Original Article

Fine-Needle Aspiration Cytology of Extramedullary Plasmacytoma: A Six-Year Case Series

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Abstract

Background: Due to its cytomorphological overlap with lymphoma or metastatic carcinoma and its protean anatomic distribution, extramedullary plasmacytoma (EMP), which accounts for less than 5% of plasma cell neoplasms, usually presents a diagnostic problem. Timely staging and treatment depend on early cytological identification.
Materials and Methods: We retrospectively reviewed 8 cases of extramedullary plasmacytoma (EMP) diagnosed on fine needle aspiration cytology (FNAC). Clinical history, imaging, laboratory data, treatment, and follow-up were retrieved from hospital records. FNAC smear samples were assessed. Cell blocks were prepared in all 8 cases and subjected to immunocytochemistry for CD138, CD38, CD45, and Ki-67 markers. In situ hybridization for κ and λ light chains was done in all cases. Descriptive analysis was performed given the small sample size.
Results: Eight patients (mean age 70.3 years; M:F = 5:3) presented with solitary soft tissue masses ranging from 2.8 to 6.5 cm. Sites included paranasal sinus (2), axilla (1), breast (1), sternum (1), orbit (1), scapula (1), and subcutaneous thigh (1). FNAC smears showed a spectrum from mature plasma cells to plasmablast-rich populations. Immunocytochemistry revealed monotypic κ-restriction in five cases and λ in three. Over a median follow-up of 15.5 months, five patients remained disease-free, two progressed to multiple myeloma, and one was lost to follow-up.
Conclusion: FNAC, combined with light-chain assessment and meticulous clinico-radiological correlation, is a rapid and reliable modality for diagnosing EMP even in resource-constrained settings. Recognizing plasmablast-rich patterns is essential because they herald aggressive behavior and a higher risk of progression to myeloma.

Keywords: Extramedullary plasmacytoma; Fine-needle aspiration cytology; Plasmablast; Light-chain restriction; Radiotherapy.

Introduction

Plasma cell neoplasms cover a broad clinical and pathological range, from asymptomatic monoclonal gammopathy of undetermined significance (MGUS) to plasma cell leukemia and advanced multiple myeloma. Among these, extramedullary plasmacytoma (EMP) is a rare entity characterized by monoclonal plasma cell proliferation occurring outside the bone marrow, in the absence of systemic disease. EMP accounts for approximately 2–4% of all plasma cell malignancies and $< 1\%$ of head and neck tumours [1]. While the upper aerodigestive tract remains the prototypical site, EMP may occur in a variety of locations including lymph nodes, skin, orbit, breast, soft tissue, and bone, often mimicking metastatic or infectious lesions [2]. Although tissue biopsy remains the gold standard for diagnosis, fine needle aspiration cytology (FNAC) has emerged as a valuable frontline modality, especially for superficial or image-guided lesions. Cytological features such as eccentric nuclei, “clock-face” chromatin, basophilic cytoplasm, and perinuclear hofs are well recognized in mature plasma

cells. However, EMP displays significant cytological heterogeneity. Plasmablast-rich variants, with prominent nucleoli and nuclear pleomorphism, can closely show similarity in high-grade lymphomas, poorly differentiated carcinomas, or sarcomas [3]. Such overlap increases the risk of diagnostic errors, specifically delaying systemic evaluation or resulting in unnecessary surgery.

Ancillary techniques like immunocytochemistry (ICC) and in situ hybridization for κ and λ light chain restriction have enhanced diagnostic specificity by confirming monoclonality [4]. Yet these methods may not be available in all settings. Moreover, while plasmablastic morphology is a well-established adverse prognostic feature in MM [5], its relevance in EMP is under-reported and poorly understood. Recent guidelines from the European Hematology Association and European Society for Medical Oncology (EHA-ESMO) focuses the importance of baseline systemic evaluation—including PET/CT, bone marrow examination, and serum free light chain analysis—to exclude occult myeloma, as up to 30% of apparent EMPs may progress to systemic disease over time [6].

Radiotherapy is the cornerstone of treatment for EMP, with involved-field doses of 40–50 Gy achieving local control rates approaching 90% [7]. However, factors such as age > 65 years, tumour size > 5 cm, high M-protein levels, and plasmablastic histology have all been associated with increased risk of progression to MM [8]. These risk factors are particularly relevant in resource-constrained settings where long-term surveillance may be challenging. In this context, we undertook a retrospective audit of all cytologically diagnosed EMP cases encountered in our institution over a three-year period. We aimed to characterise the clinico-cytological features, correlate findings with ancillary investigations, and assess short-term outcomes following standard therapy. Particular attention was paid to plasmablast-rich cytology as a potential marker of aggressive biological behaviour.

Objectives:

To describe the clinico-cytological spectrum of EMP diagnosed on FNAC. To evaluate the utility of ancillary studies (cell block ICC and radiological staging) in confirming EMP. To document treatment modalities and short-term clinical outcomes.

This six year study adds to the limited body of literature on EMP in low-to-middle-income countries and reinforces the pragmatic role of FNAC in early diagnosis and treatment planning for this rare plasma cell neoplasm.

Materials and Methods

Study Design and Setting

This was a retrospective, descriptive case series conducted in the Department of Pathology at a Tertiary Care Hospital. All cases were identified and analysed over a six year period, from May 2018 to January 2025. Ethical clearance was obtained from the Institutional Ethics Committee. Since the study comprised of retrospective analysis of data from records, hence informed consent from patients was not required.

Case Selection

Cytopathology archives were searched using keywords ”plasmacytoma” and ”plasma cell neoplasm.” Inclusion criteria were: (i) fine needle aspiration cytology (FNAC) smears showing a predominant plasma cell population with or without plasmablasts, (ii) availability of relevant clinical data, radiology, and immunocytochemistry, and (iii) absence of systemic multiple myeloma at the time of diagnosis. Cases with inadequate cellularity (< 50 plasma cells) or incomplete clinical workup were excluded.

Cytology Procedure and Smear Evaluation

FNAC was performed under aseptic conditions using a 22-gauge needle with or without image guidance depending on lesion location. Two to three passes were made per case. Smears were stained with May-Grünwald-Giemsa (air-dried) and Papanicolaou (alcohol-fixed). Cell blocks were prepared using the plasma-thrombin clot method when sufficient material remained.

All smears were independently reviewed by two senior cytopathologists. Cytomorphological features assessed included: Cellularity (scant/moderate/high). Maturation pattern (mature plasma cells vs plasmablasts). Nuclear pleomorphism. Mitotic figures (count per 10 high-power fields). Background elements (necrosis, amyloid, inflammatory cells). Discrepancies in interpretation were resolved by joint review.

Ancillary Investigations

Immunocytochemistry (ICC) was performed on formalin-fixed paraffin-embedded cell block sections using antibodies against CD138, CD38, CD45, and Ki-67 (ready-to-use monoclonal clones). In situ hybridisation for κ and λ light chains was carried out in all cases using chromogenic detection systems to demonstrate light chain restriction.

To exclude systemic multiple myeloma, each patient underwent: Whole-body fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT), Serum protein electrophoresis, Serum free light chain assay, Bone marrow aspirate and trephine biopsy

All test results were retrieved from the institutional electronic medical records.

Treatment and Follow-Up

Details of treatment modalities—radiotherapy dose, surgical intervention, and any systemic therapy—were noted from oncology files. Follow-up data were collected until 31 March 2025. Clinical outcomes were classified as: Disease-free, Progression to multiple myeloma, Lost to follow-up.

Progression-free survival (PFS) was calculated from the date of cytological diagnosis to the date of confirmed systemic progression or last clinical contact.

Data Analysis

Due to the limited sample size, descriptive statistics were used. Data were compiled and analysed using Microsoft® Excel (Version 2021), and results were expressed as counts, percentages, and medians.

Results

Clinical Profile

Eight patients (5 males, 3 females) aged between 58 and 90 years (mean age: 70.3 years) presented with solitary, painless soft tissue masses located at diverse anatomical sites. The most common presenting complaints were painless lumps or site-specific symptoms such as proptosis, nasal obstruction, and headache. Tumour sizes ranged from 2.8 cm to 6.5 cm, and symptom duration ranged from 1 to 10 months. None of the patients exhibited classical systemic features of multiple myeloma such as hypercalcaemia, renal dysfunction, anaemia, or bone lesions (CRAB criteria). The Bone marrow examination was normocellular in all cases (Table 1).

Table 1: Clinicodemographic Profile

Case	Age/Sex	Site	Size (cm)	Duration	Presenting Symptom
1	90/M	Axilla	3.2	8 m	Painless lump
2	78/M	Sternum	6.0	5 m	Dull ache
3	79/F	Orbit	4.5	4 m	Proptosis
4	67/F	Paranasal sinus	5.0	3 m	Nasal obstruction
5	58/M	Breast	2.8	1 m	Lump
6	66/M	Scapula	4.2	6 m	Shoulder pain
7	81/F	Thigh	5.8	9 m	Subcutaneous lump
8	72/M	Paranasal sinus	3.9	2 m	Headache

Cytological Findings

All FNAC smears were adequately cellular, exhibiting a range from mature plasma cells to highly atypical plasmablasts. Plasmablast-rich smears ($\geq$ 70%) were observed in three cases (Cases 3, 6, and 7), which also demonstrated higher mitotic activity (5–7/10 hpf), marked pleomorphism, and background necrosis. Cases dominated by mature plasma cells showed minimal atypia and lower Ki-67 indices. Amyloid-like extracellular material was noted in one case (Case 4), which showed a mixed population of mature cells and plasmablasts (Table 2, Figure 1).

Table 2: Cytomorphological Features

Case	Cellularity	Plasmablasts (%)	Mitoses (per 10 hpf)	Necrosis	Ki-67 (%)
1	High	0%	0	Absent	5%
2	High	60%	3	Focal	20%
3	Hypercellular	80%	6	Present	35%
4	Moderate	30%	2	Absent	15%
5	High	0%	0	Absent	5%
6	High	75%	5	Present	30%
7	Hypercellular	85%	7	Present	40%
8	Moderate	20%	1	Absent	10%

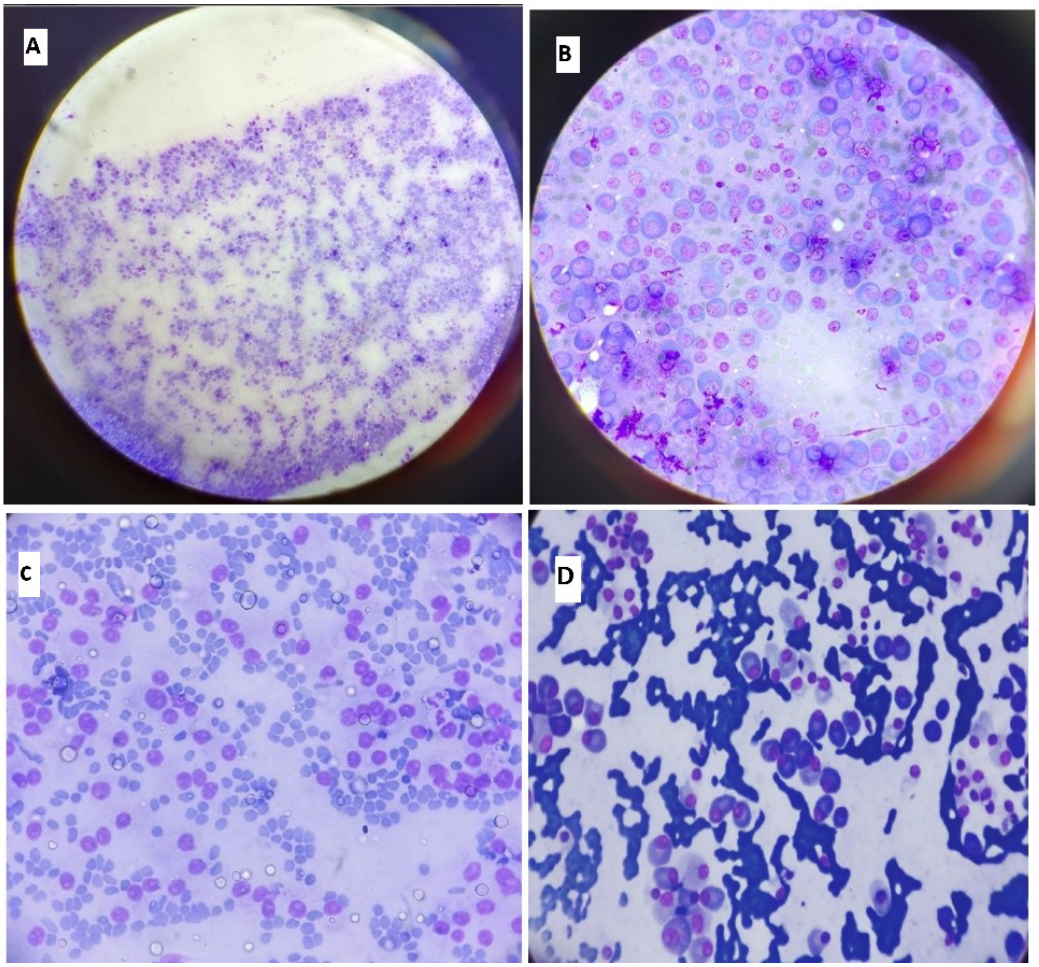

Figure 1: Cytopathology Findings (Clockwise from left upper corner) **A.** Highly cellular smear demonstrating sheets of plasma cells, Giemsa stain (100x). **B.** Smear showing plasma cells with eccentric, cartwheel nucleus, perinuclear hof, abundant basophilic cytoplasm, Giemsa stain (400x). **C.** Smear showing immature and mature plasma cells, Giemsa stain (400x). **D.** Cytological smear shows immature plasmablasts with prominent nucleoli, Leishman stain (200x).

Ancillary Investigations

Immunocytochemistry performed on cell block sections revealed the diffuse CD138 and CD38 positivity in all cases. CD45 was uniformly negative, ruling out lymphoma. Light chain restriction was demonstrable in all eight cases: κ restriction in five and λ in three. The whole-body FDG PET/CT showed no evidence of systemic disease or skeletal involvement, confirming the solitary nature of each lesion. SUVmax values ranged from 6.2 to 12.1. M-protein was not detected in six patients, while two patients (Cases 3 and 6) had low-level M-spikes (0.4 g/dL and 0.6 g/dL, respectively). Bone marrow studies showed no clonal plasma cell proliferation (Table 3).

Table 3: Ancillary Investigations

Case	PET SUV	M protein	Light Chain	BM Biopsy
1	6.5	None	κ	Normal
2	9.8	None	κ	Normal
3	11.2	0.4 g/dL	λ	Normal
4	7.9	None	κ	Normal
5	6.2	None	λ	Normal
6	10.5	0.6 g/dL	κ	Normal
7	12.1	None	λ	Normal
8	7.1	None	κ	Normal

Treatment and Follow-Up

All patients were treated with involved-field radiotherapy (40–50 Gy), administered in 20–25 fractions. One patient (Case 2) with a large sternal lesion underwent surgical curettage and internal fixation prior to radiation. At a median follow-up of 15.5 months (range: 6–18 months), four patients achieved complete response and remained disease-free, whereas one patient had stable disease. Two patients (Cases 2 and 7) progressed to multiple myeloma. A 78-year-old man (Case 2) with a 6 cm sternal extramedullary plasmacytoma containing $\sim 60\%$ plasmablasts responded only partially to surgery and radiotherapy and, within ten months, developed bone pain and anaemia; bone marrow aspirate revealed 15% clonal plasma cells and skeletal imaging showed multiple lytic lesions, leading to systemic therapy. An 81-year-old woman (Case 7) with a 5.8 cm thigh lesion rich in plasmablasts showed a similarly rapid course: after a partial response to 50 Gy radiotherapy, she developed fatigue and weight loss at nine months, and investigations (serum electrophoresis, PET/CT, bone marrow biopsy) confirmed disseminated myeloma requiring systemic therapy, although she was lost to follow-up. One patient (Case 3) was lost to follow-up after 6 months despite initial complete metabolic response (Table 4).

Table 4: Treatment and Outcome

Case	Therapy	Response	Follow-up	Outcome
1	RT 40 Gy	CR	18 m	Disease-free
2	RT 50 Gy + Surgery	PR $\rightarrow$ MM	16 m	MM at 12 m
3	RT 45 Gy	CR	6 m	Lost to follow up
4	RT 40 Gy	CR	15 m	Disease-free
5	RT 40 Gy	CR	17 m	Disease-free
6	RT 45 Gy	PR	14 m	Stable disease
7	RT 50 Gy	PR $\rightarrow$ MM	13 m	MM at 9 m
8	RT 45 Gy	CR	16 m	Disease-free

Discussion

This six-year retrospective audit highlights the rarity of extramedullary plasmacytoma (EMP), which constituted just 0.15% of all FNACs performed at our institution, comparable to earlier cytology-based studies reporting similar low yields. The demographic profile in our series—mean age of 70.3 years with a male predominance—aligns with established literature describing EMP as a disease of older adults with a mild male bias.

Anatomical distribution in our cohort was notably diverse. While the upper aerodigestive tract remains the most frequent site of EMP involvement, several patients in our series had lesions at unusual sites such as the breast, scapula, thigh, and orbit. This anatomical heterogeneity, increasingly reported in recent studies, underscores the importance of maintaining a broad differential when evaluating solitary soft tissue masses.

Cytologically, FNAC proved to be a reliable diagnostic modality, yielding adequate material in all cases. Classical features such as mature plasma cells with eccentric nuclei and perinuclear hofs were seen in lower-grade cases, whereas plasmablast-rich smears were characterised by pleomorphism, high mitotic activity, and elevated Ki-67 indices—up to 40% in some cases. Although plasmablast-rich morphology is well established as a poor prognostic indicator in multiple myeloma [9], its role in EMP is less well defined. Our observation that two plasmablast-dominant cases progressed to multiple myeloma within a year supports earlier suggestions that high-grade cytological features may signify aggressive biological behaviour in EMP [10].

Differentiating EMP from its cytological mimics is important and crucial. Plasmablastic lymphoma (PBL), in particular, shares morphologic overlapping similarity with plasmablast-rich EMP but typically arises in immunocompromised hosts and expresses CD45 and EBV-related markers—none of which were present in our cohort. In such contexts, immunocytochemistry and light chain analysis are indispensable. All cases in our series demonstrated clear monotypic κ or λ restriction, confirming plasma cell clonality. These findings echo the results of Goel et al. who also emphasised the value of ICC in establishing a cytological diagnosis of EMP [11].

Comprehensive staging remains critical, as 10–30% of EMPs may progress to systemic myeloma over time [12]. In accordance with international recommendations, all our patients underwent PET/CT, serum protein electrophoresis, free light chain assays, and bone marrow biopsy to exclude occult systemic disease. While no skeletal system involvement was found at baseline, progression to multiple myeloma in two cases reinforces the view that baseline negativity does not preclude future dissemination [13].

Radiotherapy remains the cornerstone of EMP management. Current international guidelines recommend involved-field radiotherapy at doses ≥ 40 Gy, which achieve local control rates of up to 90% [14]. All patients in our cohort received radiotherapy; five remained disease-free at follow-up, and one had stable local disease. The need for additional surgical intervention in the sternal lesion also reflects the necessity of a multidisciplinary approach for lesions involving weight-bearing or structurally critical sites [15].

Our findings highlight the prognostic importance of tumour size (> 5 cm), plasmablastic morphology, and high proliferative indices, all of which have been implicated in the risk of systemic progression in previous studies [15]. These parameters should inform not only treatment decisions but also post-therapy surveillance strategies, which must include periodic imaging and serum biomarker evaluation.

Limitations

The major limitation of the study is its small sample size, which restricts the generalisability of the findings, and it is challenging to make reliable statistical inferences since extramedullary plasmacytoma is uncommon. The retrospective design has possible biases in selection and documentation. Further, in a case, poor follow-up renders impossible an evaluation of long-term outcomes. In spite of these limitations, the report offers comprehensive cytomorphological examination correlated with immunocytochemical, radiological, and clinical findings, providing cytopathologists dealing with such rare presentations with useful information.

Future Directions

Prospective, multicentre registries incorporating cytology, flow cytometry, immunophenotyping, and molecular profiling—such as MYC rearrangement analysis and next-generation sequencing—are essential to better delineate the biological spectrum between extramedullary plasmacytoma and multiple myeloma. Such efforts could clarify the prognostic relevance of plasmablast-rich morphology, identify early molecular predictors of systemic progression, and support the development of risk-adapted surveillance and treatment protocols tailored to individual disease biology.

Conclusion

According to fundamental immunocytochemistry and light chain investigations, fine needle aspiration cytology represents a rapid diagnostic approach for extramedullary plasmacytoma, especially when lesions appear at uncommon body regions. Our research identified tumor dimensions along with high Ki-67 values and plasmablast-rich cytomorphology as indicators of rapid systemic advancement, which aligns with known risk factors for aggressive disease. Current international guidelines indicate that most patients achieve lasting local disease control through radiotherapy. Our findings emphasize the importance of complete baseline staging and ongoing monitoring, because PET-negative EMPs can transform into systemic multiple myeloma. Pathologists in resource-limited settings should remain alert to solitary soft-tissue masses in unusual locations and carefully assess cytomorphological features because tumour size > 5 cm, older patient age and high plasmablast content

have been associated with poor prognosis. Early referral for baseline staging and meticulous follow-up are essential, as many of these apparently localised lesions may progress to multiple myeloma.

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