CASE REPORT

Profound hypophosphatemia in a multiple myeloma patient receiving zoledronic acid, cyclophosphamide and furosemide

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ABSTRACT

Hypophosphatemia is a rare occurrence in multiple myeloma patients due to compromised renal function. We describe a male patient who presented with acute renal failure, anemia, hypercalcemia, hyperphosphatemia, and was diagnosed with Stage IIIIB IgG kappa multiple myeloma. He subsequently developed profound hypophosphatemia during the course of his treatment, which included zoledronic acid, cyclophosphamide, and furosemide. A combination of the phosphate depleting effect of the three drugs and his improving renal function may have contributed to the profound hypophosphatemia.

Key words: hypophosphatemia, multiple myeloma, zoledronic acid, cyclophosphamide, furosemide

INTRODUCTION

Hypophosphatemia is a relatively uncommon occurrence in the general population. However, its prevalence varies considerably in hospitalized patients with severe trauma (up to 75%) or sepsis (65-80%), and among individuals with chronic alcoholism (2.5-30.4%). In adults, a normal serum phosphate concentration is typically in the range of 2.5 to 4.5 mg/dL (0.81-1.45 mmol/L). Hypophosphatemia is defined as serum phosphate concentration of less than 2.5 mg/dL (0.81 mmol/L) and severe hypophosphatemia is defined as less than 1.0 mg/dL (0.32 mmol/L). Severe hypophosphatemia that is not treated can lead to rhabdomyolysis, hemolysis, respiratory failure, and neurological abnormalities. In the setting of multiple myeloma, hypophosphatemia is rare because of the myeloma associated renal dysfunction which usually leads to renal phosphate retention instead of phosphate loss. Hypophosphatemia in patients presenting with myeloma had only been reported in isolated case reports from 1997 to-date. Caras, Kerr and Mao independently reported hypophosphatemia due to analytical interference in phosphate measurement due to paraproteins. However, the case we detail here highlights the initial presentation of a myeloma patient with hyperphosphatemia, secondary to reduced renal function, then subsequent development of profound hypophosphatemia during his clinical course. The profound hypophosphatemia was not due to analytical interference.

CASE REPORT

A 67-year-old male was transferred from an outside hospital to our institution for management of acute renal failure, anemia and hypercalcemia. Six months prior to presentation, the patient had noted a painless swelling on his scalp and the back of his head, and over the subsequent few weeks he had developed increasing generalized weakness, being unable to stand...
up from a chair and unable to drive. The patient had also lost more than 30 lbs in weight, which he attributed to his having difficulty swallowing solid foods and being on a liquid only diet. The only medication he was taking prior to admission was lisinopril 10 mg daily. His past medical history was significant for a right eyelid ptosis over the previous several months and weakness of his left quadriceps with decreased sensation to light touch on the left leg after sustaining a fall 3 years previously.

His initial set of laboratory investigations was notable for hypercalcemia, hyperphosphatemia, anemia (normochromic, normocytic), renal failure, hyperuricemia and very high total protein (Table 1). Initial Magnetic Resonance Imaging (MRI) of the brain revealed a large occipital mass (Fig. 1). Further laboratory work-up showed IgG of 8037 mg/dL (reference range: 700 -1600 mg/dL), IgA of 20 mg/dL (reference range: 70  -400 mg/dL), and IgM of 16 mg/dL (reference range: 40  -230 mg/dL). Serum protein electrophoresis revealed an IgG kappa monoclonal gammopathy (M-spike of 7.33 g/dL). MRI of the lumbar and thoracic spine showed multiple compression fractures with diffuse disease but no emergent process or cord compression. The patient’s clinical presentation and laboratory studies were consistent with Stage IIIB IgG kappa multiple myeloma.

On day 1 of admission, our patient was given 1L of 0.9% sodium chloride intravenous (IV) bolus followed by 200 mL/hour infusion for hypercalcemia and renal failure. He was also started on unfractionated heparin 5000 units subcutaneous (SQ) every 8 hours for deep vein thrombosis prophylaxis and Senna-docusate sodium for constipation relief. On day 2, the Hematology/Oncology Service was consulted. The patient was given a single dose of zoledronic acid 4 mg IV over 1 hour and continued 0.9% sodium chloride infusion at 200 mL/hour for hypercalcemia. Prednisone 20 mg peroral (PO) daily was given initially and subsequently changed to dexamethasone 10 mg PO daily (on hospital day 3). Esomeprazole 40 mg PO daily was initiated for gastrointestinal prophylaxis. To normalize his hyperuricemia (serum uric acid 13.6 mg/dL), rasburicase 6 mg was given once. A bone marrow biopsy was also obtained. On day 3, his uric acid level decreased appreciably to 3.5 mg/dL and he was then maintained on allopurinol 100 mg PO daily. His renal function was improving (serum creatinine 2.76 mg/dL) and his calcium was 9 mg/dL (within reference range). His uric acid was 0.6 mg/dL and was under control, and his phosphate concentration had normalized to 2.5 mg/dL, although at the low end of the reference range. IV hydration was continued and chemotherapy was initiated. It consisted of a reduced dose of cyclophosphamide IV at 500 mg/m2 (1175 mg) and

### Table 1, Laboratory test results from day 1 to 9 of admission

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 5</th>
<th>Day 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dL)</td>
<td>13.6</td>
<td>9.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Phosphate (mg/dL)</td>
<td>5.8</td>
<td>2.5</td>
<td>0.9</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>4.39</td>
<td>2.41</td>
<td>1.41</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>63</td>
<td>41</td>
<td>37</td>
</tr>
<tr>
<td>Uric Acid (mg/dL)</td>
<td>13.6</td>
<td>0.6</td>
<td>2.6</td>
</tr>
<tr>
<td>Lactate Dehydrogenase (U/L)</td>
<td>305</td>
<td>-</td>
<td>314</td>
</tr>
<tr>
<td>Total Protein (g/dL)</td>
<td>12.7</td>
<td>-</td>
<td>9.8</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>7.3</td>
<td>6.9</td>
<td>7.2</td>
</tr>
</tbody>
</table>

*Reference ranges are in parenthesis

![Figure 2, Serum phosphate concentration during admission](image-url)
Profound hypophosphatemia in a multiple myeloma patient have led to the drastic decrease in serum phosphate.

CONCLUSION

This case report illustrated the potential additive adverse effect of several drugs when administered together. The Naranjo adverse drug reaction probability scale in this case suggested a probable drug interaction between cyclophosphamide, zoledronic acid, and furosemide. This case also emphasized the importance of monitoring both the calcium and phosphate levels during drug treatment, and not just focusing on normalizing calcium levels, although normalizing serum calcium could theoretically normalize phosphate since the two affect each other’s homeostasis.

REFERENCES

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