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Case Report

Extramedullary Multiple Myeloma: A Rare and Aggressive Variant

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Abstract

Extramedullary multiple myeloma (EMM) is an aggressive variant of Multiple Myeloma characterized by proliferation of malignant plasma cells outside the bone marrow. It is associated with advanced disease, resistance to therapy, and poorer prognosis. We report a 63-year-old male who presented with fever, productive cough, progressive exertional dyspnoea, significant weight loss, and generalized weakness over two months. Laboratory investigations revealed severe pancytopenia, hypercalcaemia, acute kidney injury, and marked hypergammaglobulinemia with rouleaux formation on peripheral smear. Serum protein electrophoresis demonstrated a monoclonal spike, and immunotyping confirmed IgG lambda monoclonal gammopathy. Bone marrow examination showed approximately 40% abnormal plasma cells consistent with multiple myeloma. Imaging studies revealed diffuse lytic skeletal lesions and splenomegaly with multiple focal splenic lesions suggestive of extramedullary involvement. Based on clinical, laboratory, and radiological findings, a diagnosis of IgG lambda multiple myeloma with probable extramedullary disease was established. This case highlights the importance of early recognition of extramedullary manifestations, which significantly influence disease prognosis and therapeutic strategy.

Keywords

Extramedullary multiple myeloma, Plasma cell neoplasm, Splenic involvement.

Introduction

The extramedullary variant of Multiple Myeloma is characterized by the proliferation of malignant plasma cells outside the bone marrow, either at the time of initial diagnosis or during disease progression. These lesions, known as extramedullary plasmacytomas**,** may develop through hematogenous dissemination of plasma cells or by direct extension from adjacent osteolytic bone lesions. This form of the disease represents a more aggressive biological behavior and is generally associated with a poorer prognosis. Extramedullary involvement occurs when malignant plasma cells lose their adhesion to the bone marrow microenvironment, enabling them to circulate and infiltrate distant tissues. Clinically, it is considered a high-risk manifestation of myeloma and is often associated with advanced disease stage and resistance to therapy. Extramedullary disease may present either at diagnosis (primary extramedullary disease) or during relapse (secondary extramedullary disease). Diagnosis typically relies on imaging modalities such as PET-CT or MRI, supported by tissue biopsy demonstrating clonal plasma cells with immunohistochemical positivity for markers such as CD138 and CD38. Management generally follows treatment strategies for high-risk myeloma and may include combination chemotherapy, proteasome inhibitors such as Bortezomib, immunomodulatory agents such as Lenalidomide, autologous stem cell transplantation, and radiotherapy for localized lesions.

Case Presentation

A 63-year-old previously unevaluated male presented with a two-week history of fever associated with a productive cough**.** He also reported progressively worsening exertional dyspnoea, lethargy, and episodes of faintness over the preceding two months**.** During the same period, he experienced significant weight loss of approximately 8–10 kg and loss of appetite. There was no history of chest pain, abdominal pain, abdominal

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distension, lower limb oedema, or jaundice. His bowel habits were normal, and there was no history of dysphagia, regurgitation, early satiety, or rectal bleeding. He denied prior episodes of recurrent fever or respiratory tract infections and had no past or contact history suggestive of tuberculosis. There was no history of skin rash, joint pain, or swelling. During the hospital stay, he developed several episodes of haematemesis, without associated melaena or per-rectal bleeding. A few days later, his respiratory status deteriorated with increasing dyspnoea and haemoptysis, requiring supplemental oxygen. The patient had no significant past medical or surgical history, no known drug or food allergies, and no family history of malignancy or autoimmune disease. He was a manual labourer, independent in activities of daily living, a non-vegetarian, and reported occasional alcohol consumption and smoking.

On examination, he appeared chronically ill and pale. His height was 154 cm, weight 40 kg, and BMI 16.8 kg/m², indicating undernutrition. His Glasgow Coma Scale score was 14/15, and he was disoriented. There was no icterus, lymphadenopathy, or peripheral oedema. Abdominal examination revealed splenomegaly extending 3 cm below the left costal margin, without hepatomegaly or ascites. Digital rectal examination was normal. Cardiovascular examination showed a pulse rate of 100 beats/min and blood pressure of 110/60 mmHg, with normal heart sounds. Respiratory examination revealed bilateral crepitations with a respiratory rate of 26/min. Neurological examination was unremarkable.

Initial laboratory investigations demonstrated pancytopenia, with haemoglobin 6.8 g/dL, leukopenia, and severe thrombocytopenia (platelet count 15–27 $\times 10^9$/L). The peripheral blood film showed marked rouleaux formation, suggesting hypergammaglobulinemia. Inflammatory markers were elevated, with C-reactive protein rising from 20.9 mg/dL to 43.1 mg/dL and erythrocyte sedimentation rate of 125 mm/hour. Renal function tests revealed acute kidney injury, with serum creatinine rising from 359 µmol/L to 485 µmol/L, followed by gradual improvement with treatment. Urine analysis demonstrated proteinuria (2+), and the urine protein-creatinine ratio was 361.8 mg/mmol, consistent with nephrotic-range proteinuria. Biochemistry showed marked hypercalcaemia with albumin-corrected calcium levels up to 3.67 mmol/L, along with hyperuricemia (742.5 µmol/L). Liver function tests revealed hypoalbuminemia (22 g/L) and markedly elevated globulin levels (80 g/L). Serum protein electrophoresis demonstrated a monoclonal spike in the gamma region, with monoclonal protein concentration of 40.1 g/dL ***(Figure 1).***

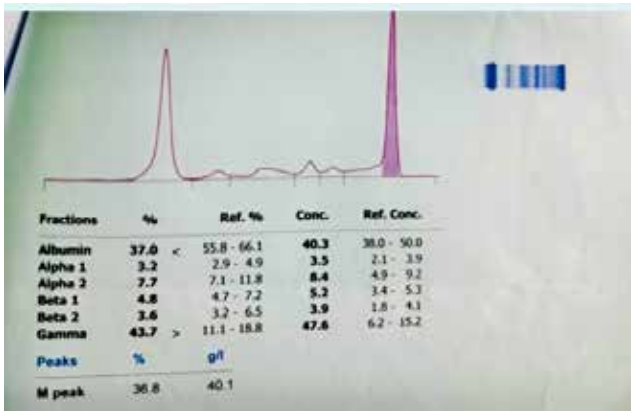

Fig- 1: Serum protein electrophoresis demonstrated a monoclonal spike in the gamma region, with monoclonal protein concentration of 40.1 g/dL

Immunotyping confirmed IgG lambda monoclonal gammopathy. Urine testing for Bence Jones protein was negative. Bone marrow aspiration and biopsy revealed approximately 40% abnormal plasma cells, including plasma blasts and multinucleated forms, confirming the diagnosis of multiple myeloma. Imaging studies supported systemic involvement. Skeletal survey and CT imaging demonstrated multiple lytic bone lesions ***(Figure 2)***

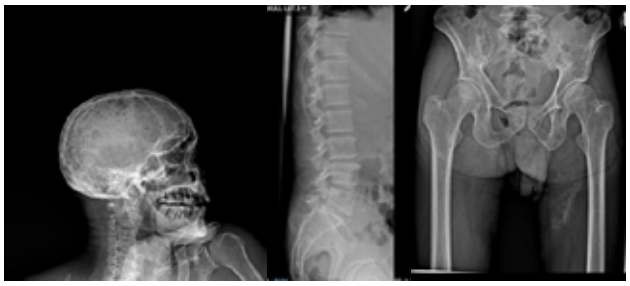

Fig-2: Skeletal survey demonstrated multiple lyric bone lesion.

Abdominal ultrasonography initially demonstrated multiple hypoechoic lesions in the liver and spleen, raising suspicion for metastatic disease or hematological malignancy. Upper gastrointestinal endoscopy performed following haematemesis showed blood-stained gastric mucosa with diffuse oozing, likely secondary to severe thrombocytopenia. Echocardiography revealed normal cardiac function with a left ventricular ejection fraction greater than 60%. Contrast-enhanced CT of the chest, abdomen, and pelvis revealed diffuse skeletal lytic lesions consistent with multiple myeloma, moderate splenomegaly with heterogeneous enhancement and multiple focal lesions suggestive of extramedullary involvement, mild ascites, and bilateral pleural effusions (left greater than right).

Based on the bone marrow findings, monoclonal gammopathy, lytic bone lesions, hypercalcaemia, renal impairment, and splenic lesions suggestive of extramedullary involvement, a diagnosis of IgG lambda multiple myeloma with possible extramedullary disease was established.

Discussion

Multiple Myeloma (MM) is defined by the presence of ≥10% clonal bone marrow plasma cells associated with clinical features such as hypercalcemia, renal impairment, anemia, or lytic bone lesions, or by the presence of specific biomarkers including ≥60% bone marrow plasma cells, an involved to uninvolved free light chain ratio ≥100, or ≥2 focal marrow lesions on MRI(1). Despite advances in diagnosis and treatment, the disease demonstrates heterogeneous clinical behavior, and a subset of patients develop more aggressive variants.

Extramedullary multiple myeloma (EMM) represents a relatively rare manifestation of MM in which malignant plasma cells acquire the ability to survive independently of the bone marrow microenvironment and infiltrate extramedullary tissues(2). The overall incidence of extramedullary disease is reported to be approximately 13%, with about 7% detected at initial diagnosis and 6–20% occurring at relapse. The median time from the initial diagnosis of MM to the development of EMM has been reported to range between 19 and 23 months(1).

Patients with EMM may present with involvement of diverse anatomical sites including lymph nodes, skin, soft tissues, the central nervous system, thoracoabdominal organs, or serous cavities. Because the presenting symptoms are often nonspecific and depend on the site of involvement, early diagnosis can be challenging. This rarity combined with atypical clinical manifestations may delay recognition of the condition and therefore affect timely management. Accurate diagnosis frequently requires extensive investigations. While extramedullary disease may occasionally present as palpable or visible masses, imaging modalities play a crucial role in detection. Magnetic resonance imaging (MRI) is particularly useful for assessing spinal and central nervous system involvement, whereas functional whole-body imaging techniques are more effective for detecting systemic extramedullary lesions. The International Myeloma Working Group recommends the use of 18F-FDG PET/CT for the evaluation of suspected extramedullary disease because of its superior sensitivity in identifying metabolically active lesions (3).

Extramedullary involvement is generally considered a more aggressive biological variant of MM and is associated with poorer prognosis compared with conventional bone marrow–confined disease. The aggressive nature of EMM can significantly influence patient outcomes and may lead to increased morbidity and reduced quality of life. Therefore, early recognition and prompt initiation of therapy are crucial. Current treatment strategies aim to achieve optimal hematologic response, eradicate extramedullary lesions, improve end-organ function, and prolong survival. Available therapeutic options include proteasome inhibitors, immunomodulatory drugs, and emerging immunotherapies such as monoclonal antibodies, bispecific antibodies, and chimeric antigen receptor T-cell therapy(4).

Given its rarity, nonspecific presentation, and aggressive clinical course, extramedullary multiple myeloma remains a diagnostic and therapeutic challenge, highlighting the need for heightened clinical suspicion and comprehensive evaluation to facilitate early diagnosis and improve patient outcomes.

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