ABSTRACT

Aim: To highlight the need to consider multiple myeloma as a probable diagnosis while evaluating a patient presenting with paraparesis and backache.

Presentation of Case: A 55 year old woman presented to a hospital in Calabar, Nigeria with complaints of low back pain and progressive difficulty in walking for three months. There was associated constipation and weight loss. She had received two units of whole blood prior to presentation on account of severe anaemia. Physical examination revealed marked cachexia, pallor, dehydration and oral candidiasis. There was bilateral lower extremity weakness and exaggerated deep tendon reflexes. Investigation revealed anaemia, elevated erythrocyte sedimentation rate, hypoalbuminemia and increased serum globulin. Corrected serum calcium and uric acid were also elevated. Radiographic studies revealed generalized osteopenia and gross reduction in vertebral body height of T6, T9, T11 and L2 with lytic lesions on the ribs and skull. She was managed with blood transfusions and cycles of systemic chemotherapy comprising of vincristine, adriamycin and dexamethasone and referred for radiotherapy.

Discussion: This case posed a diagnostic challenge. The presenting complaints suggested a compressive myelopathy which is more commonly caused by tuberculosis in our setting. Other considerations were benign or malignant tumours, HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) and neurolathyrism.

Conclusion: In the evaluation of a patient with paraparesis and backache, multiple...
myeloma should be considered. Failure to investigate for multiple myeloma will lead to delays in diagnosis and treatment. Early diagnosis can be made by demonstrating M proteins in either serum or urine, and showing more than 10% of these malignant plasma cells in the bone marrow.

Keywords: Multiple myeloma; paraparesis; back pain.

1. Introduction

Multiple myeloma or plasma cell myeloma is a haematologic malignancy caused by neoplastic plasma cells which synthesize abnormal amounts of immunoglobulins or immunoglobulin fragments [1]. This proliferation often results in osteolytic lesions, osteopenia and/or pathological fractures as well as hypercalcaemia, anaemia, recurrent infections and renal impairment [2]. Multiple myeloma is part of a spectrum of diseases ranging from monoclonal gammopathy of unknown significance (MGUS) to plasma cell leukaemia [3]. This condition is commoner in blacks with a mean age at presentation of 54 years [4].

In adults, it is the second most common haematological malignancy and accounts for 4.3% of all haematological malignancies in Calabar, Nigeria [5,6]. Typically the clinical manifestations of multiple myeloma vary as a result of the heterogenous biology spanning from the indolent or smoldering phase to the highly aggressive or terminal phase. Bone pain remains a common presentation of multiple myeloma [7].

Our case report highlights the need to consider multiple myeloma as a probable diagnosis while evaluating a patient presenting with paraparesis and backache.

2. PRESENTATION OF CASE

A 55 year old female trader presented to a tertiary health facility in Calabar, southeast Nigeria with complaints of low back pain and progressive difficulty in walking of three months duration. The low back pain was initially mild but increased in intensity and radiated down both lower limbs. The pain was aggravated by movement and there was no paraesthesia. Lower extremity weakness was progressive with associated constipation and weight loss but no urinary incontinence. She had been transfused with two units of whole blood prior to presentation due to severe anaemia.

Physical examination of the patient revealed marked cachexia, pallor, dehydration and oral candidiasis. There was tenderness over the lumbar spines and bilateral lower extremity weakness (3 out of 5) with exaggerated deep tendon reflexes. Sensation to light touch, pain and temperature were intact. Other findings on physical examination were unremarkable.

Investigation revealed anaemia with haemoglobin of 6g/dl. The leukocyte count was normal at 5.3 x10⁹/dl: neutrophils comprised 38% and lymphocytes accounted for 62% of the leukocyte count. The erythrocyte sedimentation rate was markedly elevated at 153mm/hour. The total serum protein was 7.7g/dl (6.2-8.2 g/dl) with hypoalbuminemia of 1.8g/dl (3.6-5.2 g/dl) and increased serum globulin level of 5.9g/dl (1.8-3.6g/dl) with a monoclonal M spike (IgG). Serum creatinine was normal at 68µmol/L (88-177µmol/L). Estimated glomerular filtration rate (GFR) was 108ml/min (100-130ml/min). Serum calcium was at the upper limit
of normal at 2.6 mmol/L (2.1-2.6mmol/L) and corrected calcium was also high at 3.15mmol/L (2.1-2.6mmol/L). There was also hyperuricemia of 350mcmol/L (180–300 mcml/L). Bence Jones proteins were detected in the urine by protein electrophoresis. Human Immunodeficiency Virus (HIV) screening was negative.

Radiographic studies revealed generalized osteopenia and gross reduction in vertebral body height of T6, T9, T11 and L2 on thoracolumbar x-ray. The pedicles were preserved and lytic lesions were noted on the ribs. An x-ray of the skull revealed multiple lytic lesions of varying sizes affecting all parts of the skull (see Fig. 1).

![Skull x-ray showed multiple lytic lesions](image)

Bone marrow aspiration showed clusters of malignant plasma cells constituting 30% of cells seen.

She received blood transfusion and was started on systemic chemotherapy comprising of vincristine, adriamycin and dexamethasone. She was then referred to another facility that offered radiotherapy for treatment of the spinal cord compression.

3. DISCUSSION

This case posed a diagnostic challenge in that the presenting complaints suggested a compressive myelopathy that would be more likely to be due to tuberculosis in our setting. Tuberculosis can affect the vertebral body as Pott’s disease, tuberculous spondylitis, or tuberculoma with paraparesis and bladder disturbances similar to this presentation [7].

Another consideration was a benign or malignant tumor as an extra-medullary tumor could have accounted for the symptom of radicular pain in the absence of sphincteric dysfunction. The common benign tumors that could give rise to paraparesis include osteoblastomas, giant cell tumors, aneurismal bone cysts, and hemangiomas [7]. It may have also been a primary malignancy such as chordoma, chondrosarcoma, lymphoma and Ewing's sarcoma.
Metastatic deposits could have also arisen from breast, lungs, renal cell and genitourinary cancers but the history or physical findings were no suggestive. However, the patient could not afford a further evaluation of the spine via MRI. Both osteoblastic and osteolytic metastases have been reported to cause pathologic fractures and subsequent spinal cord compression [9].

Two causes of paraparesis of toxo-metabolic origin were also considered namely HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP) and neurolathyrism. HAM/TSP is a slowly progressive myelopathy characterized by spastic lower limb weakness or paraparesis, hyperactive reflexes, and sphincter dysfunction [10]. A significant proportion of TSPs is associated with HTLV-I while the rest remain idiopathic or at least HTLV-I seronegative [11]. Neurolathyrism on the other hand is a neurologic disorder caused by excessive ingestion of Lathyrs species. Lathyrs often presents relatively rapidly after a prolonged period (months) of ingesting large amounts of the grain, often in the setting of malnutrition [12]. Lathyrs is characterised by pain or cramps in the legs or in the region of the lumbar spine followed by lower extremity weakness, sphincter dysfunction and permanent spastic paraparesis [12]. Following cessation of intoxication and the development of spasticity, the pains and the sphincter dysfunction usually subside [13].

Multiple myeloma is an incurable malignancy with a high incidence of spine involvement [7]. A study in Nigeria has shown the common presentation of multiple myeloma to be bone pain, low back pain, weakness, fever, weight loss, inability to work and bleeding [14]. The incidence of bone pain from osteolytic lesions ranges from 58% to 66% of patients with multiple myeloma [7]. Spinal cord compression following vertebral compression fractures or vertebral plasmacytoma comprises 5% of the presentation of multiple myeloma [7]. The aetiology of multiple myeloma is unknown but some studies have suggested the pivotal role of viruses in the development of multiple myeloma [15]. Diagnosis of multiple myeloma involves demonstrating the monoclonal immunoglobulins in the serum or urine, demonstration of more than 10% of malignant plasma cells in the bone marrow with or without the end organ effects like anaemia, hypercalcaemia or renal impairment. The anaemia may result from defective erythropoiesis due to insufficient erythropoietin production, invasion of bone marrow by myeloma cells, autoimmune haemolysis, high levels of IL-6 that can suppress erythropoiesis as well as mucosal bleeding that could result from platelet coating by M-protein [13].

Hypercalcaemia is seen in about 28% of multiple myeloma cases and can result from multiple mechanisms. Firstly, myeloma cells produce various cytokines including TNF-β and IL-6 that activate osteoclasts and lead to calcium washout from bones to the bloodstream. Secondly, some studies showed that myeloma cells may secrete parathyroid hormone-related peptide similarly to other malignancies like squamous cell lung carcinoma. Thirdly, serum calcium may be falsely elevated because of binding to immunoglobulins [16]. Renal impairment can be the consequence of hypercalcaemia, hyperuricemia, light deposition in the tubules, amyloidosis or recurrent infections as well as the toxic effects of some of the medications used in the treatment.

Currently, it is advocated that treatment of symptomatic patients should commence immediately [1]. Induction therapy can be done with thalidomide, lenalidomide and bortezomib. This can be combined with hematopoietic stem cell transplantation in patients under the age of sixty five without co-morbidities [17]. For those older than sixty five years of age, more conventional medications can be combined with thalidomide, lenalidomide or bortezomib [18].
The prognosis of multiple myeloma patients with CNS involvement is poor with a median survival of 1.5-2 months from diagnosis [19]. The prognosis can improve significantly with radiotherapy for spinal cord compression as myeloma is an extraordinarily radiosensitive lesion [20]. Douglas and colleagues recently published a new survival score that personalizes the treatment of patients with SCC from myeloma [20]. The leading cause of death in patients with multiple myeloma accounting for up to 54% of cases is infection as a result of granulocytopenia, immunoparesis and suppression of CD4+ cells [10].

4. CONCLUSION

In the evaluation of a patient with paraparesis and backache, multiple myeloma should be considered as a differential diagnosis. A failure to investigate for multiple myeloma multiple myeloma will lead to delays in diagnosis and treatment. Spinal cord compression following vertebral compression fractures or vertebral plasmacytoma represents a rare but devastating complication. Early diagnosis is possible and median survival can thus be extended. A high index of suspicion is thus necessary to prevent its misdiagnosis especially in settings of high tuberculosis burden.

In the treatment of multiple myeloma, a multidisciplinary approach necessitating referrals to other medical units can be adopted. Clinically trained and competent medical practitioners are required to achieve this while limiting loss to follow up.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this case report and accompanying image.

ETHICAL APPROVAL

The Health Research and Ethical Committee of the University of Calabar Teaching Hospital gave approval for this report to be written. Written informed consent of the patient in question was obtained before proceeding.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


