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Original Research Paper

Medicine

AN INTERESTING CASE OF COMPRESSION FRACTURE DIAGNOSED TO BE MULTIPLE MYELOMA

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ABSTRACT

Multiple myeloma is a malignant proliferation of plasma cells producing a monoclonal paraprotein. Multiple myeloma can present in a range of ways, for example, hypercalcaemia, hyperviscosity, renal failure and bone pains/fractures. We report an unusual presentation of multiple myeloma in the form of compression fracture. Multiple myeloma, a multicentric hematological malignancy, is the most common primary tumor of the spine. As epidural myeloma causing spinal cord compression is a rare condition, its therapeutic approach and clinical results have been reported to be diverse, and no clear guidelines for therapeutic decision have been established.

We report the case of an individual with a progressive lower back ache and bilateral weakness of lower limbs which was progressive. MRI spine done , which showed osteoporotic compression fracture. Other routine investigation revealed anaemia , hypercalcemia, reversal of A/G ratio, azotemia which lead to suspicion of multiple myeloma. The diagnosis of multiple myeloma was made on serum protein electrophoresis and bone marrow biopsy.

KEYWORDS :

Introduction:

Multiple myeloma (MM) is a plasma cell disorder characterized by clonal proliferation of malignant plasma cells in bone marrow. This can be detected by monoclonal protein in the blood or urine, and dysfunction of associated organs. It is classified as asymptomatic or symptomatic depending on the absence or presence of an organ lesion or dysfunction of the affected organ tissue. Its presentation may vary, which makes the diagnosis harder; especially in early stages where the patient has better prognosis [1-3]. The MM represents 1% of neoplastic diseases and 13% of hematologic cancers [1,3,4]. In Western countries, the adjusted annual age incidence is 5.6 cases per 100,000 people. The average diagnosis age is around 70: 37% of patients are under age 65, 26% are between the ages of 65 and 74, and 37% are 75 years of age or older [1]. The risk of infection in patients with MM increases mainly due to polyclonal hypogammaglobulinemia [4], but there are also other reasons such as: reduction of CD4 + T cells, functional impairment of the natural killer cells, abnormalities in the complement system, and occasional granulopenia [5] which constitutes the leading cause of mortality in these patients. The risk of infection exceeds 7-15 times that of a hospitalized patient for any other reason [4,5]. The diagnosis of multiple myeloma is based on the presence of at least 10% plasma cells in the bone marrow sample and the presence of monoclonal protein in serum or urine. In patients with Nonsecretory myeloma, the diagnosis is based on the presence of 30% plasma cells or evidence of plasmacytoma in the bone marrow [3].

Case Report:

A 62-year-old woman with no significant medical background, presented with lower back pain for one month and progressive lower extremity numbness and weakness. She was unable to walk unaided in the last several days and had developed lower limb weakness. A neurological examination revealed bilateral lower extremity weakness with grade 3 strength, decreased deep and superficial sensation, a tingling sensation below the umbilicus and increased knee jerk. Initial laboratory tests revealed a hemoglobin of 9.1 g/dL, white cells of 9100/mm3, erythrocyte sedimentation rate of 120 mm/h, and normal liver function test, with blood urea of 64.80 and serum creatinine of 3.13mg/dl suggestive of renal failure.Other blood tests include:

Serum calcium	9.36mg/dl
Serum Phosphorous	4.18mg/dl
Serum Uric acid	6.18mg/dl
Ionic Calcium	1.31mmol/L
Sodium	144.5mmol/L
Potassium	4.32mmol/L
Blood urea nitrogen	30.26mg/dl
Random blood sugar	97.75mg/dl

Patient's protein report showed inverse A/G ratio.
Total protein- 8.21g/dl
S. Albumin- 2.29g/dl
S. Globulin- 5.9g/dl
A/G Ratio- 4:1

On magnetic resonance imaging (MRI) of the entire spine that was taken to evaluate the neurological condition, overall marrow signal heterogeneity involving the lumbar vertebrae and the pelvic bones *-possibly osteoporotic,* needs correlation with DEXA. It showed old osteoporotic compression fracture of L5 vertebra with the fracture along the superior vertebral endplates. Mildly reduced vertebral body height seen. Mild annular disc bulge at L4-L5 level causing thecal sac indentation. The posterior disc margin abuts traversing L5 nerve roots bilaterally.

Mild annular disc bulge at L3-L4 level causing thecal sac indentation.

Screening of sacro iliac joints reveal : the sacrum , the sub articular portion of ilium and the visualized iliac bones show marked heterogenous T1/T2 hypointensity with subtle patchy hyperintense signal on STIR images.

A bone marrow biopsy and serum protein electrophoresis was performed due to findings of an A/G ratio reversal, anemia, hypercalcemia, osteoporotic changes and azotemia on laboratory tests.

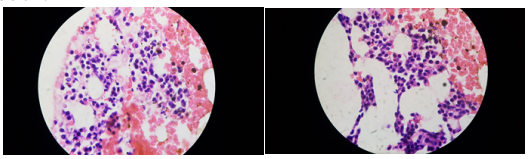
Tumor markers (CEA, PSA, CA 19-9, CA-125, and AFP) were demonstrated to be within normal range. On serum protein electrophoresis, an M-spike was present in the gamma globulin fraction, and the concentration of M-spike was 5.61 g/dL. Serum immunoelectrophoresis and immunofixation electrophoresis revealed monoclonal gammopathy immunoglobulin A(IgA), lambda type. On a quantitative immunoglobulin test, the immunoglobulin G level was 5.11 g/L (normal range is 7 to 16 g/L), the IgA level was16.1 g/L(normal range is 0.7 to 4 g/L), and the immunoglobulin M level was <0.17 g/L (normal range is 0.4 to 23 g/L).

Bone marrow aspiration showed plasma cell myeloma. Biopsy
The above-mentioned results of bone biopsy, electrophoresis, immunoelectrophoresis, and immunofixation electrophoresis proved the diagnosis of Multiple Myeloma.

The findings of multiple punched out lesion in the skull and multiple osteolytic lesions over the spine on the radiological examination were matched with MM (IgG, λ chain).

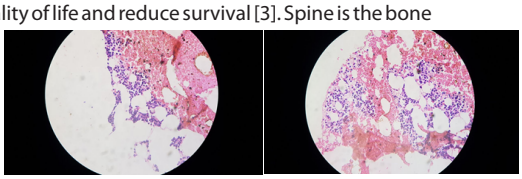
High-dose steroid therapy (dexamethasone, 40 mg/day) and initial management with fluids, anti hypertensives , and bisphosphonates were started for the patient.

The patient was referred to another hospital, where she received VAD(vincristine, Adriamycin, and dexamethasone) radiation for compression fracture, chemotherapy and bone marrow transpl antation.



Discussion:

Multiple myeloma (MM) is a clonal B-cell disorder characterized by proliferation and accumulation of B-lymphocytes and plasma cells in the bone marrow and, more rarely, at extramedullary sites. Its annual incidence is 6/100000 in western countries, thus representing the second most common hematological malignancy after non-Hodgkin lymphomas [1]. Bone disease occurs in approximately 80% of patients with newly diagnosed MM, and in 70% of the cases bone pain is the first symptom to be reported at disease onset [2]. Pathological fractures, osteolyses, osteoporosis or, in general, skeletal-related events (SRE), that include also the need for radiotherapy or surgery to the bone, can severely impair patients quality of life and reduce survival [3]. Spine is the bone



frequently affected by MM-related lesions [4]. Vertebral lesions can result in pain, permanent deformity, kyphosis, walking impairment, permanent disability, or paralysis.

Normal bone homeostasis is maintained by a balanced and continuous remodeling process performed by the coordinated activity of osteoclasts and osteoblasts. Osteoclasts are macrophage derived cells that interact with bone surface with a highly specialized portion of their cell membrane called ruffled border and produce metalloproteinases and other proteolytic enzymes capable of degrading bone matrix [5]. Osteoblasts are mesenchymal derived cells that produce bone matrix and finally differentiate to osteocytes [6]. The mechanism that causes bone disease in multiple myeloma is based upon the fact that neoplastic plasma cells, either directly or indirectly through their interaction with bone marrow stromal cells, induce an alteration in the mechanisms of bone remodeling, as demonstrated by in vitro coculture experiments [7], so that bone resorption is promoted (increased osteoclast activity) and bone formation is inhibited (reduced osteoblast activity). It is well known that osteoclasts are recruited and undergo normal maturation through the interaction of their receptor RANK (receptor activator of nuclear factor κB) with its ligand (RANK-L) produced by stromal cells, preosteoblasts, and activated T-lymphocytes [7]. The activity of RANK-L is balanced by the presence of its decoy receptor, osteoprotegerin (OPG) produced by stromal cells, and preosteoblasts [7, 8]. In MM, osteoclast activity is promoted by an increased production of RANK-L by stromal cells and preosteoblasts, a reduced production of OPG, and the upregulation of proosteoclastogenic cytokines such as Interleukin 1 (IL1)-alpha, macrophage-colony stimulating factor (M-CSF), and macrophage inflammatory protein (MIP)-1-alpha [7, 8]. This latter cytokine can activate monocytes, thus recruiting osteoclast progenitors and promoting their differentiation to mature osteoclasts [9]. Another recently identified proosteoclastogenic cytokine is activin A, a tumor-growth-factor- (TGF-) beta family member, that promotes osteoclast differentiation and inhibits osteoblast maturation [10]. The activity of osteoblasts is further reduced as malignant bone marrow plasma cells can express and secrete DKK-1, a soluble inhibitor of wnt signaling inhibitor that could potentially impair the maturation of osteoblasts [11]. Another mechanism that could contribute to impair osteoblastogenesis is the reduced production of RUNX-2-CBFA1, a transcription factor that plays a central role in promoting osteoblast maturation [12]. Osteoclasts can in turn stimulate plasma cell growth through an increased production of IL-6 [13, 14], thus contributing to the maintenance of the vicious circle.

Epidural spinal cord compression (SCC) occurs in up to 20% of patients with MM at various disease stages [15]. The pathogenetic mechanisms are induced by displacement and compression of the spinal cord, and this can be caused by either epidural invasion by neoplastic tissue arising from a vertebral mass, as described above, or by osseous fragments protruding from a fractured vertebral body. Pain is the first and more common presenting symptom [16, 17]. It is generally a mechanical pain caused by periosteal infiltration of the vertebrae, it becomes more intense in case of cough or labor, and it is further exacerbated when exerting pressure on the spinous processes. Radicular pain can also be present [16, 17]; this can be caused by nerve-root compression and it is perceived according to the dermatomal distribution of the nerve root. Motor dysfunction is the second more frequent symptom of SCC. Patients complain about weakness of lower limbs, in particular when walking or going up the stairs. Sensory symptoms such as paresthesias, tingling, or numbness can occur simultaneously or after motor dysfunction; they usually precede autonomic-sphinteric symptoms that are usually represented by bladder dysfunction [16, 17]. Prompt recognition of these symptoms and subsequent intervention is mandatory as the picture invariably proceeds to paralysis that is frequently irreversible [18]. The gold standard diagnostic procedure to evaluate SCC is spinal magnetic resonance imaging (MRI), which allows a clear identification of bone lesions, tumor masses, and neural alterations [19]. Regarding therapeutic approaches, decompressive laminectomy was frequently performed in the past but its use is now abandoned due to the residual instability of the vertebral column, to the possible delay in the beginning of antimyeloma therapy after surgery and, above all, to the sensitivity of neoplastic cells to steroids and radiotherapy, that now represent the mainstay of the treatment of SCC [16, 20]. High-dose steroids, such as Dexamethasone at doses of 40–60 mg/day for 4–6 days must be soon initiated upon recognition of SCC, aiming at obtaining both a plasmacytolitic and an antioedema effect. Radiotherapy, either 30 Gy in 10 fractions or shorter courses [20], must be also administered early, as an optimal and long-lasting local control of the disease can be achieved.

Conclusion:

We believe that better awareness of the rare clinical presentation as spontaneous vertebral compression fracture of Multiple myeloma can facilitate earlier diagnosis and earlier treatment.

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