CASE REPORT

Diagnostic dilemma in a case of osteolytic lesions

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SUMMARY

A middle-aged male patient presented with fever, polyarthralgia, polyuria, easy fatigability and weight loss for 1 month. Clinically, there was only significant pallor and a swelling over the right sternoclavicular joint. On investigation, there was anaemia, raised urea, creatinine and pus cells in urine with growth of *Escherichia coli*. There were also hypercalcaemia and osteolytic lesions over the ribs, scapula, clavicle and skull along with distorted renal corticomedullary differentiation. Although the initial diagnosis was likely to be a case of multiple myeloma, serum protein electrophoresis was negative for the monoclonal band and no Bence-Jones protein was detected in urine. Bone marrow plasma cells were less than 10%, but the serum-free light chain assay revealed altered $\kappa:\lambda$ ratio. Later in the course of the disease, a cervical lymph node appeared. The biopsy and immunohistochemistry of this lymph node revealed a CD5 positive diffuse large B-cell lymphoma, but unfortunately the patient succumbed to his illness after receiving the first cycle of Rituximab-Cyclophosphamide-Hydroxydoxorubicin-Oncovin-Prednisolone.

BACKGROUND

Multiple osteolytic lesions along with hypercalcaemia and renal compromise are a common presentation of multiple myeloma, but in our case, despite the above presenting features, other investigations like serum protein electrophoresis, urine for Bence-Jones protein and bone marrow study were not suggestive of myeloma except elevated serum-free light chain (sFLC) with altered $\kappa:\lambda$ ratio. Subsequently, the patient was diagnosed to be a case of diffuse large B-cell lymphoma. These presenting features are rarely seen with lymphoma.

CASE PRESENTATION

A 45-year-old male patient, a worker in a soap factory, presented to us with fever and multiple joint pain for 1 month. Although the fever was initially of low grade, for the past 10 days, there was high-grade fever with chill. Joint pain was mainly in the large joints of the upper and lower extremities. It was symmetric in involvement, additive in nature, used to present even at rest and was not associated with any swelling or redness. For the past few days, he had developed an increased frequency and amount (3.5–4 L/day) of urine. There was also a history of progressive generalised weakness, easy fatigability and weight loss as evidenced by loosening of his clothes for the past 1 month.

The patient was not a known diabetic or hypertensive. There were no histories of dysuria, urethral discharge, diarrhoea, redness or watering of eyes, pedal swelling or puffiness of face, low back pain

or pain in abdomen, oral ulceration or photosensitivity. Medical, personal and family histories were non-contributory.

On examination, there was marked pallor. Pulse was of 100/min, regular. Blood pressure was of 130/70 mm Hg. No significant lymphadenopathy was detected. There was no sternal tenderness and no organomegaly. Movements of the joints were also not restricted. Other systemic examinations were also within normal limits.

INVESTIGATIONS

On routine investigations, haemoglobin was 5 g/dL (13–17 g/dL; mean corpuscular volume 58 fL (83–101 fL), mean corpuscular haemoglobin 17.7 pg (27–32 pg), mean corpuscular haemoglobin concentration 30.5% (31.5–34.5%), total leucocyte count 16 400/mm³ (4000–10 000/mm³; neutrophil 79%, lymphocyte 14%), platelet 2.35 lakhs/mm³. Erythrocyte sedimentation rate was 72 mm in the first hour. Urea and creatinine were 72 (10–45) and 3.4 mg/dL (0.5–1.5 mg/dL), respectively. Uric acid was 7.1 mg/dL. Serum calcium was elevated 16.3 mg/dL that prompted us to give forced diuresis. Serum sodium was 132 mEq/L (136–149 mEq/L) and potassium 4.1 mEq/L (3.6–5.3 mEq/L). Liver function test revealed total bilirubin 1.1 mg/dL, direct bilirubin 0.6 mg/dL, aspartate aminotransferase 25 U/L, alanine aminotransferase 28 U/L, alkaline phosphatase 219 U/L. Total serum protein was 7.2 g/dL with albumin 2.7 and 4.5 g/dL. As there was microcytic and hypochromic anaemia, we did a serum iron profile and that revealed serum ferritin 820 ng/mL (50–250 ng/mL), total iron-binding capacity 251 mg/dL (251–406 mg/dL) and serum iron 158 µg/dL (41–141 µg/dL), suggestive of anaemia of chronic disease. As there was increased frequency of micturition along with polyarthralgia, we sent a urine sample for routine and microscopic examination that was reported as presence of pus cells (12–15/hpf) with trace amounts of protein. The urine sample was sent for culture sensitivity and a significant growth of *Escherichia coli* was found. As per the culture sensitivity report, the patient was put on piperacillin-tazobactam, but blood culture sensitivity revealed no growth. Ultrasonography of the whole abdomen revealed mild hepatomegaly, minimal ascites, distorted renal corticomedullary differentiation with right and left kidney size 10.9 and 11.2 cm, respectively. Chest X-ray (figure 1) showed multiple translucent areas over the ribs and clavicle. After detecting raised urea, creatinine, hypercalcaemia and osteolytic areas in chest X-ray, multiple myeloma was thought of and skull X-ray (figure 2) was carried out; there were multiple osteolytic lesions, hinting more towards myeloma.

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Figure 1 Chest X-ray showing multiple translucent areas over the ribs and clavicle.

So we did serum protein electrophoresis and immunofixation, but astonishingly it was negative for the monoclonal band. Bence-Jones protein in urine was also not detected. Only 8–9% plasma cells were found in the bone marrow aspiration study. Bone marrow trephine biopsy revealed only focal trabecular myelofibrosis. We then searched for other causes such as hyperparathyroidism for such osteolytic lesions, but serum parathyroid hormone was 6.21 ng/L (Ref 8–51 ng/L) and serum phosphate was 3.3 mg/dL (Ref 2.5–4.3 mg/dL). Upper and lower gastrointestinal endoscopies were carried out to rule out any gastrointestinal malignancy. Then we did an sFLC assay that was reported as κ light chain 144 mg/L (Ref 3.3–19.4 mg/L), λ light chain 51.5 mg/L (Ref 5.71–26.3 mg/L) along with altered κ/λ ratio 2.818 (Ref 0.26–1.65). Meanwhile, as the patient's condition was getting worse day by day, we consulted with the haematology department of our hospital and they suggested the possibility of light chain myeloma. As per their advice, we started Bortezomib-Thalidomide-Dexamethasone (BTD).

During our ward rounds, about 6 days after starting BTD, we found a new enlargement of a cervical lymph node. Biopsy of

Figure 2 Skull X-ray showing multiple osteolytic lesions.

Figure 3 Lymph node biopsy showing sheets of lymphoid cells, plasma cells and small lymphocytes.

this node was carried out and there were sheets of lymphoid cells, plasma cells and small lymphocytes along with scattered immunoblasts, suggestive of lymphoproliferative disorder (figures 3 and 4). Immunohistochemistry of the lymph node was carried out and it revealed tumour cells expressing CD20 and CD5 and that were immunonegative for CD30, CD10, CD23, Cyclin D1 and SOX11. The Mib-1 labelling index was approximately 50–60%. The final impression was non-Hodgkin's lymphoma of diffuse large B-cell phenotype.

DIFFERENTIAL DIAGNOSIS

- Reactive arthritis
- Light chain myeloma

TREATMENT

At first, piperacillin-tazobactam was started as per the urine culture sensitivity report and intravenous fluid with lasix was given to manage hypercalcaemia. However, when the patient did not respond to these and his clinical condition started to deteriorate, BTD was started after consulting with the haematology department of our hospital as light chain myeloma was thought of initially. After the lymph node biopsy report was made available, we stopped BTD and shifted to Rituximab-Cyclophosphamide-Hydroxydoxorubicin-Oncovin-Prednisolone (R-CHOP).

Figure 4 Lymph node biopsy showing scattered immunoblasts.

OUTCOME AND FOLLOW-UP

Unfortunately, the patient succumbed to his illness after receiving the first cycle of R-CHOP.

DISCUSSION

The presentation with hypercalcaemia, renal failure and osteolytic lesions is common in case of multiple myeloma. However, some alternative diagnosis must be thought of if serum protein electrophoresis, urine for Bence-Jones protein and bone marrow biopsy do not fit well with that of myeloma.¹ Osteolysis is found in 5–15% of cases of malignant lymphoma while hypercalcaemia may present in 10% of cases, but the presence of both osteolysis and hypercalcaemia as initial manifestations of lymphoma is a bit uncommon. Secretion of osteoclast-activating factors such as MIP-1 α by the tumour cells may be the underlying pathophysiology of such osteolytic lesions.² This sort of bony lesions may arise from other malignancies too like those from small round blue cell tumours, acute myelogenous leukaemia, acute lymphoblastic leukaemia, precursor B lymphoblastic lymphoma, etc.^{3–4} On the other hand, nowadays sFLC estimation is not confined only to the domain of myeloma; rather, sFLC ratio is used as a prognostic factor in multiple myeloma, Waldenström macroglobulinaemia and amyloid light chain amyloidosis. It can also suggest the progression of monoclonal gammopathy of unknown significance, solitary plasmacytoma and

smouldering multiple myeloma into multiple myeloma. Its application in the domain of B-cell non-Hodgkin lymphoma (NHL) or chronic lymphocytic leukaemia is also flourishing,^{5–9} and in diffuse large B-cell lymphomas, increased sFLC has been demonstrated as an independent, adverse prognostic factor for overall, event-free survival.⁵

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Learning points

- Lymphoma can also cause osteolytic lesions in the bones.
- Besides myeloma, serum-free light chain can also become elevated in lymphoma.
- Early diagnosis and treatment of diffuse large B-cell lymphoma is of utmost importance to save the patient's life.

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