RESEARCH PAPER

When the Liver Lies: Plasma Cell Myeloma Mimicking Hepatic Metastasis of Unknown Primary — A Pathological Perspective

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ABSTRACT

Background: Extramedullary plasma cell myeloma (PCM) with hepatic space-occupying lesions mimicking hypervascular metastases of unknown primary is exceedingly rare and diagnostically challenging.

Case Summary: A 60-year-old male with T2DM presented with back pain and bilateral lower limb weakness. Imaging revealed multiple hypervascular hepatic lesions, peripancreatic calcified masses, and extensive lytic skeletal lesions with D11 vertebral compression fracture. Tumour markers were normal. EUS-guided fine needle biopsy (EUS-FNB) yielded cores showing small round blue cells in sheets with eccentric nuclei and salt-and-pepper chromatin. Immunohistochemistry (IHC) demonstrated diffuse membranous CD138 positivity with synaptophysin negativity, confirming plasma cell myeloma.

Conclusion: EUS-FNB with IHC is pivotal in establishing the pathological diagnosis of hepatic extramedullary myeloma, preventing misdiagnosis as an epithelial metastasis and ensuring timely haematological management.

Keywords: Plasma cell myeloma; Extramedullary myeloma; Hepatic metastasis; EUS-guided fine needle biopsy; CD138 immunohistochemistry
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INTRODUCTION

Multiple myeloma (MM), classified under plasma cell neoplasms (PCN) in the WHO 5th Edition Classification of Haematolymphoid Tumours (WHO-HAEM5, 2022), is a malignant clonal proliferation of terminally differentiated plasma cells [1]. Extramedullary myeloma (EMM) — growth of myelomatous tissue independent of the bone marrow microenvironment — occurs in 1–2% of patients at diagnosis [2]. Hepatic involvement with space-occupying lesions is a particularly rare and histologically deceptive manifestation of EMM [3,4].

Pathologically, myelomatous hepatic lesions consist of infiltrating sheets of neoplastic plasma cells that may lack the classic "clock-face" chromatin pattern, instead displaying immature morphology with prominent nucleoli or a plasmablastic appearance, rendering cytomorphology alone insufficient for diagnosis [5]. IHC characterisation — particularly CD138, CD38, MUM1/IRF4, and light chain restriction — is essential for definitive lineage assignment [6]. EUS-guided FNB has emerged as the preferred minimally invasive modality for obtaining adequate core tissue from hepatic lesions, with a diagnostic accuracy of 95–100% and a unique advantage in simultaneously enabling IHC [7,8].

CASE REPORT

A 60-year-old male with a known history of Type 2 Diabetes Mellitus presented with progressive back pain of four months duration, bilateral lower limb weakness, and reduced sensation. He was referred from an outside facility following PET-CT findings demonstrating hepatic space-occupying lesions (SOLs), peripancreatic lesions, and multiple skeletal metastases. On examination, vital signs were stable with a blood pressure of 130/90 mmHg and SpO2 of 98% on room air. Abdominal examination revealed diffuse tenderness. Tumour markers were within normal limits — CA19-9 at 2.44 U/mL and CEA at 2.54 ng/mL. Liver function tests demonstrated mild

hyperbilirubinaemia with a total bilirubin of 1.23 mg/dL, while transaminases and alkaline phosphatase remained normal.

Contrast-enhanced CT of the abdomen revealed multiple hypodense hepatic lesions exhibiting arterial-phase hyperenhancement with venous-phase washout, the largest measuring 2.7×2.6 cm in segment V of the right lobe. Peripancreatic calcified masses measuring up to 3.5×2.6 cm were identified, raising the differential diagnosis of neuroendocrine tumour versus calcified lymphadenopathy. Extensive lytic bone lesions were noted involving the D11 through L3 vertebrae, sacrum, and acetabulum, with a wedge compression fracture at D11 causing significant spinal canal narrowing.

EUS-guided fine needle biopsy was performed using a linear echoendoscope from the largest hepatic lesion, yielding multiple grey-brown core fragments ranging from 0.1 to 0.4 cm in length. Histological sections showed tumour tissue against a background of haemorrhage. On H&E examination,(Figure 1) tumour cells were arranged predominantly in cohesive sheets and singly, displaying round to polygonal nuclei with eccentric placement, salt-and-pepper stippled chromatin characteristic of neuroendocrine or plasma cell lineage, and scant to moderate pale cytoplasm. Gland formation and squamoid differentiation were absent. The overall morphological pattern was consistent with a small round blue cell tumour (SRBCT) with plasmacytic features, and the differential diagnosis at this stage encompassed plasma cell myeloma/plasmacytoma, neuroendocrine tumour Grade 2–3, diffuse large B-cell lymphoma, and poorly differentiated carcinoma.

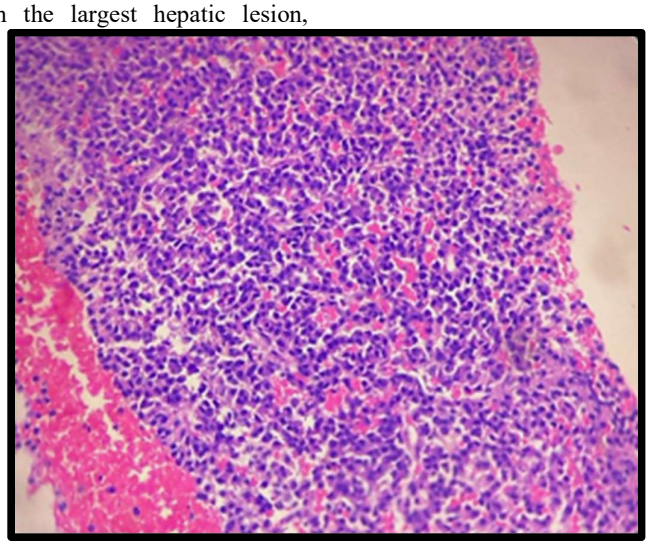

Figure 1. H&E stain (×400): Sheets of small round blue cells with round-to-polygonal eccentric nuclei, salt-and-pepper chromatin, and scant cytoplasm — morphology consistent with plasmacytic differentiation. Background haemorrhage is noted.

A targeted IHC panel was applied to establish lineage. CD138 (syndecan-1), a transmembrane heparan sulphate proteoglycan expressed on mature plasma cells and lost upon neoplastic dedifferentiation in lymphomas, showed strong and diffuse membranous positivity on tumour cells [Figure 2 a,b]. Synaptophysin — a presynaptic vesicle membrane protein used to confirm neuroendocrine differentiation — was entirely negative [Figure 3], effectively excluding metastatic NET.

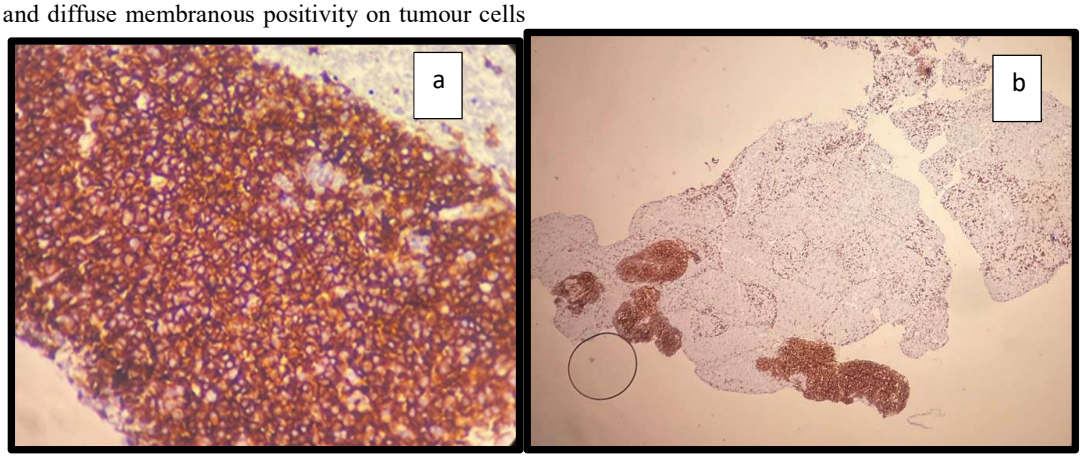

Figure 2 a,b. IHC — CD138 (×400): Strong diffuse membranous CD138 positivity on tumour cells, confirming plasma cell lineage. CD138 is the lineage-defining marker for plasma cell myeloma .

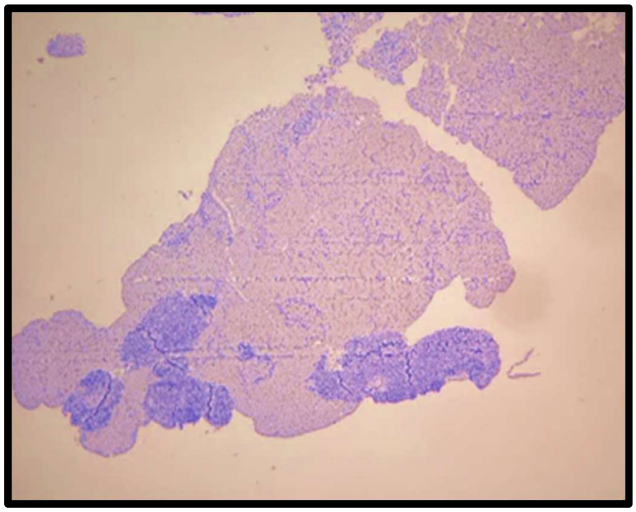

Figure 3. IHC — Synaptophysin (×400): Complete absence of synaptophysin expression in tumour cells,.

Final Pathological Impression: Features consistent with PLASMA CELL MYELOMA — EUS-guided liver biopsy. (CD138 positive; Synaptophysin negative.)

DISCUSSION

From a pathological standpoint, hepatic EMM represents a diagnostic challenge because neoplastic plasma cells — particularly in extramedullary sites — frequently exhibit immature or plasmablastic morphology, losing the characteristic clock-face chromatin and cartwheel nuclear pattern of mature marrow plasma cells [5]. In such cases, SRBCT morphology with salt-and-pepper chromatin raises a broad differential including NET Grade 3, small cell carcinoma, lymphoma, and plasmacytoma. The critical differentiator is IHC.

Per WHO-HAEM5 (2022), plasma cell myeloma/multiple myeloma is defined by ≥10% clonal marrow plasma cells or a biopsy-confirmed plasmacytoma, with at least one myeloma-defining event [1]. The recommended IHC panel for plasma cell lineage confirmation includes CD138, CD38, MUM1/IRF4, and cytoplasmic light chain restriction (kappa/lambda); CD138 remains the most widely used single marker, exhibiting strong membranous staining in 96–100% of plasma cell neoplasms [6]. In the present case, CD138 membranous positivity was unequivocal, and synaptophysin negativity excluded the primary radiological differential of NET. Chromogranin A was not performed; however, synaptophysin negativity alone, in combination with CD138 positivity, is sufficient to redirect the diagnosis.

The morphological deception in this case was heightened by the CECT characteristics: arterial hyperenhancement with venous washout classically suggests HCC or hypervascular metastases (renal cell carcinoma, NET, thyroid, choriocarcinoma). The peripancreatic calcified masses further misdirected towards a pancreatic NET with hepatic spread. Normal tumour markers (CA19-9, CEA) appropriately weakened the adenocarcinoma hypothesis but did not by themselves indicate a haematological aetiology. This pattern — hypervascular hepatic SOLs, lytic bone lesions without osteoblastic reaction, and negative epithelial markers — should prompt the pathologist to include plasma cell myeloma in the differential, as MM uniquely produces osteolytic lesions without new bone formation [2].

Recent literature corroborates the rarity and diagnostic complexity of hepatic EMM. Pu et al. (2025) reported hepatic MM as the initial manifestation with atypical imaging, and confirmed that histopathological verification is indispensable [4]. Skołozdrzy et al. (2024) emphasised that myelomatous hepatic lesions can mimic primary or secondary liver tumours on all imaging modalities, and biopsy with IHC is mandatory [3]. Singh et al. (2021) highlighted that hepatic EMM carries a poor prognosis and necessitates early tissue diagnosis for appropriate staging [9].

Regarding tissue acquisition, EUS-FNB using 19–22G needles achieves diagnostic accuracy of 95–100% for focal liver lesions, superior to FNA (86.7%), and provides tissue cores adequate for IHC — an absolute requirement when SRBCT morphology is encountered [7,8]. Tantău et al. (2024) confirmed EUS-FNB as the preferred modality for hepatic lesion characterisation, particularly for left lobe and caudate lesions inaccessible percutaneously [10]. The present case involved a caudate/perihilar lesion between the portal vein and IVC, precisely where percutaneous biopsy carries higher vascular risk — underscoring the safety advantage of the EUS route.

CONCLUSION

This case demonstrates that plasma cell myeloma can present as hypervascular hepatic SOLs closely mimicking an unknown primary malignancy. The pathological diagnosis rested on meticulous IHC interpretation: CD138

membranous positivity confirmed plasma cell lineage while synaptophysin negativity excluded neuroendocrine aetiology. EUS-FNB provided adequate core tissue for this analysis safely and accurately. Pathologists reviewing hepatic SRBCT morphology — particularly in the presence of lytic bone lesions and normal epithelial markers — must maintain plasma cell myeloma as an active differential and apply a comprehensive IHC panel. Timely pathological diagnosis is the keystone of appropriate haematological management in extramedullary myeloma.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest pertaining to the publication of this case report.

SOURCE OF FUNDING

None.

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