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Non Secretory Multiple Myeloma With Paraplegia - A Rare Case Report

Medical Science

KEYWORDS : Non Secretary Multiple Myeloma , Paraplegia , Metastasis , Lytic bone lesions, Plasmacytosis.

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ABSTRACT

A 42 year old lady presented to us with sudden onset flaccid paraplegia. Spinal magnetic resonance imaging showed multiple lytic and sclerotic lesions at various levels. Thorough work up for metastasis with unknown primary and skeletal survey were performed which ruled out the evidence of any primary malignancy. The bone marrow examination showed plasmacytosis , which confirmed the diagnosis of Multiple Myeloma (Non Secretory variant) . The patient was subsequently started on steroids and chemotherapy for myeloma. Non Secretory Multiple Myeloma (NSMM), is a rare variant of the classic form of MM which shows plasmacytosis & skeletal lytic lesions but no monoclonal gammopathy in serum / urine. To our best knowledge this is the first case , we are reporting from India, of NSMM with paraplegia with diffuse osteosclerosis & osteolytic lesions.

INTRODUCTION:

Multiple Myeloma(MM) is a B-cell malignancy characterized by accumulation of monoclonal plasma cells. It accounts for 1% of all malignant diseases and represents about 10% of all hematological malignancies.1 Reported incidence of NSMM is 1-5% of all the MM cases.2 Typically, the disease involves bone marrow and breaks through the cortex , invading the surrounding tissue. Usually, MM is a widespread and multicentric disease, with the most common localization being the spine. Therefore, collapse of vertebral bodies with narrowing of the spinal canal and circumscribed tumor extension into the adjacent epidural space is one of the common complications of this disease.3 Spinal cord compression occurs approximately in 5% of patients with MM.4 We report a case of MM that caused paraplegia without collapse of vertebrae/ tumor mass but presented with features of non- compressive myelopathy due to the infiltration of Myeloma cells & degeneration of Spinal cord.

CASE REPORT :

A 42yr old female patient with history of fatigue & vague body pains from 1 year, suffered a severe back pain associated with pain & heaviness in both lower limbs for 1 week , now presented with sudden weakness of both lower limbs,associated with sensory loss & bladder and bowel incontinence. On examination, patient was conscious & coherent. She was of thin built, moderately nourished. Pallor was present and her vitals were stable. Neurological examination revealed a complete flaccid paraplegia; weakness was also involving trunk muscles and loss of superficial & deep reflexes in both lower limbs, abdominal reflex absent. All modalities of sensations decreased (nearly 75% loss), below the level of L1-L2. Plantars were non-responsive both sides. At this point, we were of an opinion that she had a non-compressive myelopathy i.e; AcuteTransverseMyelitis. Initial laboratory studies revealed a HB % of 8.1 g/ dl, TC-5000cells/cu.mm, PlateletCount:2lakhs, Erythrocyte Sedimentation Rate=30, PeripheralSmear showed Dimorphic anemia. Her Random blood sugar-136g/dl, Serum Sodium=140 meq/l, Potassium=4.1 meq/l, Creatinine=1.5 mg/dl, Urea=46 mg/ dl. On MRI spine, features of Marrow Reconversion, Multiple Mixed Lytic and Sclerotic lesions at various levels of vertebrae , Degenerative/Demyelinating metastatic focus involving central part of spinal cord was observed which was extending from midpart of D3 vertebra to midpart of D4 vertebra.

Figure – 1 : Magnetic Resonance Imaging(MRI) Spine showing a Small Demyelinating metastatic focus{black arrow head} involving spinal cord between D3-D4 vertebrae.

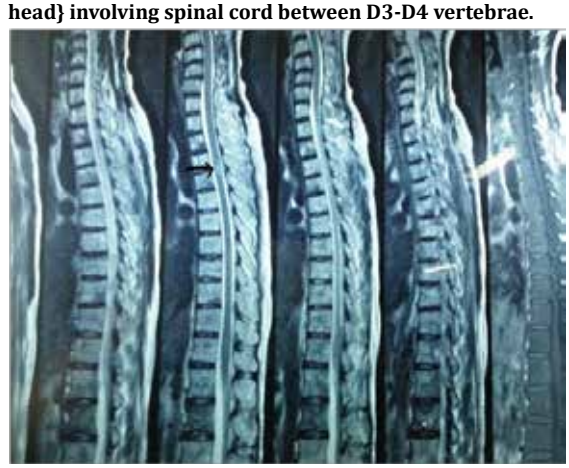
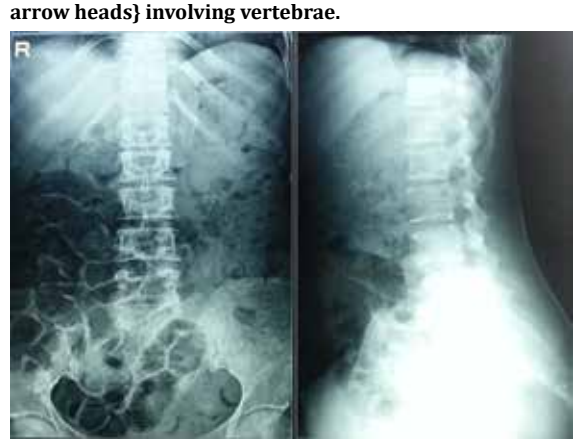


Figure -2 : MRI Spine showing multiple lytic lesions{white arrow heads} involving vertebrae.



Plain radiographs of thoracic and lumbar spine showed only osteoporotic changes but no evidence of fracture/ collapsed vertebrae

Figure – 3 : Plain Radiograph of Spine showing No Fracture/ Collapse of Vertebrae.

Figure -4 : Plain Radigraph of Skull in AP & lateral views showing multiple punched out lytic lesions(Black Arrow Heads) involving both the tables of cranial vault & mandible.

Lumbar puncture was done & CSF findings were normal. Tests for Human Immuno deficiency Virus & Tuberculosis were Negative. At this stage we were left with a differential diagnosis of Multiple myeloma/Metastasis with unknown primary. Then we have gone out with a detailed skeletal survey and work up for identifying any unknown primary with bone metastases. In this course, Ultrasonogram of abdomen and pelvis, Ultrasonogram of neck and mammography for breast, Pap smear were done and found no abnormality. Then we evaluated for Multiple myeloma with Serum Calcium=9.6 gm/dl, Serum AlkalinePhosphatase=1080; Urine Bence Jones proteins were negative,Serum Albumin=3.1 mg/ dl.

Plain radiographs of skull, pelvis and long bones were taken which showed multiple lytic (punched out lesions) in skull, mandible, pelvis with no evidence of fractures.

Figure – 5 : Plain Radiograph of Pelvis & Hip joints showing multiple lytic lesions involving the iliac bones & both the femurs along with osteoporotic changes .

Bone marrow aspiration and biopsy showed Increased Plasma cells(>10%) (Figure -6 here). Serum protein electrophoresis showed mild increase in the alpha-1&2, decreased gamma globulin levels and M-protien was present in small quantities (<2g/dl) which is considered as Negative. Hence, the patient was diagnosed as a case of Non Secretory Multiple Myeloma and as the patient was symptomatic, the chemotherapy regimen of Vincristine, Adriamycin and Dexamethasone along with Pamidronate, Calcium, Vitamin-D, Iron, Folicacid were started and within few days, the patient showed a mild improvement clinically (in the form of regained sensations, mild improvement in lowerlimb power from 0/5 to 2/5). The patient was counselled to receive adjuvant radiotherapy and chemotherapy under the supervision of oncologist and was referred to an oncology centre for follow up.

DISCUSSION : Multiple myeloma (MM) is a malignant proliferation of plasma cells, usually showing diffuse/multiple bone involvement with prediliction of the spine. The median age at diagnosis is 62 yrs constituting only 1% of all the malignant diseases. 1 Only 2-3 % of the cases are reported in patients below the age of 30yrs.5 Non secretory Multiple Myeloma(NSMM) is a rare variant of the classic form of MM in which no gammopathy can be demonstrated in the serum or urine making the diagnosis more difficult.6 It accounts for 1% - 5% of all the cases of MM.2 The clinical presentation & radiological findings of MM & NSMM are similar. A frequent complication of MM is pathological fractures. Bony involvement is typically of lytic in nature.1 Diffuse osteopenia may suggest myelomatous involvemernt before the lytic lesions are apparent. Marrow replacement may be seen in some areas. Most reported cases of NSMM show the presence of lytic lesions on skeletal radiography. A diffuse osteosclerosis has been reported in very few cases in literature.7 So we describe a rare case of 42 yr old Indian woman with NSMM causing diffuse osteosclerosis interspersed with osteolytic lesions & bone marrow biopsy showing plasmacytosis. She also had osteopenia & features of marrow replacement radiographically.

In MM, Spinal cord compression has been reported in 6 – 18% of the patients.8 Since paraplegia may be the first manifestation of MM,it is important to consider this diagnosis in cases of Atraumatic / unexplained paraplegias. Paraplegia is usually caused by the primary involvement of the vertebral body with tumour extension into the adjacent spinal canal.3 NSMM was associated with a higher incidence of neurological presentation even with minimal lytic lesions.9 In these cases , plain radiograph / computerized tomography generally show a large lytic bony lesion or a collapse of vertebral body in the corresponding segment. Magnetic Resonance Imaging has been established as a sensitive method in detecting localized/ diffuse lesions in MM.3,10 Plain X-Ray remains the gold standard imaging procedure for staging newly diagnosed & relapsed MM according to the International Myeloma Working Group Consensus Statement. (Table-1 here) . Also, simple radiography is indicated for the evaluation of skeletal lesions & skeletal survey is performed when MM is in the differential diagnosis. The marrow infiltration process may involve any bone,but the predominant sites include vertebral column, skull, ribs, pelvis, femur & mandible.11,12,13,14,15,16. The typical radiographic appearance is a well-defined/discrete punched-out lytic lesions, solitary/multiple. Permeative lytic lesions with blurred outlines are a rare pattern which is radiologically indistinguishable from skeletal metastases. Involvement of skull, jaw & oral cavity in MM has been often reported In literature. 17. In NSMM, a lower incidence of Hypogammaglobulinemia & lower median percentage of plasma cells in the bone marrow are reported.9 We made a diagnosis of NSMM in this middle aged woman with the help of lytic lesions of bones including Vertebrae, mandible, skull, pelvis & long bones, a plasmacytosis (>10%) in bone marrow. A review of the literature for MM in young - indicates that monoclonal gammopathy is seen in Human Immuno Deficiency Virus(HIV) infected patients due to malignant transformation of more differentiated lymphoid cells.9 Though our patient is negative for HIV serology, it is important to know that MM is added to the list of neoplastic diseases associated with HIV Infection.

Differential diagnosis of such a case is mainly Metastases with

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unknown primary (breast/thyroid/lung/leukemia), which is difficult to differentiate prior to biopsy on the basis of signal intensity & morphology on Magnetic Resonance Imaging.18,19,20. Hence the support of bone marrow was taken as an important consideration in the Diagnosis of NSMM.

The median survival of patients with MM is approximately 2.5 yrs, but with spinal involvement,75% of the patients die within 1 yr of diagnosis.21,22. MM is highly treatable but rarely curable. The major challenge here is , to diagnose & separate the stable, asymptomatic group of patients who do not require treatment from rapidly progressive, symptomatic myeloma who should be treated immediately. Improvements in prognosis have occurred because of the introduction of chemotherapy & newer therapies such as pulse steroids, thalidomide, lenalidomide, Bortezumab & autologous/allogenic stem cell transplantation.23 Paraplegia in MM has frequently been regarded as a strong indication for surgical intervention. The use of Radiation therapy alone has been occasionally reported successful but not sufficiently stressed.8 In the clinical situation of our case , we opined that the patient did not need a spine surgery as she had no cord compression due to fractured/collapsed vertebrae , she needed an adjuvant Radio & chemotherapy. So she was referred to an Oncology centre.

CONCLUSION : While the entity of Non Secretary Multiple Myeloma(NSMM) is rare, its diagnosis may be delayed / unrecognized if too much reliance is placed on the presence of a serum/ urinary M component. NSMM is characterized radiographycally by classic lytic lesions & plasmacytosis/myeloma cells on bone marrow. Also, Paraplegia may be the 1st manifestation of MM, hence it is important to be considered as a Differential diagnosis in cases of Non-traumatic Paraplegia.

MGUS(MONOGAMMOPATHY OF UNKNOWN SIGNIFICANCE)	< 10% Plasma cells in bone marrow	Monoclonal M protein <3 g/dl in serum	End organ damage (renal failure/ lytic bone lesions) Are Absent
ASYMPTOMATIC (SMOLDERING) MULTIPLE MYELOMA	>/= 10% plasmacells	>/= 3 g/dl in serum/ urine	Absent
SYMPTOMATIC MULTIPLE MYELOMA	Plasma cells present (any amount)	Present in serum/ urine/both	Present
NON SECRETORY MULTIPLE MYELOMA	>10% plasma cells	None	Present
SOLITARY/ MULTIPLE PLASMACYTOMAS	Plasma cells at the site of bony/ extra medullary tumor	May / may not be present	None other than localized bone lesions.

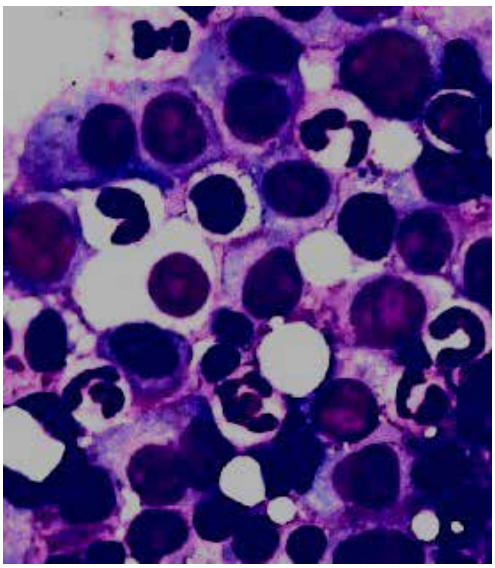

Figure – 6 : Bone Marrow picture showing Plasmacytosis .

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