Case Report

Beyond the Bone Marrow: Extramedullary Multiple Myeloma Mimicking Soft Tissue Tumors – A Case Series

Gurusamy S[1], Arasirajesh[2], Ramasundari Ilambirai M[3]

[1]Assistant professor, Department of Pathology, Tirunelveli Medical college, Tirunelveli, Tamil Nadu, India.[2]Professor, Department of Pathology, Tirunelveli Medical college, Tirunelveli, Tamil Nadu, India,[3]Assistant Professor, Department of Pathology, Tirunelveli Medical college, Tirunelveli, Tamil Nadu, India.

Abstract

Background: Extramedullary multiple myeloma (EMM) is an uncommon manifestation of multiple myeloma, characterized by the proliferation of malignant plasma cells outside the bone marrow. It occurs in approximately 7%–18% of patients and may involve soft tissues. Extramedullary lesions can mimic primary or metastatic soft tissue neoplasms, creating a diagnostic challenge. **Case Series:** We present a case series of patients with secondary extramedullary multiple myeloma presenting as unusual soft tissue masses. The lesions occurred at atypical sites and clinically and radiologically simulated other soft tissue tumors. Histopathological examination, supported by appropriate immunohistochemical evaluation, was essential for establishing the diagnosis of extramedullary plasma cell neoplasm. **Conclusion:** Extramedullary multiple myeloma should be considered in the differential diagnosis of an unexplained soft tissue mass. Recognition of its unusual presentations and appropriate use of histopathology and immunohistochemistry are crucial for accurate diagnosis. Early identification of extramedullary disease is clinically important because of its association with aggressive disease behavior and adverse prognosis.

Keywords: Extramedullary multiple myeloma; plasma cell neoplasm; extramedullary disease; soft tissue tumor; immunohistochemistry.

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INTRODUCTION

Multiple myeloma is a clonal plasma cell malignancy characterized by the uncontrolled proliferation of abnormal plasma cells within the bone marrow, resulting in end-organ damage. Clinically manifested as CRAB features such as hypercalcemia, renal failure, anemia and multiple lytic bone lesions. According to the WHO and the International Myeloma Working Group, the diagnosis of Multiple Myeloma requires ≥10 % clonal bone marrow plasma cells or a biopsy-proven plasmacytoma, in addition to evidence of myeloma defining criteria. These include one or more CRAB features or else biomarkers of malignancy such as a clonal bone marrow plasma cell percentage ≥ 60 %, an involved/uninvolved serum free light chain ratio ≥ 100, or more than one focal lytic lesion on imaging.[1] Extramedullary Multiple Myeloma is a rare and aggressive variant of multiple myeloma in which malignant plasma cells infiltrate tissues outside the bone marrow, including soft tissues and visceral organs. It may occur at initial diagnosis or during relapse, with a reported incidence ranging from 7 % - 18 %.[2,3] Despite improvements in imaging and therapeutic strategies, Extramedullary Multiple Myeloma remains a clinical challenge due to its heterogeneous presentations, poor response to conventional treatments, and poor prognosis.[3,4] Although Extramedullary plasmacytoma (EMM) is increasingly recognized, involvement of soft tissue masses are rare and often misdiagnosed, contributing to delayed treatment. This case series report describes rarecases of secondary extramedullary multiple myeloma clinically presented as lung, breast and soft tissue masses, an exceptionally uncommon sites of involvement. It aims to underscore the diagnostic challenges and clinical implications of atypical soft tissue presentations, emphasizing the importance of early recognition to facilitate timely and appropriate treatment.

CASE 1

A 62 year old female presented with complaints of breathlessness and right-sided chest pain of several weeks duration. There was no significant history of hemoptysis or fever. CT chest showed a mass lesion in the right lung, raising suspicion for primary lung carcinoma.A core needle biopsy was performed from the lung lesion. Microscopic examination showed diffuse sheets of plasma cells with eccentric nuclei, coarse chromatin, and abundant basophilic cytoplasm.Occasional immature forms were identified.Immunohistochemical analysis demonstrated diffuse positivity for CD138. Tumor cells were negative for cytokeratin, thereby excluding epithelial malignancy.In view of the plasma cell morphology, further systemic evaluation was advised. Bone marrow examination revealed increased plasma cells. Serum protein electrophoresis demonstrated monoclonal

Address for correspondence: Dr. Gurusamy S,
Assistant professor, Department of Pathology, Tirunelveli Medical college, Tirunelveli, Tamil Nadu, India.
E-mail: gurusamy208@gmail.com

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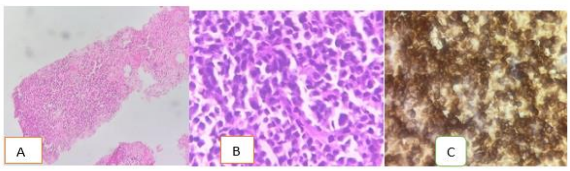
gammopathy.Correlating the histopathological, immunohistochemical, and laboratory findings, a final diagnosis of plasma cell myeloma with pulmonary involvement was rendered.

FIGURE: 1

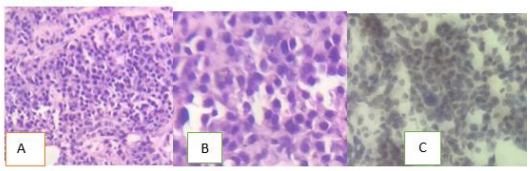


A. H&E section from lung biopsy shows sheets of plasma cells. (4x view)
B. H&E section from lung biopsy shows tumor cells with abundant basophilic cytoplasm, perinuclear hof, larger nuclei with remarkable nucleoli resembling immature plasma cells. (40x view)
C. Immunohistochemical analysis demonstrated diffuse positivity for CD138.

CASE 2

A 50 year old female presented with a palpable lump in the breast for 3 months duration. The swelling was gradually progressive and associated with mild discomfort. There was no history of nipple discharge or constitutional symptoms. Radiological evaluation demonstrated a suspicious breast lesion, and a provisional diagnosis of breast carcinoma was considered. Fine needle aspiration cytology was performed and showed atypical cells suspicious for malignancy. Subsequently, a core needle biopsy was obtained. Microscopic examination revealed diffuse sheets of atypical plasma cells infiltrating the breast tissue. The cells exhibited eccentric nuclei, coarse chromatin, conspicuous nucleoli, and moderate amounts of basophilic cytoplasm. Occasional binucleated and pleomorphic forms were seen. Immunohistochemical analysis demonstrated diffuse positivity for CD138 and MUM1, confirming plasma cell lineage. The histomorphological and immunophenotypic features favored plasmacytoma. Further systemic evaluation was undertaken to exclude associated plasma cell myeloma. MRI revealed multiple lytic lesions involving the axial skeleton. Laboratory investigations showed elevated serum beta-2 microglobulin levels. Based on the clinicopathological, radiological, and laboratory findings, a final diagnosis of extramedullary plasmacytoma of the breast associated with underlying plasma cell myeloma was made.

FIGURE: 2

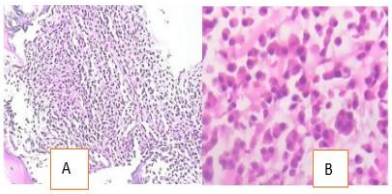


A. H&E section from breast mass shows sheets of plasma cells. (10x view)
B. H&E section from breast shows tumor cells with abundant basophilic cytoplasm, perinuclear hof, larger nuclei with immature plasma cells. (40x view)
C. Immunohistochemical analysis demonstrated positivity for Mum1.

CASE 3

A 55 year old male presented with complaints of back pain and progressive weakness of both lower limbs for several weeks. The patient also had difficulty in walking and restricted movements. There was no significant history of trauma. MRI of the spine revealed a paraspinal soft tissue mass with features suggestive of a malignant neoplasm. Radiological differential diagnoses included soft tissue sarcoma, lymphoma, and metastatic malignancy. CT guided biopsy was performed from the paraspinal lesion. Histopathological examination showed diffuse sheets of plasma cells infiltrating the soft tissue. The tumor cells exhibited eccentric nuclei, coarse chromatin, and moderate to abundant basophilic cytoplasm. Occasional atypical and binucleated plasma cells were identified. Immunohistochemical analysis demonstrated diffuse membranous positivity for CD138, confirming plasma cell lineage. In view of the histopathological findings, further systemic evaluation was undertaken. Bone marrow examination revealed increased plasma cells. Positron emission tomography scan demonstrated multiple metabolically active skeletal lesions involving the axial skeleton. Based on the clinicopathological, immunohistochemical, and radiological findings, a final diagnosis of plasma cell myeloma presenting as a paraspinal mass was established.

FIGURE: 3



A. H&E section from soft tissue mass shows sheets of plasma cells. (10x view)
B. H&E section from soft tissue mass shows tumor cells with abundant basophilic cytoplasm, with larger nuclei. (40x view)

Discussion

Extramedullary multiple myeloma (EMM) is an uncommon and aggressive manifestation of plasma cell myeloma characterized by infiltration of clonal plasma cells beyond the bone marrow into soft tissues or visceral organs. It may be present at initial diagnosis or develop during relapse. Its incidence varies from 7% - 18% of myeloma cases. EMM is clinically significant because it often behaves more aggressively than typical medullary disease and is associated with inferior response to therapy and poor prognosis.[5] The three cases in this series illustrate the protean nature of EMM and its tendency to mimic primary malignancies of the involved site. Pulmonary involvement may simulate primary lung carcinoma, breast involvement may be mistaken for invasive breast cancer, and paraspinal soft tissue disease may resemble sarcoma, or metastatic tumor. These overlapping clinical and radiologic features make diagnosis challenging and frequently delay appropriate and early treatment. Histopathological examination

remains the diagnostic cornerstone. The presence of diffuse sheets of atypical plasma cells with eccentric nuclei, coarse chromatin, abundant basophilic cytoplasm, perinuclear hof, and occasional binucleation should prompt consideration of a plasma cell neoplasm. Immunohistochemistry is essential for confirmation, with CD138 and MUM1 supporting plasma cell differentiation, while negativity for cytokeratin and other lineage-specific markers helps to exclude epithelial malignancy and other mimics.

Extramedullary plasmacytomas can occur in various organs, including the skin, lungs, gastrointestinal tract, bladder, and head and neck. EMM masquerading as a pulmonary nodule is extremely rare and associated with aggressive terminal phase of myeloma.[6]

In review of previous literature only 5% of patients with extramedullary plasmacytomas have coexistent multiple myeloma.[7,8] The occurrence of plasmacytoma in breast, either as an isolated Extramedullary plasmacytoma or as a manifestation of widespread Multiple Myeloma, is infrequent. Breast plasmacytoma represents 1.5% of all plasmacytoma cases.[9-11]

Extramedullary multiple myeloma as a paraspinal soft tissue mass is distinct from those involving visceral organs or lymph nodes. They represent an aggressive manifestation of Multiple Myeloma, marked by the capacity of malignant clones or subclones to proliferate and persist independently of the bone marrow microenvironment.[12]

This aggressive behavior is associated with high-risk genetic alterations, increased proliferation, evasion of programmed cell death, and resistance to treatment.[13]

Breast and pulmonary plasmacytomas are particularly rare, and their presentation often leads to an initial diagnosis of carcinoma. Similarly, paraspinal soft tissue involvement is a recognized but uncommon manifestation of advanced myeloma and usually indicates biologically aggressive disease. Such extramedullary spread reflects the ability of malignant plasma cell clones to survive and proliferate independently of the bone marrow microenvironment.[14]

Treatment depends on whether the disease is solitary or part of disseminated myeloma. Local radiotherapy may be useful for palliation or local control in selected cases, but systemic therapy is required when extramedullary disease is associated with underlying myeloma. Because soft tissue involvement is linked to shorter progression-free and overall survival, early recognition is crucial to avoid unnecessary surgery and to initiate timely myeloma directed therapy.

The median overall survival for all multiple myeloma patients with Extramedullary disease at presentation is less when compared to paraskeletallesions. This is because in Extramedullary lesions like in breast or lungs, the myeloma cells are less dependent on the bone marrow microenvironment and they represent clones with greater ability for dissemination and drug resistance.

Conclusion

Recognition of unusual presentations of Extramedullary plasmacytoma is crucial because treatment strategies differ significantly from those used for primary soft tissue malignancies.

Early biopsy, careful morphologic assessment, immunohistochemistry, and systemic workup are essential for accurate diagnosis.

Early diagnosis can facilitate prompt initiation of chemotherapy, radiotherapy, or targeted therapy and help to prevent complications and hence prognosis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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