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Review Article

Rare Locations of Plasma Cell Tumour: A Single-Centre Experience

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Abstract

Extramedullary involvement, also known as Extramedullary Disease (EMD), represents a highly aggressive variant of plasma cell dyscrasias. It is characterised by the presence of plasma cell clones that proliferate independently of the bone marrow microenvironment. While EMD most commonly affects the skin and soft tissues, in cases of disease relapse, it may extend to internal organs, including the liver, kidneys, central nervous system, chest wall, pleura, and pericardium.

The reported incidence of EMD varies. A comprehensive review of the literature indicates that in newly diagnosed Multiple Myeloma (MM) patients, the incidence ranges from 0.5% to 4.5%. However, in relapsed or refractory MM, the incidence increases markedly, reaching between 3.4% and 14%. Prognosis remains poor, particularly when the paravertebral region is involved, as this often leads to vertebral body fractures that complicate treatment and worsen outcomes.

Current data on therapeutic responses are primarily based on retrospective studies. Therefore, prospective trials are needed to more accurately assess the efficacy of various treatment regimens. This study presents a cohort of patients with paravertebral plasma cell tumours, with a specific focus on tumour location, associated vertebral fractures, available treatment strategies, and clinical responses following induction therapy.

More Information

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Keywords: Plasma cell dyscrasias; Paravertebral location; Therapy; Pathogenesis; Therapeutic response

Abbreviations: MM: Multiple Myeloma; EMD: Extramedullary Disease; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; NMRI: Nuclear Magnetic Resonance Imaging; IMiDs: Immuno-modulatory Drugs; PI: Proteasome Inhibitor; PFS: Progression-free Survival; OS: Overall Survival; ASCT: Autologous Stem Cell Transplantation

Introduction

Multiple Myeloma (MM) is a haematological malignancy characterised by the presence of over 10% clonal plasma cells in the bone marrow, accompanied by clinical evidence of end-organ damage—commonly including hypercalcemia, renal insufficiency, anaemia, and lytic bone lesions. In most cases, plasma cell infiltration is confined to the skeletal system; however, in instances of extramedullary involvement, soft tissue masses develop outside the bone marrow, marking a more aggressive disease phenotype (Table 1).

Methods

A retrospective analysis was conducted on a cohort of patients treated at the Neurosurgery Clinic of the Military Medical Academy in Sofia between 2015 and 2024 (Table 2).

Results

During this period, 14 patients diagnosed with paravertebral extramedullary plasmacytoma were followed. Thoracic vertebral involvement was observed in 57% of cases, while lumbar vertebral involvement was identified in 28% of the patients. Magnetic Resonance Imaging (MRI) served as the primary diagnostic modality in 71% of cases, whereas only four patients underwent Computed Tomography (CT) scans.

At the time of diagnosis, more than 70% of patients presented with clinical and laboratory markers of active disease, including anaemia, renal insufficiency, and either pathological fractures or osteolytic bone lesions. All patients underwent immunohistochemical assessment, which confirmed the diagnosis of plasmacytoma through histological evaluation.

Discussion

This extramedullary variant of myeloma is associated with high-risk cytogenetic features, increased proliferative capacity of malignant cells, resistance to therapy, and evasion of apoptosis [1,2]. Extramedullary plasmacytomas can arise through two primary mechanisms: (1) direct extension

Table 1: Plasma cell neoplasms – extramedullary location (adapted from Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, et al. The International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15:e538–e548).

Plasma cell neoplasm	Definition
Extramedullary disease	An aggressive form of multiple myeloma characterised by the presence of soft-tissue plasmacytomas that result from haematogenous spread
Paraskeletal plasmacytoma	A form of multiple myeloma characterised by the presence of soft-tissue plasmacytomas that occur due to direct growth from skeletal tumours following cortical bone disruption
Solitary plasmacytoma	A single mass of clonal plasma cells (bone or extramedullary) with no or minimal bone marrow plasmacytosis and with no other symptoms than those derived from the primary lesion
Plasma cell leukaemia	A rare and aggressive variant of myeloma characterised by the presence of circulating plasma cells; diagnosis is based upon the percentage (≥20%) and absolute number (≥2 × 109/L) of plasma cells in peripheral blood

Table 2: Retrospective analysis of a series of patients who underwent treatment at the Neurosurgery Clinic of the Military Medical Academy Sofia for the period 2015–2024

Location	Clinical and laboratory characteristics	Immunohistochemistry	Diagnostic method	Therapeutic option
L5 vertebral biopsy, pathological fracture	Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD 56+	MRI	CyBorD
Th8, Th11, L5 vertebral biopsy	Bone lesions.	CD 138+/CD56+	MRI	CyBorD
Biopsy of paravertebral soft tissue mass not involving vertebral bodies. Pathological fractures of Th3-Th5	Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD56+	CT scan	n/a
The vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micro mol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD56+	MRI	n/a
Biopsy of paravertebral soft tissue mass, without evidence of vertebral body involvement	Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micromol/L (>2mg/dL); Bone lesions.	CD 138+/CD56+	CT scan	CyBorD
C7-Th 1 vertebral biopsy	Bone lesions	CD 138+/CD56+	CT scan	n/a
The vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micro mol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions	CD 138+/CD56+	MRI	n/a
L3 vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micro mol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions	CD 138+/CD56+	MRI	n/a
L5 vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micro mol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions	CD 138+/CD56+	MRI	CyBorD
The vertebral biopsy, biopsy of the fourth rib	Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD56+	MRI	CyBorD
The vertebral biopsy	Bone lesions	CD 138+/CD56+	CT scan	n/a
Th8-Th9-Th10 vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micro mol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD56+	MRI	n/a
Th4-Th7 vertebral biopsy	Renal insufficiency: creatinine clearance <40 mL per minute or serum creatinine >177 micromol/L (>2mg/dL); Anaemia: haemoglobin value of >20g/L below the lowest limit of normal, or a haemoglobin value <100g/L; Bone lesions.	CD 138+/CD56+	MRI	CyBorD
Th2-Th3 vertebral biopsy	n/a	CD 138+/CD56+	MRI	CyBorD

from osseous lesions following cortical bone destruction, and (2) haematogenous spread to internal organs, with rare cases attributed to iatrogenic dissemination during invasive procedures [3,4] (Figure 1).

Genetically, these lesions often exhibit high-risk abnormalities, including del(17p), t(4;14), t(14;16), gain(1q21), and overexpression of oncogenes such as MYC and MAFB, alongside the loss of CD56 expression. These alterations collectively indicate a high-risk disease profile [5-9,11].

Imaging plays a pivotal role in the diagnostic workup of MM. Nuclear magnetic resonance imaging (NMRI) remains a widely used modality for evaluating disease within the central nervous system and axial skeleton. However, for the detection of extramedullary disease beyond the central and peripheral nervous systems, functional imaging is essential.

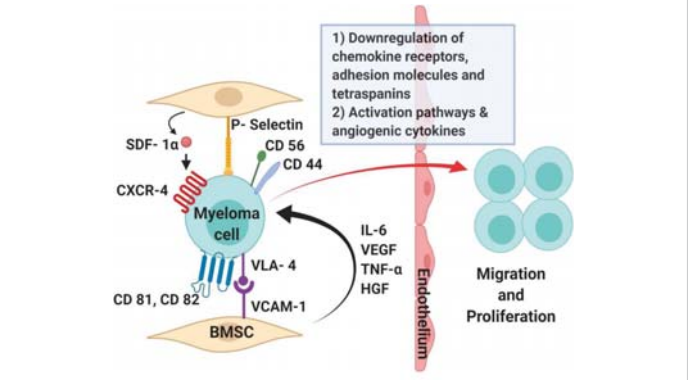

Figure 1: Mechanism of extramedullary dissemination of myeloma. SDF-1- Stromal cell-derived factor-1, CXCR-4- Chemokine receptor type 4, VLA-4- Very late antigen-4, VCAM-1- Vascular cell adhesion protein-1, VEGF- Vascular endothelial growth factor, TNF-α- Tumour necrosis factor-alpha, HGF- Hepatocyte growth factor, IL-6- Interleukin-6. (Adapted from Bansal, R., Rakshit, S., & Kumar, S. Extramedullary disease in multiple myeloma. Blood Cancer J 11, 161 (2021). https://doi.org/10.1038/s41408-021-00527-y).

The International Myeloma Working Group (IMWG) recommends ^18F-FDG PET/CT as the imaging modality of choice for identifying extramedullary disease [13].

Before the widespread implementation of PET/CT, the reported incidence of extramedullary involvement at diagnosis was relatively low, ranging from 1.7% to 4.5% [3]. However, with the advent of advanced imaging, recent studies have shown an increased detection rate, now estimated between 6% and 10% [12-15]. In a cohort study involving 3,744 patients with newly diagnosed plasmacytomas, the overall incidence of soft-tissue involvement was 18.2%, with paraskeletal lesions accounting for 14.5% and true extramedullary disease for 3.7% [16].

Survival outcomes also differ based on disease localisation [17]. Five-year Overall Survival (OS) was reported at 63% for both patients with and without bone-related plasmacytomas at diagnosis. However, five-year disease-free survival was 47% in those with bone-related plasmacytomas compared to 35% in those without. Moreau, et al. further identified the absence of extramedullary foci at diagnosis as an independent prognostic factor for improved progression-free survival and overall survival [18].

Several studies have explored therapeutic options and outcomes in patients with extramedullary involvement in multiple myeloma. One study examined a cohort of 267 newly diagnosed patients treated with Immunomodulatory Drugs (IMiDs) or Proteasome Inhibitor (PI)-based regimens, including 243 patients with paraskeletal soft-tissue plasmacytomas. The reported median Progression-free Survival (PFS) was 26.1 months.

In a retrospective analysis by Batsukh, et al. outcomes were assessed in 64 newly diagnosed patients with soft-tissue plasmacytomas receiving various IMiD- or PI-based treatments [19]. The median PFS for patients with bone-related plasmacytomas was approximately 16 months, while the median Overall Survival (OS) was 27.8 months, indicating a poorer prognosis in this subgroup.

Beksac, et al. conducted a multicentre, multinational retrospective study involving 226 patients with multiple myeloma and plasmacytoma involvement [17]. Among these, 176 patients presented with Extramedullary Disease (EMD), and 50 had paraskeletal plasmacytomas. The entire cohort received a median of two lines of therapy, and 44% underwent Autologous Stem Cell Transplantation (ASCT) following their plasmacytoma diagnosis. In the paraskeletal group, the median PFS was 51.7 months ($p = 0.034$), and the OS had not yet been reached ($p = 0.002$), highlighting a more favourable prognosis in comparison to other extramedullary forms.

Collectively, the findings suggest that paravertebral plasmacytoma involvement is associated with improved PFS and OS relative to other extramedullary localisations. Autologous stem cell transplantation, used as a consolidation strategy, contributes to a more durable therapeutic response. Nevertheless, the presence of adverse cytogenetic features remains a key negative prognostic factor, associated with reduced survival and diminished response to treatment.

The majority of patients received treatment regimens based on proteasome inhibitors. However, treatment data were incomplete for a subset of the cohort. In patients without neurological deficits, pathological vertebral fractures were managed using multi-level percutaneous vertebroplasty [20,21]. This minimally invasive approach provided effective analgesia and allowed for the timely continuation of systemic haematological therapy [22-24].

Despite its benefits, vertebroplasty presents limitations, particularly in cases involving extensive vertebral body destruction or when bone loss has not been previously addressed, increasing the risk of cement leakage [25-30]. In patients with severe vertebral height loss, balloon kyphoplasty may be indicated; however, when multiple vertebral levels are affected, this approach may significantly increase the financial burden due to the need for additional instrumentation sets. We have outlined an example of the surgical management of a patient with multiple vertebral body fractures [31].

Conclusion

Soft-tissue plasmacytomas represent an especially aggressive form of Multiple Myeloma (MM), typically detected either at the time of initial diagnosis or during disease relapse. The primary diagnostic tool for identifying these lesions is Nuclear Magnetic Resonance Imaging (NMRI), which remains both accessible and highly informative. Although low-intensity scanning has not yet been established as a recognised diagnostic method, it serves as a useful alternative when NMRI is not feasible for assessing specific plasmacytoma locations.

Clinical reviews indicate that the thoracic spine is the most frequently affected site for plasmacytomas. The reason for this anatomical predilection remains unclear and warrants further investigation in future studies. Pathological vertebral fractures are common in these cases and often result in significant patient disability. These fractures typically present with axial back pain alone, making them suitable candidates for minimally invasive treatment, such as percutaneous vertebroplasty. This procedure enhances spinal stability, alleviates pain, prevents further vertebral collapse, and reduces the risk of neurological complications—ultimately improving the patient's quality of life.

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