Case Report

Pott's Disease and Multiple Myeloma in the Bone Marrow: A Rare Coincidence

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Abstract

Pott's disease also known as tuberculosis (TB) spondylitis is the most dangerous form of musculoskeletal TB. It is associated with neurological deficits. Multiple myeloma (MM) is characterised by bone degradation and suppression of the immune system. It often presents itself as bone pain and anaemia. Coexistence of Pott's disease and TB is a rare occurrence. However, we present a patient with persistent back pain and anaemia, who was initially diagnosed with TB. Despite treatment with anti-TB medication for six months, he developed bone pains, lower limb numbness, and pallor. On radiographic, laboratory, and pathologic investigations, MM with Pott's disease was diagnosed. This case points out the fact that MM may coincide with active or recurrent TB. Due to the similarity of their clinical symptoms, one of them may be ignored, and this will lead to serious complications for the patient.

Keywords: Anaemia, bone pain, case report, multiple myeloma, tuberculosis spondylitis

Introduction

Multiple myeloma (MM) is a neoplasm of terminally differentiated B lymphocytes called plasma cells. It is characterised by the formation of multifocal tumor masses, suppression of normal immunoglobulin (Ig) production, and the proliferation of a single clone of plasma cells that produce a monoclonal protein resulting in bone pain, osteolytic lesions, hypercalcaemia, anaemia, and/or soft-tissue plasmacytomas. The global annual incidence of MM is 4/100,000. The median age at diagnosis is 65 years in Western Countries, 58 years in Nigeria, and 68 years in Asian populations with the incidence being lower in Asian populations and Africans compared to the Western Countries.[1] It occurs mainly in the elderly (50–70) years with a male-to-female ratio of 2.3:1. Causative agent is currently unknown but risk factors include exposure to pesticides, and herbicides, ionizing radiation, and chronic antigenic stimulation.[1] Majority of myeloma cells express the membrane phenotype of plasma cells (cytoplasmic Ig, PC-1, PCA1, and CD38). MM arises from the malignant transformation of a B lymphoid stem cell committed to produce plasma cells. Signs and symptoms of MM include anaemia, neutropenia, thrombocytopenia recurrent infections due to immunoparesis, lytic bone lesions, renal impairment/failure, haemorrhagic tendencies, and hyperviscosity syndrome. Laboratory features of MM show bone marrow hyperplasia, elevated erythrocyte sedimentation rate (ESR) >100 mm/h Westergren method, elevated β2 microglobulin levels, hypoalbuminaemia, and hypercalcaemia. Bone marrow smear shows plasmacytosis >10%.[2] Radiological findings show osteolytic bone lesions in skeletal X-ray survey. The new international staging system has classified MM based on laboratory parameters, radiologic findings, and immunological features into three stages, namely Stage I with median survival age >five years, Stage II with median survival age >three years, and Stage III with median survival age ~two years.[2] This staging system does not accurately predict disease-free survival. Other factors affecting prognosis are shown in Table 1. MM is treated using cyclophosphamide with or without prednisolone, interferon alpha, combination

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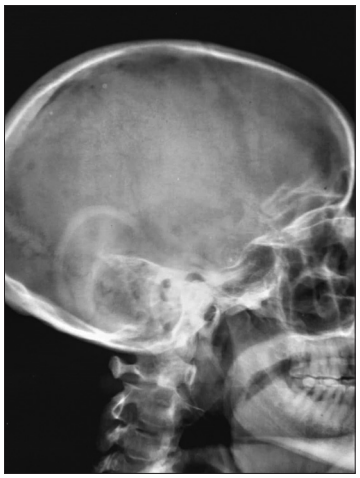

Figure 1: Lateral view of skull X-ray showing multiple punched-out lytic lesions

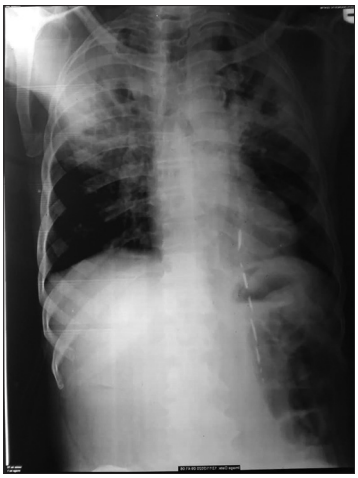

Figure 2: Frontal chest radiograph showing multiple cavitary lesions and recticulonodular opacities

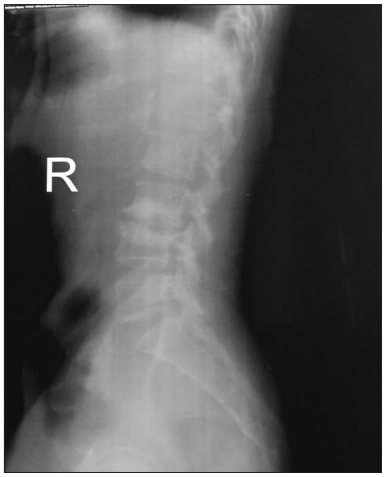

Figure 3: Lateral view of lumbosacral X-Ray showing sclerosis of the adjacent end plates of L3 and L4 vertebral bodies with obliteration of their intervertebral disc space

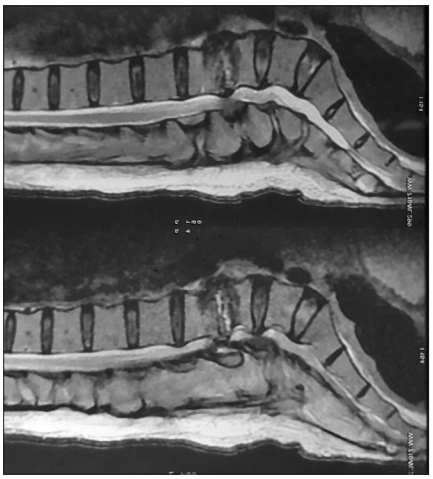

Figure 4: Magnetic resonance imaging sagittal view of the lumbosacral region showing wedged collapse of the L3 and L4 with herniation of the disc content causing severe canal stenosis

Table 1: Favorable prognostic factors in multiple myeloma

Parameters	Range
β2 microglobulin	≤2.5 mg/dL
C-reactive protein	≥4.0 mg/ml
Plasma cell labelling index	<1%
Serum albumin	>3 g/dL
Serum albumin (g/dL)	>3
Absence of plasmatic morphology	
No chromosome 13 abnormalities	

chemotherapy, or high-dose chemotherapy, followed by autologous stem-cell transplantation.[1]

In rare cases, MM occurs coincidentally with tuberculous spondylitis also known as Pott disease. This is a form of tuberculosis (TB) infection caused by *Mycobacterium tuberculosis* involving the spine, causing the collapse of vertebral bodies.[2] Although the thoracolumbar junction seems to be the most common site for spinal column involvement, any part of the spine can be affected. Furthermore, the incidence of neurologic complications in spinal TB varies from 10% to 43%. The first lumbar vertebral body is most commonly infected, with involvement of more than one vertebral body also being typical. Infection may spread to contiguous vertebral bodies or skip multiple levels; it commonly spreads beneath the anterior longitudinal ligament (and, less commonly, the posterior longitudinal ligament).[2] Destruction and anterior collapse of the vertebral body may result in deformity. Spinal TB is treated using antituberculosis drugs. The efficacy of antituberculosis drugs and other conservative means has been shown in several studies for the treatment of spinal TB in the absence of neurologic deficit, instability, and deformity regardless of the presence of paravertebral abscess. Combination of rifampicin, isoniazid, ethambutol, and pyrazinamide for two months, followed by the combination of rifampicin and isoniazid for a total period of six, nine, 12, or 18 months, is the most frequent protocol used for the treatment of spinal TB.[2]

Case Report

In December 2020, a 72-year-old Nigerian male referred from a Private Hospital to our Haematology outpatient clinic at the University of Medical Sciences Teaching Hospital Complex, Ondo, presented with complaints of disabling back pain, anaemia, and difficulty in walking. There was no history of pathological fracture, weight loss, coughing, or sputum. There were also no symptoms of bladder or bowel dysfunction with the patient not being a known hypertensive or diabetic. Seven months before presentation, the patient had received a combination of anti-TB drugs rifampicin, isoniazid, ethambutol, and pyrazinamide for two months, followed by the combination of rifampicin and isoniazid for a period of six months. Physical examination revealed pallor, lower limbs numbness, and generalised bone pain.

Investigations done include a full blood count which showed low packed cell volume (22.3%), haemoglobin (7.2 g/dL), white blood cell (11,300/mm^3), neutrophils (53.1%), lymphocyte (40%), platelet count, (147,000) plateletcrit (0.13%), red blood cells (2.90×10^{12}/l), and mean corpuscular haemoglobin concentration (32.3 g/L). Basophils, eosinophils, and monocytes were in the normal reference range. Mean corpuscular volume (76.7%) and mean corpuscular haemoglobin (24.8%) were slightly lower than normal. Other laboratory findings showed serum protein electrophoresis with immunofixation and monoclonal gammopathy (IgG was elevated with free lambda light chains).

ESR was > 130 mm/hr (↑), calcium was 2.19 mmol/L (N), beta-2-microglobulin serum of 4.9 µg/mL (↑), CRP 69 mg/L (↓), urea 4.2 mmol/L (N), creatinine of 89.4µmol/L (N), total protein of 7.1mg/dL (N) Albumin of 2.1 mg/dL (↓) and globulin of 5.0mg/dL (↑). Peripheral blood film showed normocytic, normochromic, hypochromic, microcytic red cells, relative lymphocytosis with the rouleaux formation, and adequate platelet. Qualitative Bence Jones protein was also detected in urine samples (using Hcl and heat test methods). The patient was admitted for a bone marrow aspiration which revealed hyperplasia with plasmacytosis. Plain radiograph of skull showed multiple punched out lytic lesions in the skull predominantly in the parietal bones [Figure 1]. Chest X-ray revealed wide spread reticulonodular opacities with cavitory lesions in both lung fields, sparing the lung bases indicating active tuberculosis [Figure 2]. The Lateral view of lumbosacral X-Ray revealed sclerosis of the adjacent end plates of L3 and L4 vertebral bodies with obliteration of their intervertebral disc space [Figure 3]. MRI-scan of the Lumbosacral spine showed severe L3/L4 degenerative disc changes with superimposed inflammatory process and significant spinal canal narrowing at the level [Figures 4, 5 and 6]. Other Lumbar intervertebral discs showed mild desiccation but were normal in height [Figure 7]. Ziehl-Neelsen staining for Mycobacterium tuberculosis was negative while Gene expert and mantoux tests were positive. After making the diagnosis of MM, he was commenced on standard MM therapy, (Cyclophosphamide 200mg/m^2 daily for 4 days, thalidomide 100 mg daily for 4 days, IV dexamethasone 60mg/m^2 daily for 4 days, and zoledronic acid 4mg stat) on a monthly cycle. All other supportive treatment were included in the management.

Blood samples of the patient were sent to the TB multidrug center in Ibadan. While waiting for the result, the patient was commenced on the WHO 12 month's regimen (rifampicin, ethambutol, pyrazinamide, and isoniazid for two months) followed by rifampicin and isoniazid for 10 months.

The neurological status of the patient recovered completely, and the patient was able to move around without support after the second cycle of MM therapy. His condition has consistently improved since.

Discussion

Pott's disease usually results from an extraspinal source of infection and haematogenous dissemination manifesting

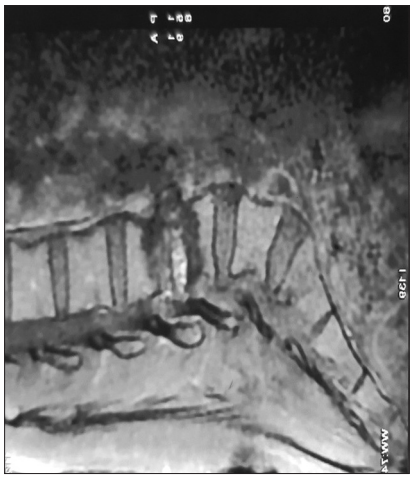

Figure 5: Magnetic resonance imaging sagittal view of the lumbosacral region distortion of the L$ and L5 showing wedged collapse of the L3 and L4 with herniation of the disc content causing severe canal stenosis

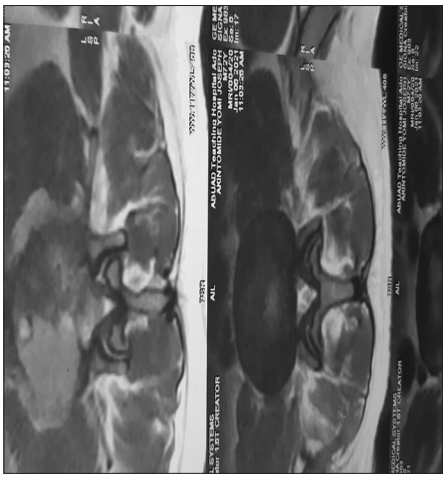

Figure 6: MRI axial view showing irregularity and heterogeneity of the L3/L4 disc material

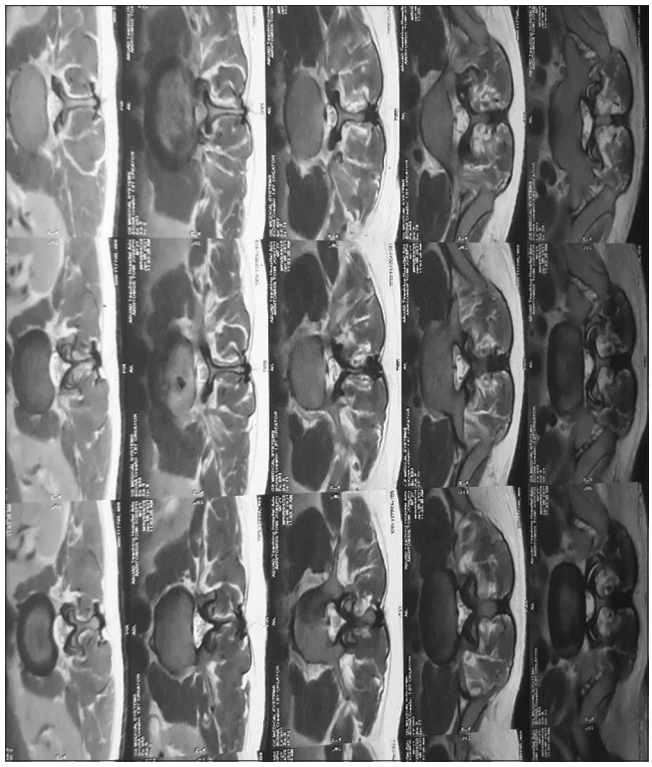

Figure 7: Multilevel magnetic resonance imaging axial cuts of the lumbar region showing varying degrees of disc desiccation

as a combination of osteomyelitis and arthritis involving more than one vertebrae.[3] It is the most dangerous form of musculoskeletal TB because it can cause bone destruction, deformity, and paraplegia and it is associated with neurological deficits. It most commonly involves the thoracic and lumbosacral spine with some variations.[4] The lower thoracic vertebrae make up the most common area of involvement (40%–50%), followed closely by the lumbar spine (35%–40%). Differentiating spinal TB from pyogenic and fungal vertebral osteomyelitis as well as primary and metastatic spinal tumors may be difficult when only clinical and radiographic findings are considered.[5] A history of TB, a positive skin test, and an elevated ESR may be useful in the diagnosis of spinal TB. The ESR and CRP recorded for this patient >130 mm/h and 69 mg/L were quite higher than the 50 mm/h and 47 mg/L, respectively, recorded by Prinsen *et al*.[6] The Ziehl–Neelsen staining for *M. tuberculosis* was negative for this reported case while Prinsen *et al*., (2013) reported a positive Ziehl–Neelsen staining for *M. tuberculosis*. Biopsy plays a valuable role in the diagnosis of spinal TB infection. Among the various types of imaging modalities, MRI has the ability to diagnose the disease earlier and more accurately than computed tomography (CT) scan due to its ability to penetrate soft tissues easily. The most distinguishing feature of spinal TB is bone destruction with relative preservation of the intervertebral disc and heterogeneous enhancement. Spinal TB if diagnosed early can be treated using a combination of rifampicin, isoniazid, ethambutol, and pyrazinamide for two months, followed by the combination of rifampicin and isoniazid for a total period of six, nine, 12, or 18 months.[7] Using multidrug therapy, the recurrence rate for skeletal TB is approximately 2%. Currently, multidrug-resistant TB is a global concern and is encountered in 3% of all new cases and 12% of retreatment cases. For the treatment of multidrug-resistant TB, an average of six anti-TB drugs for at least 24 months is recommended by the WHO.[8]

MM (also known as Kahler's disease) is a clonal B-cell disorder characterised by the proliferation and accumulation of B-lymphocytes and plasma cells in the bone marrow and, more rarely, at extramedullary sites. Bone pain and vertebral lesions are the most common symptom of the disease, affecting nearly 70% of the patients. This could be attributed to the fact that vertebral bodies contain a high amount of haematopoietic bone marrow so that a large surface of the haematopoietic niche is adjacent to osteoblasts, osteoclasts, or other stroma cells involved in bone remodeling. Motor dysfunction is the second-most frequent symptom of MM. Patients often complain of weakness of lower limbs, particularly during movement.[9] Diagnosis of MM is often done using MRI which is the most sensitive and specific imaging technique for detecting spinal lesions. It allows morphological detection of vertebral compression fractures alongside the ability to evaluate the characteristics of bone marrow infiltration by the disease. It also possesses several advantages over other imaging techniques such as X-ray and CT scans for diagnosing spinal alterations in MM patients.[10]

Treatment of MM-related spinal lesions is based upon a multidisciplinary approach, as both medical, surgical, and minimally invasive techniques are employed. Antimyeloma therapy, bisphosphonates, novel drugs (denosumab), radiotherapy, surgery, and vertebral augmentation are some treatment options for MM.[9]

Conclusion

We have described the case of a patient that presented with recurrent TB. Series of investigations revealed the coexistence of TB and MM which rarely occur together. We conclude that in patients with recurrent tuberculous spondylitis without improvement of symptoms after appropriate antituberculous medication, the presence of immunosuppressing disease such as MM should be suspected, and in such cases, investigations to aid the diagnosis of both conditions should be carried out so as to avoid severe complications from missing out on either disease.

Declaration of patient consent

The authors certify that we have obtained all appropriate consent forms including the patient's consent for his images and clinical information to be reported in the Journal. The patient understands that his name and initials will not be published and dues efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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