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Case Report

Multiple myeloma complicated by melioidosis - a case report

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Introduction

Infection is the leading cause of morbidity and mortality in patients with multiple myeloma (MM). Patient comorbidities, MM organ involvement and therapeutic strategies affect immune function and increase the risk of opportunistic infections [1]. Here, we present a case of a 71-year-old diabetic patient with a history of prolonged fever and constitutional symptoms found to have multiple abscesses involving the anterior abdominal wall and spleen. She was diagnosed with MM complicated by melioidosis. The development of new medical therapies has dramatically improved the survival of patients with MM. Our case highlights the fact that infection affects treatment outcomes, and survival in MM.

Melioidosis is a potentially fatal infection caused by a Gram-negative, aerobic, non-spore-forming, motile bacillus, *Burkholderia pseudomallei.* It is found in contaminated soil and groundwater and spreads through percutaneous inoculation, inhalation and ingestion [2]. Melioidosis is endemic in Northern Australia and Southeast Asia. During the period from 2006 to May 2017, 250 cases of melioidosis were reported in Sri Lanka which is now considered an endemic region. Males comprised the highest proportion (71.6%). The affected individuals generally had well-known predisposing factors such as diabetes mellitus (65.2%), end stage renal failure, chronic pulmonary disease and immunodeficiency. The mortality rate was 20.4% [2,3]. The clinical presentation of melioidosis varies from acute septicaemia to a chronic infection characterized by a multisite abscesses.

MM is a neoplastic proliferation of monoclonal plasma cells in the bone marrow. This results in over-production of a monoclonal paraprotein (M protein), bone destruction and

displacement of other haematopoietic cell lineages. Susceptibility to infection is, in part, due to a reduction in normal immunoglobulin production, defects in the complement cascade and other factors related to MM [4].

Case report

A 71-year-old female from Kilinochchi presented with fever of three months duration. She had a history of poorly controlled diabetes mellitus and hypertension for more than 20 years. Fever spikes occurred nearly every other day and were associated with loss of appetite. She had lost nearly 5kg in weight over 4 months. She had no respiratory symptoms or contact history of tuberculosis. She complained of a throbbing type, left hypochondriac pain for the last two weeks. She denied any genitourinary symptoms and had no history of altered bowel habits. She had no hair loss, rash or mouth ulcers. She denied any history of recent exposure to animals. She had been treated for a recurrent right side breast abscess six months previously. She denied any history of blood transfusion or high-risk sexual behaviour. She had not traveled abroad recently. She denied any family history of haematological malignancy or autoimmune disease. She was a farmer.

Examination revealed that she was febrile and pale. She did not have cervical or axillary lymphadenopathy and had no peripheral stigmata of infective endocarditis. Respiratory and cardiovascular examination findings were unremarkable. She had mild left hypochondrial tenderness without clinically palpable organomegaly.

Her blood investigations revealed elevated inflammatory markers and a significantly elevated serum globulin with reversed albumin globulin ratio and high normal serum calcium raising the suspicion of multiple myeloma. Her renal function was normal, urine Bence-Jones protein was negative, and the skeletal survey did not show lytic lesions. But blood picture assessment revealed normocytic, normochromic anaemia with marked rouleaux formation. Serum protein electrophoresis showed high levels of monoclonal proteins (55.8 g/L). The bone marrow biopsy showed that more than 60% of the marrow nucleated cells were abnormal plasma cells, including a few blast cells and multinucleate forms.

Ultrasound scan of the abdomen done to evaluate left hypochondrial pain showed multiple focal lesions in the spleen without splenomegaly. Contrast computed tomography of the abdomen revealed an enlarged spleen with multiple, focal, non-enhancing, irregular, hypodense areas seen posteriorly and multiple soft tissue nodules in the anterior abdominal wall confined to the subcutaneous tissue, possibly abscesses.

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Table 1: summary of investigation

Investigation	Results
WBC	9,980x 10^9/L (N-77%, L-17%)
Hb	8.6g/dL (MCV-83.2, MCHC-32)
PLT	201,000
CRP	72 mg/l
ESR	150mm in 1st hour
Blood culture	No growth
Liver function test	AST-25 U/l, ALT-29 U/l, ALP-103U/l, Total protein-129 g/l, Albumin-23 g/l, Globulin-106 g/l, T. Bilirubin 6.7 µmol/l , INR1.1
Renal function	Serum creatinine-80 µmol/l, Na^+ -130 mmol/l, K^+ -3.5 mmol/l
Serum calcium	2.35 mmol/l
Blood picture	Normocytic normochromic anaemia with marked rouleaux formation Compatible with anaemia of chronic disease
Urine Bence-Jones protein	Not detected
Chest Xray	No significant abnormality detected
Skeletal survey	No lytic lesions were seen
Mantoux Test	Negative
2D echo	Normal study
Melioidosis antibody	1:320 (repeated 2 times)
USS Abdomen	Multiple focal lesions in spleen without splenomegaly.
CECT Abdomen	Spleen enlarged with multiple focal non enhancing lesions and irregular hypodense area seen posteriorly and no para-aortic lymphadenopathy. Multiple soft tissue nodules in anterior abdominal wall confined to subcutaneous tissue? Abscess (large size- 2cm*2.3cm) Possible differential diagnosis are melioidosis and tuberculosis
Serum protein electrophoresis	Monoclonal protein - 55.8g/l
Bone marrow biopsy	More than 60% of the marrow nucleated cells are abnormal plasma cells including a few blast cells and multinucleated forms

Discussion

New treatment options, introduced in recent decades, have improved the survival of patients with MM. But disease-related complications, such as infections, nephropathy and neuropathy are becoming of greater concern in patients who survive longer. A weak immune response predicts a heightened risk of infection. The Medical Research Council (MRC) estimates that nearly 50% of deaths in the first two months after diagnosis are associated with infection. Bacterial infection is the most common cause of death (48%), followed by fungal infections at 28% and mycobacterial infections at 7% [5].

The risk of severe infection is approximately thirty times and the incidence of pneumonia thirteen times greater than the general population. The risk of infection is related to a

number of factors including impaired host defense and organ damage associated with the disease. The reduced response in producing immunoglobulins, delay in IgM synthesis and high level of paraprotein affect humoral immunity. The reduction of circulating and functional neutrophil leukocytes, T lymphocytes and dendritic cells further impair the host's defense. Interleukin (IL-6 and IL-10) released by myeloma cells affect the Th1/Th2 ratio, thereby reducing the immune response of Th1 cells [6].

Melioidosis should be considered as a differential diagnosis when an immunocompromised patient presents with multiple musculoskeletal abscess or visceral abscesses. *B pseudomallei* is identified as a causative organism of splenic abscess in patients with risk factors who reside in endemic areas. The results of logistic analysis show that diabetes mellitus, occupational exposure, preexisting renal diseases, and thalassaemia are significant independent risk factors for melioidosis [7]. Diabetes, uncontrolled hyperglycemia and bone marrow infiltration by myeloma impair innate immunity, specifically neutrophils. Neutropenia increases susceptibility to septicaemia [8].

Our patient received a diagnosis of melioidosis presenting with anterior abdominal wall and splenic abscesses on a background of immunodeficiency due to MM. Following a multi-disciplinary team discussion, our patient was treated intravenously with ceftazidime 2g every eight hours for two weeks, followed by eradication therapy with combined doxycycline and cotrimoxazole. Low dose chemotherapy for MM was initiated during the eradication phase. Unfortunately, she died within one month. Our case highlights the fact that, even though new therapies have improved outcome in MM, infection plays a major role in survival.

Conclusion

Immune dysfunction is one of the hallmarks of MM. It is multi-factorial in origin and carries an increased risk of infectious complications which are a major cause of morbidity and mortality. This case emphasizes the importance of detecting and managing opportunistic infections in immunocompromised patients.

Informed consent

Informed consent was obtained from the patient

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