CASE REPORT

A Case of Symptomatic Severe Hypercalcemia in a 72-Year-Old Man

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CASE PRESENTATION

A 72-year-old gentleman was referred to the internal medicine clinic with a one-month history of cognitive and functional decline. Further history revealed progressive confusion, recurrent falls, abdominal pain associated with constipation, an unintentional 30-pound weight loss, and nocturnal sweats for the past two years. His past medical history and family history were non-contributory. Physical exam was remarkable for tenderness in the coccyx region but was otherwise normal. His initial screening blood work showed a serum calcium level of 3.37 mmol/L (normal range 2.15-2.55). This suggested that his symptoms were likely a result of the elevated calcium and he was admitted to the inpatient internal medicine service for urgent treatment and further investigations.

Upon admission he was immediately started on intravenous normal saline 250 mL/h to help excrete the calcium and was given a single dose of intravenous pamidronate 90 mg to inhibit further calcium release. Further inpatient investigations were performed to assess etiology, and revealed an albumin level of 20 g/L (normal 35-52) and corrected calcium level of 3.69 mmol/L. The serum PTH level was 0.5 pmol/L (normal 1.6-6.9), suggesting that the parathyroid gland was responding appropriately to the elevated serum calcium. The CBC demonstrated pancytopenia with a hemoglobin of 99 g/L (normal 135-170), leukocytes of 3.8 × 10^9 /L (normal 4-10), and thrombocytes of 92 × 10^9 /L (normal 150-400). His hematocrit was 0.24 L/L (normal 0.4-0.5) and the reticulocyte count was normal at 43 × 10^9 /L, suggesting that the bone marrow (BM) was not able to respond appropriately to the anemia. Moreover, the near-normal MCV of 97.3 fL (normal 79-97) favored an intrinsic BM disease. Amongst other blood tests, the creatinine was elevated at 169 µmol/L (normal 62-120). We did not have a previous creatinine for comparison. The symptomatic hypercalcemia, normocytic anemia, renal failure, and deep coccyx bony pain was suspicious for multiple myeloma and we proceeded with further diagnostic workup.

Peripheral blood smear demonstrated rouleaux formation of red blood cells, ESR was 116 mm/h (normal 0-10), and protein level was 110 g/L (normal 64-83). Serum protein electrophoresis was performed to find the source of elevated protein and this demonstrated an abnormally elevated IgG lambda monoclonal protein. Urine protein electrophoresis was also performed and demonstrated the elevated monoclonal protein, along with free lambda light chains. As expected, serum IgG immunoglobulin was elevated at 72.3 g/L (normal 6-13) and the other immunoglobulins were low, suggesting immune dysfunction secondary to suppressed plasma cell function. The presence of free light chains in the urine suggested that renal failure was secondary to tubular damage from cast nephropathy. The skeletal survey did not show any lytic lesions consistent with myeloma except degenerative changes in the vertebrae, which may be the cause for our patient’s bony pain.

BM biopsy revealed more than 60% infiltration of plasma cells and the flow cytometry markers were indicative of both monoclonal plasma cells and lambda light chains. These investigations suggested immune suppression and BM infiltration from an elevated monoclonal protein. Coupled with the clinical presentation of anemia, hypercalcemia, and renal failure, this confirmed a diagnosis of IgG multiple myeloma (MM).

INITIAL PRESENTATION, EPIDEMIOLOGY, AND PATHOGENESIS OF MM

Hypercalcemia is a frequent problem among hospitalized patients with an estimated prevalence of 15%. The majority of cases are caused by primary hyperparathyroidism or malignancy. MM, a consequence of the latter, is a malignancy of plasma cells resulting in clonal proliferation of immunoglobulins. It causes extreme abnormal bone remodeling with over 80% of myeloma patients having bone disease, 73% presenting with anemia at diagnosis, and 30% having renal insufficiency. It accounts for 1% of all cancers and roughly 10% of all haematological malignancies. It is thought that almost all MM patients start off with asymptomatic monoclonal gammopathy of undetermined significance (MGUS), which then progresses to MM at a rate of 1% each year. Sometimes there is an intermediate stage known as smouldering MM (SMM), which progresses to MM at a rate of 10% each year for the first five years.

DIAGNOSIS AND TREATMENT OF MM

Diagnosis of MM is based on serum and/or urine identification of monoclonal immunoglobulins or the presence of heavy or light chains, evidence of proliferation of plasma cells on BM, and inspection of lytic bone lesions. These diagnostic criteria can differentiate between MGUS, SMM, and MM. Symptomatic MM requires >10% infiltration of clonal plasma cells on BM biopsy and evidence of end-organ damage, commonly known as the CRAB criteria: hypercalcemia, renal insufficiency, anemia, and bone lesions.

Symptomatic MM requires immediate treatment. Standard
treatment for healthy patients younger than 65 years includes induction therapy followed by autologous stem cell transplantation. Patients older than 65 years with significant comorbidities should receive chemotherapy. Two therapies are recommended in this clinical setting based on level 1A evidence: (1) melphalan/prednisone/thalidomide (MPT) and (2) bortezomib/melphalan/prednisone (VMD).^{8,9}

**CASE CONCLUSION**

Clinically, our patient responded well to IV fluids and pamidronate. The corrected calcium improved to 2.47 mmol/L and this coincided with an improvement in his mentation and abdominal symptoms. The hematology service was consulted for definitive management of MM. Given that our patient likely had lambda light chain cast nephropathy as the cause of renal failure, the hematologist suggested a pulse cycle of dexamethasone 40mg IV for 4 days on, 4 days off, and repeated once. These cycles were a part of a chemotherapy regime consisting of oral melphalan and intravenous bortezomib. Given our patient’s advanced age, he was not a candidate for BM transplant. He was discharged with a normal serum calcium, full recovery from symptoms, and a prescription including instructions for the oral 4 mg pulse dexamethasone cycle. The hematology service took over further care and chemotherapy on an outpatient basis.

Our patient's follow-up includes bloodwork, serum and urine protein electrophoresis, creatinine, and calcium levels every 2-3 months. Furthermore, new onset of bone pain warrants thorough investigations to detect new bone lesions.\(^7\) Considering MM patients are living longer nowadays and suffering from resulting bone disease, it is important for future therapies to target novel mediators of bone destruction.\(^10\)

**REFERENCES**