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Multiple Myeloma Presenting with A Large Bone Swelling& Review of Literature – A Case Report

KEYWORDS: solitary bony lesion, multiple myeloma, plasma cell infiltration

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ABSTRACT *Multiple myeloma is a hematological malignancy with plasma cell infiltration of bone marrow and carries a poor prognosis. Solitary bone plasmacytoma is the precursor of multiple myeloma, which usually progress to the later in 2-3 years. Early progression depends on certain factors like the size of the lesion. Early diagnosis and appropriate therapy favours the outcome of the patient. Here we present a case of multiple myeloma presenting as a solitary large bony lesion and also review the literature on multiple myeloma to highlight the need for an early diagnosis and treatment.*

Introduction:
Multiple myeloma is a neoplastic monoclonal proliferation of plasma cells, characterized by triad of bone marrow infiltration by plasma cells, lytic bone leisions and presence of M protein in serum or urine. Other common features include anemia, renal failure and bone pain[1]. Patients commonly presents with bone pain or pathological fractures or as an incidental osteolytic lesions on routine diagnostic imaging for other conditions. It is very rare for a case of multiple myeloma to present as a large cystic to mixed consistency space occupying leision. Solitary bone plasmacytoma (SBP)is a precursor of multiple myeloma(MM) with a good prognosis involving a single bone leision with no or low plasma cell infiltration of bone marrow (<5%). Multiple myeloma follows a course of disease from relatively benign monoclonal gammopathy to symptomatic multiple myeloma. Diagnosis of disease at an early stage or level improves the prognosis and is associated with good outcome. Here we report a case of multiple myeloma which was missed at the early stage of SBP by other medical professionals and landed to us in late stage of MM.

Case report:
A 60 year old female patient presented to our outpatient department with complaints of swelling over the scalp for the past 1 year, for which she was under consultation to many local medical professionals , who advised her surgical excision. Patient denied any history of swelling in other areas. The swelling was gradually progressive and attained the present state and was painless. She has no complaint of cough or dyspnea. She is not a smoker or an alcoholic. She had no past medical history and was on no medications. On examination she was conscious and coherent. A large cystic to mixed consistency , non tender, immobile lesion was found on the left parietal area. Neurological and other system examination did not reveal any significant findings.

Fine needle aspiration cytology of the lesion showed plenty of plasma cells and biopsy of the same confirmed it(figure 1). A provisional diagnosis of SBP was thought and investigative workup was started. Computed tomography of brain revealed other osteolytic lesions along with this large solitary, bone eroding lesion with mass effect over cerebrum(figure 2). Bone marrow biopsy of the patient showed more than 30% plasma cell infiltration(figure 3). She was found to be anemic with hemoglobin of 7.8gm%, normal serum calcium (8.9mg/dl) and a serum creatinine of 0.6 mg/dL. Serum protein electrophoresis showed a reversal of albumin to globulin ratio(0.42). M peak (monoclonal protein) was found to be 5.28g/dl. Total IgM was 33.0mg/dL, IgG 693 mg/dL and IgA was 5970mg/dL with albumin of 3.03gm%(figure 4). This reflects that it is an IgA myeloma with only a marginal decline in uninvolved immunoglobulins. Her serum Beta2 microglobulin level was 5801ng/mL, falling into stage III MM with poor prognosis. On the basis of above investigations she was diagnosed to be a case of multiple myeloma presenting with solitary bone leision. Treatment was planned with glucocorticoids and a chemotherapeutic agents vincristine and doxorubicin. But the patient is not willing and had left to a higher institute.

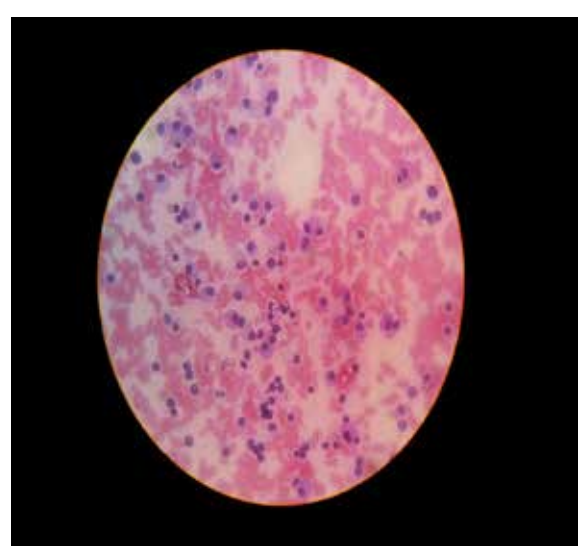

Figure 1: Microscopic examination of the biopsy from

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lesion showing plenty of plasma cells(cells with eccentricnucleus with perinuclear halo)

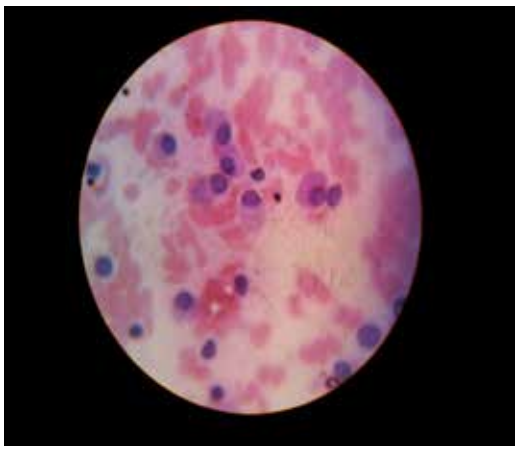

Figure 2: Bone marrow biopsy showing more than 30% of plasma cells in the nucleated cells

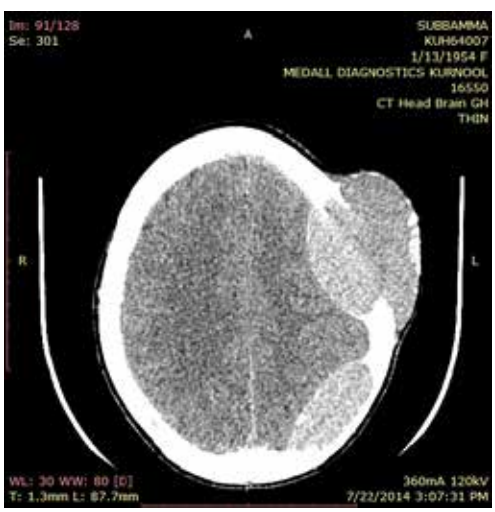

Figure 3: Computed tomography of brain showing other osteolytic lesions along with this large solitary, bone eroding lesion with mass effect over cerebrum

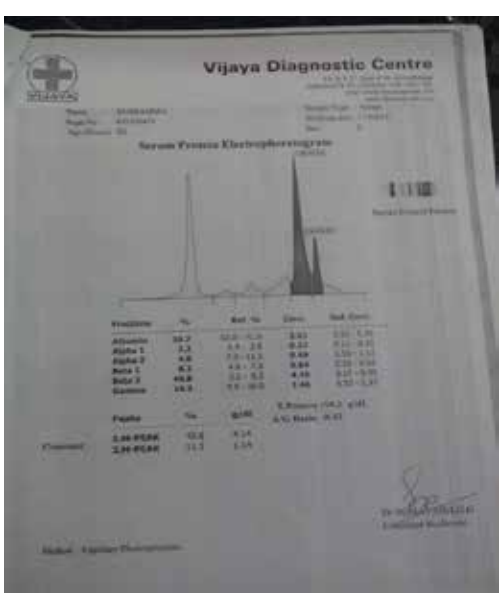

Figure 4 : Serum protein electrophoresis showing monoclonal m band and other proteins.

Discussion:

Multiple myeloma, is one of the plasma cell dyscrasias and refers to an incurable clonal B-cell malignancy with an annual incidence of 1% of all malignancies and 10% of all hematological malignancies[2].

Plasma cell dyscrasias can be subdivided into the following heads:

- Monoclonal gammopathy of unknown significance (MGUS)
- Plasmacytoma—solitary mass of neoplastic monoclonal plasma cells in either bone(SBP) or soft tissue (extramedullary)
- Asymptomatic myeloma
- Symptomatic myeloma.

This classification depends on plasma cells on bone marrow biopsy, monoclonal paraproteins, symptoms like anemia, renal failure, hypercalcemia etc… This classification represents a spectrum of disease progression than separate entities. The prognosis depends on the class of the disease in which it was diagnosed.

Monoclonal gammopathy of unknown significance is a premalignant condition with an annual incidence of 3.2% in patients above 50 years of age. Approximately 1–2% of these patients develop multiple myeloma every year. It is characterized by a monoclonal paraprotein band (M-protein) less than 3 g/dL ,plasma cells less than 10% on bone marrow examination and no evidence of hypercalcemia, renal failure, anemia or bony lesions.

A solitary bone plasmacytoma is a single area of bone destruction due to clonal plasma cells with bone marrow plasma cell infiltration not exceeding 5% of all nucleated cells with absence of any bone lesions, anemia or hypercalcemia or renal failure. It affects <5% of patients with plasma cell myeloma. Two thirds of the patients are men with a median age of presentation of 55 years about 10 years younger than patients with MM. Electrophoresis of serum and urine samples reveals monoclonal protein in 24-72% with SBP, although the levels of the protein are much lower than those patients with MM. with disease progression, monoclonal protein may be found in serum or urine in some patients[3]. The preserved level of uninvolved immunoglobulins in SBP, provide evidence that tumour load is low. SBP often represents an early manifestation of MM in some cases. The median time of progression to MM is 2-3 years. Size of the leision predict conversion to MM[4].

Asymptomatic multiple myeloma is an intermediate phase in the spectrum of multiple myeloma and is also known as smoldering myeloma. It is characterized by serum paraprotein greater than 3 g/dL [and/or] clonal plasma cells greater than 10% on bone marrow biopsy and no myeloma-related organ or tissue impairment viz. Hypercalcemia, Renal insufficiency, Anemia and Bone lesions (CRAB).

The average duration of progression from smoldering myeloma to symptomatic disease is less than 2 years.

A progressive disease was defined by an elevation of serum myeloma protein to atleast 5.0g/dl, an unequivocal increase in size or number of bone lesions or an obvious complication of myeloma such as fracture, anemia, hypercalcemia or renal failure. The dominant prognostic factors predictive of early progression are serum monoclonal pro-

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tein level above 30g/L, IgA heavy chain type, Bence Jones protein excretion value above 50mg/day with median time to progression of 17 months.

Symptomatic multiple myeloma as defined by International myeloma working group

(IMWG) in 2003 and subsequently revised in 2009, the criteria for symptomatic multiple myeloma includes:[5]

- Clonal plasma cells greater than 10% on bone marrow biopsy or (in any quantity) in a biopsy from other tissues (plasmacytoma)
- A monoclonal protein (paraprotein) in either serum or urine
- Evidence of end-organ damage related to the plasma cell disorder (commonly referred to as "CRAB" symptoms):
  - Hypercalcemia (> 10.5 mg/dL or > 0.5 mg above normal limits)
  - Renal insufficiency attributable to myeloma (creatinine > 2 mg/dL)
  - Anemia (hemoglobin <10 g/dL or <2 g/dL below normal limits)
  - Bone lesions (lytic lesions or osteoporosis with compression fracture)

Often patients presents with symptoms of bone pain, osteoporosis, pathological fracture or as an incidental finding on routine diagnostic imaging. It is very rare for a case of multiple myeloma to present as a large space occupying bone lesion. All patients of multiple myeloma should undergo a battery of investigations which would aid in diagnosis as well as direct prognosis and monitoring.

These include-

- Complete and differential blood counts
- Serum albumin, serum calcium, serum creatinine
- Serum β2-microglobulin, C-reactive protein, lactate dehydrogenase (LDH)
- Quantitative immunoglobulins
- Free light chain assay
- Serum and urine electrophoresis
- Serum protein immunofixation
- Radiological skeletal bone survey
- Cytogenetics, fluorescent in situ hybridization (FISH)
- Gene expression profiling (GEP).

Monoclonal gammopathy of unknown significance and asymptomatic myeloma are both premalignant condition with a definite proportion transforming into overt multiple myeloma every year. It is imperative that monitoring of such patients be undertaken at regular intervals so as to identify and arrest the disease at an early stage.[6]

An international staging for system for multiple myeloma based on serum beta 2 microglobulin level was devised which is as follows[7],[figure]. Therapy for different classes of disease differs. For MGUS no therapy is needed. For SBP treatment of choice is radiotherapy. For multiple myeloma conventional therapy include glucocorticoids, melphalan, chemotherapeutics like doxorubicin, vincristine etc.. Novel therapies include immunomodulators like thalidomide, lenalidomide and a proteosome inhibitor like Bortezomib.

In our case the patient presented with a large cystic to mixed consistency lesion over the scalp which on biopsy showed plasmacells and on subsequent evaluation diagnosed as MM. She had the same lesion for about a year, but she was all been missed in her diagnosis before our consultation. If it was being diagnosed earlier in the stage of SBP, there might have been a chance for radiotherapy and a favourable outcome. Now she landed in a progressive disease with bad prognosis. This clearly shows how a delay in diagnosis, particularly in a disease like multiple myeloma costs the life of patient. Eventhough MM is a malignant one early diagnosis in MGUS or SBP level and appropriate therapy and follow up prolongs the life of the patient. We present this case to review the literature of multiple myeloma and educate the need for early diagnosis and intervention.

Conclusion:

Multiple myeloma a malignant plasma cell disorder has a spectrum of classes with worsening prognosis. The earlier the diagnosis, the better will be the outcome. High index of suspicion and complete investigative work up is necessary to make a diagnosis, stage the disease and choose the modality of treatment.

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