Case Studies

Hyperphosphatemia in a Patient with Respiratory Problems

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CLINICAL HISTORY

Patient: 48-year-old white male.

Chief Complaint: Fever and chills, dyspnea, and productive cough.

History of Present Illness: The patient was symptomatic for 2 weeks prior to admission and unresponsive to outpatient treatments. The only positive finding on physical examination was a high oral temperature (38°C). Positive laboratory findings at the time of admission include macrocytic anemia (Hb: 11 g/dL, MCV:110 fl) associated with leucopenia and thrombocytopenia, raised ESR, positive CRP, and most notably, hyperphosphatemia (14.7 mg/dL; reference range: 2.5–5.0 mg/dL) accompanied with normal serum calcium, PTH, and mildly disturbed renal function tests (**Table 1**). Chest X-ray and spiral CT scan showed consolidation of the anterior segment of the right upper lobe of the lung (**Figure 1**).

The pneumonia was successfully treated with the antibiotic regimen consisting of ceftazidime, clindamycin, and erythromycin.

Because of intractable pancytopenia, the patient underwent bone marrow aspiration-biopsy that showed increased plasma cells consistent with plasma-cell dyscrasia (**Figure 2**); immunohistochemical staining of the biopsy specimen revealed λ light chain restriction (**Figure 3**). Serum total protein and IgG were significantly raised, while IgM and IgA levels were low. The serum β2 –microglobulin level was high, and the urine was positive for Bence-Jones protein. Serum protein electrophoresis (SPE) revealed an M-spike in the gamma-region of the gel (**Figure 4**).

Keywords: plasma cell dyscrasia, multiple myeloma, pseudohyperphosphatemia, hyperglobulinemia

Questions

1. What are the most notable clinical and laboratory findings in this case?
2. What is the best explanation for hyperphosphatemia in this patient?
3. What are the other possible causes of pseudohyperphosphatemia?
4. What is the analytical source of pseudohyperphosphatemia secondary to hyperglobulinemia?
5. What are the methods to resolve the problem?
6. Does this finding alter the patient's prognosis?

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Possible Answers

1. Hyperphosphatemia with normal serum calcium and only mildly disturbed renal function tests, pancytopenia with monoclonal bone marrow plasmacytosis with λ light chain restriction and serum M component by electrophoresis; lobar consolidation of the lung responsive to antibiotic therapy.

2. The hyperphosphatemia was paradoxical because it occurred in the presence of normal serum calcium. There are a few conditions that are characterized by hyperphosphatemia and normocalcemia, such as cortical hyperostosis[1] and tumoral calcinosis,[2] but neither of these conditions is consistent with this patient's symptoms.

The most likely cause of apparent hyperphosphatemia in this case is hypergammaglobulinemia which can result from plasma cell dyscrasia or infection. The persistence of hyperphosphatemia after antibiotic treatment, and the monoclonal immunoglobulin band on SPE eliminated infection as the cause.

3. Hyperimmuneglobulinemia, hyperlipidemia, hyperbilirubinemia, and in vitro hemolysis can cause a pseudohyperphosphatemia[3-8] as explained below.

Figure 1

Spiral CT scan showing alveolar consolidation in the anterior segment of right upper lobe.

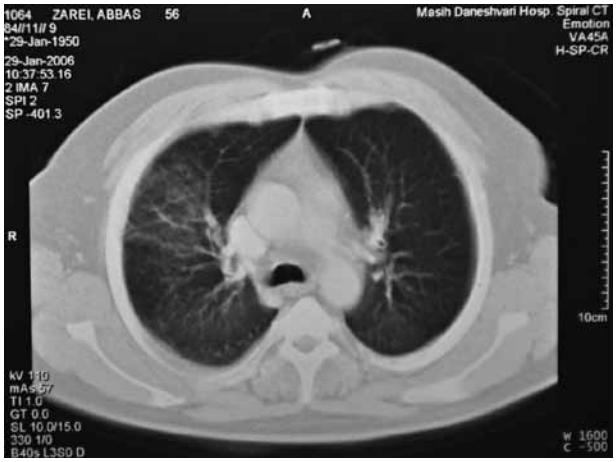
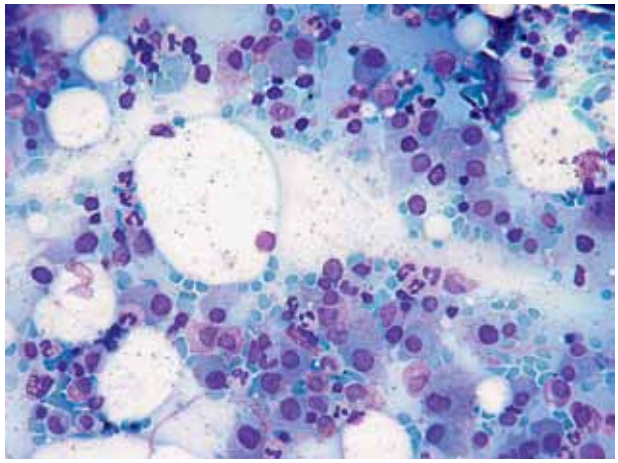


Figure 2

Bone marrow aspiration smear showing plasmacytosis (×40).



4. The usual colorimetric method for measuring inorganic phosphate is based on the addition of phosphomolybdic acid to the specimen; its reduction causes a color change that is measured spectrophotometrically.[5,6] Turbidity in hyperproteinemic specimens can result in falsely high absorbance.[7]

Table 1. Biochemical Data of the Case

Variable	Patient's Data	Normal Range
Hemoglobin (g/dL)	11	14-17.5
WBC count (×10³) (cells/μL)	3	4-11 ×10³
Platelet (×10³) (cells/μL)	69	150-450 × 10³
ESR (mm/h)	128	<20
Total protein (g/dL)	10	6.4-8.3
Serum albumin (g/dL)	2.2	3.5-5.5
Serum phosphate (mg/dL)	14.7	2.5-5
Serum calcium (mg/dL)	10	8.1-10.4
Urea (mg/dL)	84	10-50
Serum creatinine (mg/dL)	1.2	0.7-1.4
Serum uric acid (mg/dL)	9	3.5-7.2
Creatinine clearance (mL/min)	~51	110-120
IgG (mg/dL)	9,000	800-1,700
IgM (mg/dL)	<10	50-370
IgA (mg/dL)	22	85-490
PTH (pg/mL)	36.5	10-62
TSH (μU/mL)	6.4	0.4-6.2

WBC, white blood cell; ESR, erythrocyte sedimentation rate; IgG, immunoglobulin G; IgM, immunoglobulin M; IgA, immunoglobulin A; PTH, parathyroid hormone; TSH, thyroid-stimulating hormone.

Hyperproteinemia is not always associated with pseudohyperphosphatemia, suggesting that both the physicochemical properties and the quantity of protein are important factors.[3] Pseudohyperphosphatemia in multiple myeloma, for example, may be due to the presence of phosphate binding globulin.[9] Interestingly, pseudohyperphosphatemia may occur intermittently in spite of similar levels of abnormal immunoglobulin.

5. Analytical methods that separate proteins from serum before measuring inorganic phosphorus are not susceptible to the interference from turbidity in hyperproteinemic specimens. However, methods that rely on diluting serum proteins prior to measurement of phosphate are vulnerable to falsely elevated phosphate results because the dilution may not be adequate in severe hyperglobulinemia.

Use of a purine nucleoside phosphorylase-based enzymatic method, followed by converting the phosphomolybdate complex to a heteropolymolybdate may also eliminate the protein interference. Accurate measurements of phosphate can also be obtained with the phosphomolybdate calorimetric assay after appropriate chemotherapeutic regimen.[10]

6. Hyperphosphatemia is a negative prognostic factor in multiple myeloma,[11] but pseudohyperphosphatemia due to hyperimmunoglobulinemia should be ruled out before interpreting the laboratory result. LM

Figure 3

Immunohistochemical study of Bone marrow biopsy showing diffuse staining for λ light chain.

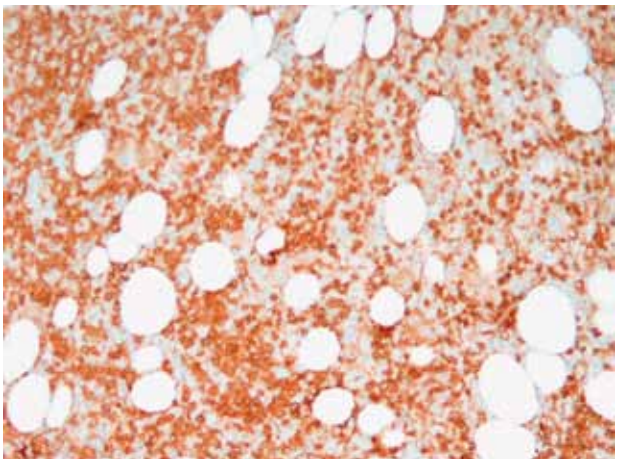
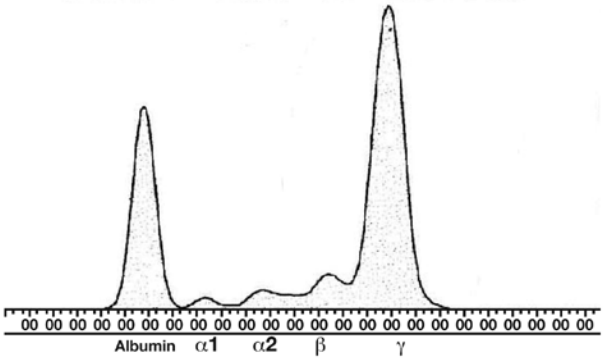


Figure 4

Serum protein electrophoresis showing an M spike in gamma region.



Total values and normal ranges						
No.	Fraction	(%)	Flag	Normal (%)	g/dL	Normal (g/dL)
1	Albumin	31.8		52-62	3.1	3-6
2	α1	1.5		2-6	0.2	0.1-0.4
3	α2	4.1		8-13	0.4	0.5-1.1
4	β	6.9		13-19	0.7	0.6-1.3
5	γ	55.6		15-23	5.6	0.7-1.8
Total Protein:		10	H	6-8 g/dL		
A/G Ratio:		0.4	L	1-2		

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