, muscle cramps, and arrhythmia, accompanied by generalized precipitation of calcium phosphate into soft tissues, especially vascular walls, causing morbidity as well as mortality.[1] Therefore, when severe hyperphosphatemia is detected, immediate

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correction of both the hyperphosphatemia and its etiology are important to prevent organ damage. However, spurious hyperphosphatemia, also known as pseudo-hyperphosphatemia, occurs occasionally, and the physician must be aware of this mimicking condition, as unnecessary phosphate-lowering intervention can be detrimental to the patient. Herein we present a case of spurious hyperphosphatemia in a patient with multiple myeloma (MM). The patient's medical record and related literature were reviewed in March 2020 and this case report was completed in April 2020.

Case report

A 57-year-old Thai man was referred to the orthopedic out-patient department of our institution due to a left distal femur fracture after falling from standing height. A plain film of the left femur showed multiple osteolytic lesions, and he was immediately admitted for a bone biopsy. His past medical history and physical examination were unremarkable, aside from conjunctival pallor and painful swelling in his left thigh. The laboratory findings revealed moderate impairment of renal function, severe hypercalcemia, and, surprisingly, extremely high serum phosphate as measured by the Roche Cobas Molybdate Ultraviolet method (Table 1). The blood sample collection and handling were checked and met the standard laboratory protocols.

Serum immunofixation and protein electrophoresis revealed immunoglobulin G monoclonal gammopathy Kappa type. Bone marrow clonal plasma cells were ninety-nine percent. These investigations confirmed the diagnosis of MM in this patient.

Unlike true hyperphosphatemia, our patient with extremely high serum phosphate did not have any hyperphosphatemic complications. Therefore, spurious hyperphosphatemia from hyperglobulinemia was suspected. To confirm this hypothesis, a blood sample was deproteinized with sulfosalicylic acid, and a few hours later his serum phosphate was retested, and had normalized to 3.5 milligrams per deciliter, confirming our suspicion of spurious hyperphosphatemia. Following a course of chemotherapy for MM (bortezomib, cyclophosphamide, and dexamethasone), the patient's serum biochemical values returned to normal within a month (Table 2).

Table 1 Patient's laboratory results

Parameter	Patient's value	Normal value
Serum studies		
Creatinine (mg/dL)	2.40	0.67-1.17
eGFR (mL/min/1.73 m^2)	30.00	-
Calcium (mg/dL)	14.60	8.60-10.20
Phosphate (mg/dL)	23.60	2.70-4.50
Uric acid (mg/dL)	12.10	3.40-5.20
Albumin (g/dL)	2.50	3.50-5.20
Total protein (g/dL)	13.00	6.40-8.30
Triglycerides (mg/dL)	122.00	0.00-150.00
Total bilirubin (mg/dL)	4.66	0.00-1.20
Parathyroid hormone (pg/mL)	9.48	11.00-62.00
Complete blood count		
Hemoglobin (g/dL)	9.90	13.00-18.00
Leukocyte count (per mm^3)	5,020.00	4,500.00-10,000.00
Platelet count (per mm^3)	200,000.00	150,000.00-450,000.00

eGFR=estimated glomerular filtration rate, mg/dL=milligrams per deciliter, mL/min/1.73 m^2=milliliters per minute per 1.73 square meters, g/dL=grams per deciliter, pg/mL=picograms per milliliter, mm^3=cubic millimeter

Table 2 Baseline, post-deproteinization, and post-chemotherapy laboratory results

Serum parameter	Baseline	After deproteinization	2 months after chemotherapy
Creatinine (mg/dL)	2.40	1.89	0.97
eGFR (mL/min/1.73 m^2)	30.00	39.00	87.00
Calcium (mg/dL)	14.60	13.90	9.10
Parathyroid hormone (pg/mL)	9.48	–	–
Phosphorus (mg/dL)	23.60	3.50	4.10
Total bilirubin (mg/dL)	4.66	–	0.31
Globulin (g/dL)	10.50	–	4.00

eGFR=estimated glomerular filtration rate, mg/dL=milligrams per deciliter, mL/min/1.73 m^2=milliliters per minute per 1.73 square meters, pg/mL=picograms per milliliter, mm^3=cubic millimeter

Discussion

Hyperphosphatemia in MM can be diagnosed by obvious clues such as renal insufficiency and tumor lysis syndrome.[1] However, in our case, elevated serum phosphorus levels in the absence of these clinical signs and the accompanying hypocalcemia were key indicators of spurious hyperphosphatemia. To avoid unnecessary treatment, it is important for physicians to recognize this condition and know how to measure the exact level of serum phosphate by using available techniques in their institutes.

The molybdate assay is a widely used colorimetric assay for serum phosphate measurement. The ammonium molybdate in this assay reacts with phosphate ions to produce a colored complex which indicates the presence of inorganic phosphate. Many reports have demonstrated an interference effect by increasing optical density from hyperlipidemia, hyperbilirubinemia, and hyperglobulinemia leading to a misdiagnosis of hyperphosphatemia.[2–5]

Spurious hyperphosphatemia secondary to hyperglobulinemia has been documented in many case reports with various suggested techniques for assessing the patient's exact serum phosphate levels. Removal of serum protein by deproteinization of the serum using sulfosalicylic acid[4,6,7], ultrafiltration[8–10], and dialysis[5] have been proposed but their reliability has not yet been fully assessed. Atomic absorption spectrophotometry[11–13] has been found to be a more reliable serum phosphate test than the colorimetric assay, however, its high cost and lack of availability limit its practical usefulness. Serum phosphate and globulin were found to be positively correlated in several case reports.[6,7,12] Nevertheless, the level of globulin which begins to affect the test has not yet been identified.

Spuriously hyperbilirubinemia has also been reported in patients with hyperglobulinemia.[14] Because the patient's serum total bilirubin was mildly isolated elevated, it was remeasured 2 months after the chemotherapy and, as well as the serum phosphate, the result was normal. That the serum calcium and creatinine levels normalized after the chemotherapy but not with deproteinization of the serum indicates that they were true abnormalities caused by the patient's MM.

Our case is another example of an MM patient with spurious hyperphosphatemia whose serum phosphate level could be corrected by deproteinization with sulfosalicylic acid which was confirmed by the spontaneous normalization of the serum phosphate after a course of chemotherapy for MM. This supports the effectiveness of this simple and low-cost technique in detecting a high level of serum phosphate from a cause other than true hyperphosphatemia, such as hyperglobulinemia, as in our case.

Conclusion

Deproteinization of a blood sample in an MM patient with asymptomatic and apparent hyperphosphatemia can reveal spurious hyperphosphatemia, thus avoiding unnecessary phosphate-lowering intervention.

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