CASE REPORT

Streptococcus pneumoniae bacteraemia leading to the diagnosis of multiple myelomaSavita Shahani,¹ Lokesh Shahani²

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Accepted 31 August 2014

SUMMARY

Multiple myeloma (MM) is a malignant plasma cell disorder characterised by the neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. Anaemia, bone pain from lytic lesions, hypercalcaemia and renal failure are the most common presentations at diagnosis; however, the presence of infection at the time of diagnosis is rarely reported. The author reports an elderly male presenting with isolated fever and initial blood cultures positive for *Streptococcus pneumoniae*. Investigating the patient's underlying immunodeficient state predisposing him to this infection, serum and urine immunofixation electrophoresis identified monoclonal IgG λ and bone marrow biopsy revealed diffuse plasma cell infiltration that comprised 35% of the cellular elements, which were all consistent with MM. This case report highlights the importance of considering MM in asymptomatic elderly patients who present with acute pneumococcal infection without an apparent predisposing factor.

BACKGROUND

Multiple myeloma (MM) is a malignant plasma cell disorder and accounts for 10% of all haematological malignancies.¹ It is characterised by the neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin. Immune dysfunction in MM is multifactorial, resulting from impaired lymphocyte function, suppression of normal plasma cell function and hypogammaglobulinemia. A review of 1027 patients newly diagnosed with MM at Mayo clinic identified anaemia, bone pain from lytic lesions, hypercalcaemia and renal failure as the most common presentations.² The presence of infection as the initial clinical presentation is rarely reported. The author reports a case of a patient presenting with isolated pneumococcal bacteraemia and on investigating his cause of immune dysfunction was diagnosed with MM.

CASE PRESENTATION

The author reports a 67-year-old man presenting to the physician's office with fever. He had been in relatively good health with no previously diagnosed medical condition and just had isolated fever for 2 days prior to his presentation. On examination by his outpatient doctor, the patient was found to be febrile; however, he was haemodynamically stable. Blood cultures were drawn in the physician office which turned positive 18 h later and hence the patient was hospitalised for further investigation.

On admission, the patient continued to be febrile; however, he denied having any associated

symptoms. He mentioned using acetaminophen for his fever; however, he denied using any medication on a chronic basis. He denied having any sick contacts and also any family history for recurrent infections or malignancy. The patient was a married retired male in a monogamous relation and denied the use of alcohol, tobacco or other illicit drugs.

On examination, the patient was febrile (T=39.3°C) with signs of sepsis such as tachycardia (98 bpm) and hypotension (86/64 mm Hg). The remainder of his detailed physical examination was unremarkable. The patient's tachycardia and hypotension responded to 3 L of normal saline. The patient's laboratory results were remarkable for leukocytosis (white cell count=12 400 cells/mm³) with 78% neutrophils. He did not have any evidence of anaemia, renal failure or elevated serum calcium or alkaline phosphatase. Laboratory abnormalities included discrepancies between elevated total protein and albumin levels (total protein=10.2 g/dL, and albumin=2.2 g/dL) and mild (1+) proteinuria on the urine dipstick. Patient's results of his blood cultures were finalised and it grew *Streptococcus pneumoniae* which was penicillin and ceftriaxone susceptible. The minimal inhibitory concentration for the antimicrobials was as follows: penicillin=0.06 µg/mL, ceftriaxone=0.03 µg/mL.

INVESTIGATIONS

In order to investigate the patient's underlying immunodeficient condition predisposing him to *S. pneumoniae* bacteraemia, a HIV ELISA was ordered, which was negative. The patient did not have any evidence of invasive disease leading to otitis media, sinusitis, meningitis or pneumonia. He had a chest X-ray and a transthoracic echocardiogram, which did not show any evidence of lung or cardiac involvement. Owing to the discrepancy between the elevated total protein and albumin levels and proteinuria, as well as recognising the association of MM in an elderly male presenting with isolated pneumococcal bacteraemia as reported in the literature,^{2,3} a workup for MM was ordered. Serum protein electrophoresis was ordered, which revealed an abnormal band measuring 3.37 g/dL in the γ region. Serum and urine immunofixation electrophoresis identified monoclonal IgG λ with reduced IgA and IgM levels. Bone marrow biopsy revealed diffuse plasma cell infiltration that comprised 35% of the cellular elements. All the above findings were consistent with a diagnosis of MM. The patient had a skeletal survey which did not reveal lytic lesions. At this

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To cite: Shahani S, Shahani L. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-204472

time, he was diagnosed with smouldering or asymptomatic MM and therapy for MM was deferred at this time.

OUTCOME AND FOLLOW-UP

The patient was treated with 14 days of intravenous ceftriaxone secondary to its convenient dosing pattern. He completed his therapy with resolution of his symptoms. The patient was followed up at the haematology clinic and is in the preparation stage for chemotherapy and possible autologous haematopoietic cell transplantation.

DISCUSSION

The association between MM and invasive pneumococcal infection has been well reported previously. Among the various types of haematological malignancies, patients with MM had the highest risk for invasive pneumococcal infection as reported in a population-based study from Canada. Compared to the rate of invasive pneumococcal infection in the general adult population (11.0 cases/100 000 per year), there were significantly increased rates of invasive pneumococcal infection in those with MM (673.9 cases/100 000 per year, OR 62.8).² Age greater than 65 years was a risk factor for recurrent invasive pneumococcal infection.⁴ Further, in a case series of 17 patients with acute bacterial infection as the only presenting feature of MM, bacteraemia was noted in 91% of *S. pneumoniae* infection and was the only sign of infection in two cases.³ The median age of these 17 patients in this study was 65.5 years and the monoclonal paraprotein identified was IgG in 92%, as was the case for our patient. The study emphasised pneumococcal bacteraemia as a possible red flag for MM in patients without other predisposing conditions for pneumococcal infections.³

The reported patient was worked up for MM because of the discrepancy between the elevated total protein and albumin levels and proteinuria. Other features such as anaemia, renal failure, bone pain, weight loss and a global feeling of ill health in an elderly patient presenting with pneumococcal bacteraemia should serve as a red flag for workup of MM.^{3 5} Our patient was diagnosed earlier in his course of MM and did not have any secondary complications such as renal failure or skeletal metastasis at diagnosis. A higher frequency of complications is observed among patients diagnosed later in their disease. A prolonged delay in diagnosis has been associated with a significant negative effect on disease-free survival.⁵

Patients with MM are susceptible to infection due to multiple reasons, with the major defect being in the humoral immunity. Close to 75% of patients have a diminished production of polyclonal immunoglobulins, which leads to a defective antibody response to an antigenic stimulus.^{6 7} However, other mechanisms which have been identified include a defect in the C3b binding capacity to *S. pneumoniae*, which has been correlated with the incidence of pneumococcal infections. Further, as opsonisation with a complement is essential for granulocyte interaction with *S. pneumoniae*, the defect in the complement system predisposes these patients towards infections.⁸

Host defences against *S. pneumoniae* are primarily mediated via humoral factors such as antibody formation, complement system and phagocytosis. Defective antibody formation such as congenital causes (agammaglobulinemia) and secondary causes

(MM, lymphoma, HIV infection, chronic lymphoid leukaemia) have been linked to the greatest susceptibility to pneumococcal infection. Neutropenia and neutrophilic dysfunction (cirrhosis, steroids use, diabetes) as well as defective clearance of the bacteria due to asplenia also predispose the patients to invasive pneumococcal disease. Understanding this risk, the Infectious Disease Society of America recommends the 13-valent pneumococcal conjugate vaccine followed by a 23-valent pneumococcal polysaccharide vaccine after at least 8 weeks for patients with haematological malignancies, including MM.⁹ This case report highlights the importance of considering various immune deficiencies in asymptomatic elderly patients who present with acute pneumococcal infection without an apparent predisposing factor.

Learning points

- ▶ Multiple myeloma (MM) is a malignant plasma cell disorder characterised by the neoplastic proliferation of a single clone of plasma cells producing a monoclonal immunoglobulin.
- ▶ Anaemia, bone pain from lytic lesions, hypercalcaemia and renal failure are the most common presentations at diagnosis; however, the presence of infection at the time of diagnosis is seldom reported.
- ▶ Patients with MM are susceptible to infection due to multiple reasons, with the major defect being in the humoral immunity.
- ▶ It is important to consider MM in asymptomatic elderly patients who present with acute pneumococcal infection without an apparent predisposing factor.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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