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Rare Atypical Presentation of Multiple Myeloma with Ataxia and Intracranial Plasmacytoma

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Abstract

Plasmacytomas are accumulation of clonal plasma cells. It can be osseous or extra medullary. We report a case of 56 year old man, who presented with profound neurological symptoms due to an intracranial soft tissue mass, which was diagnosed as dural plasmacytoma impinging the cerebellar area and was found later to be associated with multiple myeloma (MM). Most common clinical presentation of MM is anemia, bone pain, pathological fractures, infection and spinal cord compression etc. Atypical presentation can also be a part of manifestation in MM, especially in those, with involvement of rare extra medullary site such as central nervous system (CNS).

Keywords: Extramedullary myeloma, Intracranial dural plasmacytoma , Plasma cell neoplasm, Multiple myeloma, Ataxia, Revised International Staging System (R-ISS), International Myeloma Working Group (IMWG), Serum β2 microglobulin, Lactic Dehydrogenase

Introduction

MM is a malignant entity in plasma cell dyscrasias. There is monoclonal proliferation of plasma cells that can either occur in the bone marrow (osseous) or in soft tissue extra medullary myeloma (EMM). MM is characterized by osteolytic lesion, anemia, hypercalcemia and renal failure / end organ failure[1]. Accumulation of clonal plasma cells is known as plasmacytomas. It constitutes less than 5% plasma cell dyscrasias and about 25% of them are associated with MM [2,3]. CNS involvement is extremely rare and accounts for less than 1% cases.[4,5] Extra medullary plasmacytomas may manifest as primary disease or in association with MM. It can present in extreme rare site of central nervous site or may occur in the dura, leptomeninges . We report a case of 56 year old man with dural plasmacytoma in the cerebellar area with MM, which was diagnosed later on detail investigations.

Case Report

A 56 year old male was admitted at neurology deptartment with complains of walking difficulty for 2 months, pain in bilateral throrax for 3 months and vomiting for 1 month. He had low backache since 10-12 years, which was managed with local maneuver at his village. On neurological examination, he had slow, broad based ataxic gait with tremors and reduced bilateral arm swing. Neurological examination revealed hypotonia, reduced fine motor function, bradykinesia of grade 1, gross reduction in muscle power, bilateral reduced plantar reflexes. He was provisionally diagnosed as parkinsonism with prolapsed, herniated, or extruded intervertebral disc (PIVD). Therefore, he was advised for Magnetic Resonance Imaging (MRI) of brain and whole spine. Vitals were within normal limits. Liver, spleen, lymph node were unremarkable.

The blood investigation revealed hemoglobin of 9.3 gm/dl, total leucocyte count of 6,800 cells/microliter and platelets of 2,14,000/microliter. The peripheral smear showed microcytic, hypochromic anemia, anisocytosis and rouleaux formation but no atypical cell was found. Thyroid and liver function was normal. MRI of brain showed multiple lytic lesions involving all calvarial bones (frontal, bilateral parietal, temporal and occipital bone) with a soft tissue component, measuring 3.4*3.3 cm at right side of occipital bone indenting right cerebellar hemisphere, which was radiologically reported as metastasis (Figure 1. A, B, C). The patient was referred to medical oncology for further evaluation for malignancy and its further management.

Anemia, rouleaux formation in peripheral smear and multiple osteolytic lesions in the skull provided a hint, so as to rule out MM. MRI of spine showed extensive lytic lesions involving all vertebral bodies and posterior elements. Skeletal survey revealed osteolytic lesions in ribs, sternum, pelvic bones, upper end of femur and sacrum. Few more blood investigations were done. Patient had impaired renal function with blood urea 56mg/dl and serum creatinine of 3.55 mg/dl. He had hypercalcemia with serum calcium level of 15.2 mg/dl. Serum albumin was 2.88 gm/dl and serum globulin was 7.81gm/dl with Albumin to Globulin (A/G) ratio was 0.36. Serum LDH was 1100 U/L and protein electrophoresis showed M band of 4.75gm/dl seen in gamma region. Cerebro-spinal fluid (CSF) was paucicellular with few dispersed population of plasmablast cells with occasional mature lymphocytes.

Immunofixation showed monoclonal gammopathy with IgG and kappa. Serum free light chain assay showed kappa light chain of 1300mg/L and lambda light chain of 44.5mg/L and Serum free light chain ratio was 25.21 (Figure 2. A, B, C). Serum Beta2 Microglobulin was 13.5 mg/L. Bone marrow aspiration showed myeloma marrow with 61% plasma cells of those includes plasmablasts also (Figure 2. A, B, C).

Flow Cytometry (FCM) gated 13.6% plasma cells, which expressed CD38, CD138, Cy Kappa, CD81, CD56 and negative for Cy Lambda, CD 45, CD117, CD19, CD20 and CD5 (Figure 3. A, B, C). The patient was diagnosed with MM Revised International Staging System (R-ISS) stage III as per International Myeloma Working Group (IMWG). He had acute manifestation of the disease with severe worsening of neurological symptoms, for which bone marrow biopsy, intra-cranial biopsy from intracranial soft tissue mass and Flouroscent In Situ Hybridization (FISH) was deferred. Aggressive strategy was not adopted due to poor prognosis and the treatment was planned with palliative intent. He received radiation therapy to the brain, cervical and dorsolumbar vertebra and systemic therapy

with bortezomib, dexamethasone and thalidomide. At present, the patient is on treatment and follow up.

Discussion

Most common sites of presentation of extra medullary plasmacytomas are upper respiratory tract (nasal cavity and sinuses, nasopharynx, and larynx) in over 80% cases.[1]The involvement of CNS is an extremely rare location for extra medullary site and accounts for less than 1% of MM patients [5]. MM presenting as an intracranial dural plasmacytoma is very rare. A largest retrospective study from 38 centers across 20 countries was conducted on 172 patients of MM over a period of 10 years. It was found that MM could present in the form of leptomeningeal involvement (57%) or as cerebral mass lesion (53%) or as both (19%)[6]. Another study found a total of 14 cases over a period of 26 years, of which occipital tumor like our case presented were only 3 [4].

The most common presenting symptom in intracranial involvement include extremity weakness, change of mental status, cranial nerve palsies, visual changes, radiculopathy, headache, seizures.[7] Ataxic gait was an unique feature. They are also associated with complex chromosomal translocations, high tumor burden and plasma blasts in peripheral blood [5]. For staging the disease, the R-ISS of IMWG was used [7]. Our case had serum β2 microglobulin > 5.5 mg/L and high LDH, that met the criteria of R-ISS stage III. The prognosis is poor and median overall survival (OS) from time of diagnosis of CNS involvement is between 1.5 - 3 months [8]. Due to reduced response to injectable analgesics, whole spine radiation was given for pain management. The intent of treatment was palliative in our case because of its advanced stage. A long standing complain of low backache was ignored for more than a decade and the neurological manifestation was misinterpreted as Parkinsonism with PIVD. In various literatures, the common agents mostly used in treatment are thalidomide, bendamustine, bortezomib, lenalidomide and new immunomodulatory drugs (IMiDs), all these have shown to increase survival time [9].

Conclusion

Intracranial plasmacytomas may exhibit a benign course. When it is associated with MM at presentation, has an aggressive course of disease with an overall poor prognosis despite of multimodality treatment [4,5]. Overall survival in osteodural plasmacytomas even with newer modalities of treatment is 25 months [9]. Hence the use of novel agents and allogenic transplant in this subset of patients needs further evaluation.

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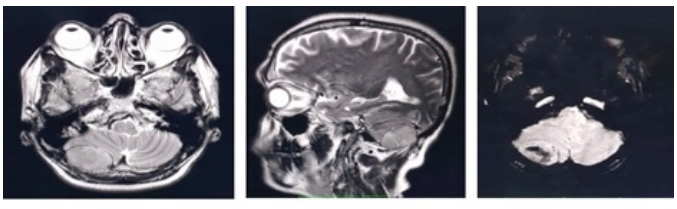
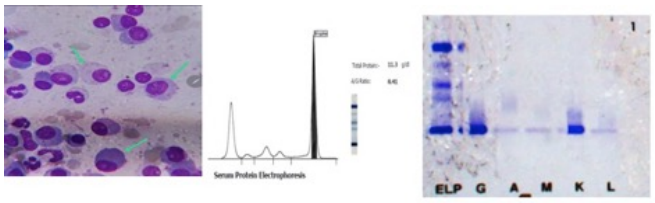
Legend Figures



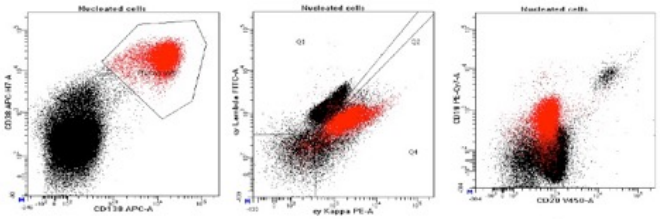
A B C

Figure 1: MRI Brain: (A) Axial T2 section showing soft tissue lesion of size 3.4 x 3.3cm size at the right side of occipital lobe indenting the right cerebellar lobe. (B) Sagittal T2 image showing occipital lytic lesion with soft tissue component. (C) GRE image showing hemorrhage inside the lesion



A B C

Figure 2: (A) Bone marrow aspiration at 100X shows dispersed population of plasmablast large cells with eccentric nuclei, open chromatin with 1-2 nucleoli) and plasma cells, (B) Serum protein electrophoresis with M spike in gamma region, (C) Serum Immunofixation showing monoclonal gammopathy seen with IgG and Kappa.



A B C

Figure 3: Immunophenotyping show atypical plasma cell populations are: (A) Positive for CD38, CD138, (B) Positive for cytoplasmic Kappa and negative for cytoplasmic Lambda, (C) Negative for CD 19.