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Case Report

Pathology Section

Lymphoplasmacytic Lymphoma Mimicking Plasma Cell Neoplasm: A Rare Case Report

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ABSTRACT

Lymphoplasmacytic Lymphoma (LPL) is an uncommon B-cell neoplasm that may closely mimic plasma cell disorders, leading to diagnostic uncertainty. We report the case of a 56-year-old man who presented with fatigue and bone pain. Bone marrow evaluation revealed an admixture of plasma cells and plasmacytoid lymphocytes, showing significant morphological overlap between LPL and plasma cell neoplasm. An extended Immunohistochemical (IHC) panel demonstrated CD20 and CD79a positivity in B-lymphoid cells, CD138 positivity in plasma cells, and kappa light-chain restriction, consistent with a clonal B-cell proliferation with plasmacytic differentiation. Correlation of clinical, radiological, and laboratory findings established the final diagnosis of LPL. This case emphasises the limitations of relying solely on morphology and highlights the essential role of immunophenotyping in differentiating LPL from plasma cell neoplasms. The distinction carries therapeutic and prognostic significance; LPL typically responds to rituximab-based regimens targeting B cells, whereas plasma cell neoplasms require anti-myeloma therapy. Recognising such atypical marrow presentations is crucial to prevent misclassification, enable appropriate management, and improve patient outcomes.

Keywords: B-cell neoplasms, Differential diagnosis, Immunophenotyping, Prognosis, Waldenström macroglobulinaemia

CASE REPORT

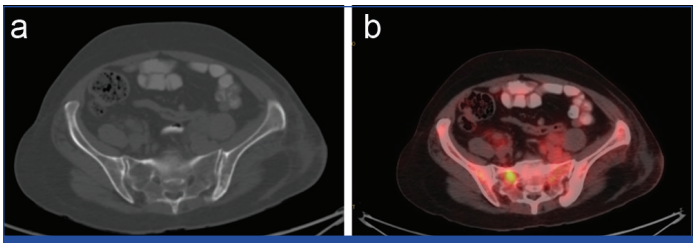
A 56-year-old male presented to the outpatient department with complaints of generalised fatigue and severe bone pain that had progressively worsened over the past few months. There was no history of fever, weight loss, night sweats, or recurrent infections. The patient did not report any bleeding manifestations or neurological symptoms or any other past history.

On general examination, the patient appeared pale but had no lymphadenopathy. Systemic examination revealed hepatosplenomegaly (Liver measures 17 cm in craniocaudal span, spleen measures 14 cm), while other findings were unremarkable.

Laboratory investigations: Complete blood count revealed pancytopenia with haemoglobin 11.5 g/dL (13.0-17.0 g/dL), total white blood cell count 2.6×10^6/µL ($4.0–10.0\times10^6$/µL), and platelet count 97×10^3/µL ($150-450\times10^3$/µL). Additional parameters included an erythrocyte sedimentation rate of 85 mm/h (0-15 mm/h), globulin 4.10 g/dL (2.0-3.5 g/dL), and direct bilirubin 0.45 mg/dL (0.0-0.3 mg/dL)- all elevated compared to normal limits. Peripheral smear showed pancytopenia with relative lymphocytosis with mild thrombocytopenia. No morphological abnormality could be appreciated in the lymphocytes on the peripheral smear.

Radiological findings showed hypermetabolic lesions in the sacrum [Table/Fig-1]. No lesions were noted elsewhere. Based on these findings, a provisional diagnosis of plasma cell dyscrasia was made. The differential diagnoses included multiple myeloma, LPL, and other small B-cell lymphomas with plasmacytic differentiation.

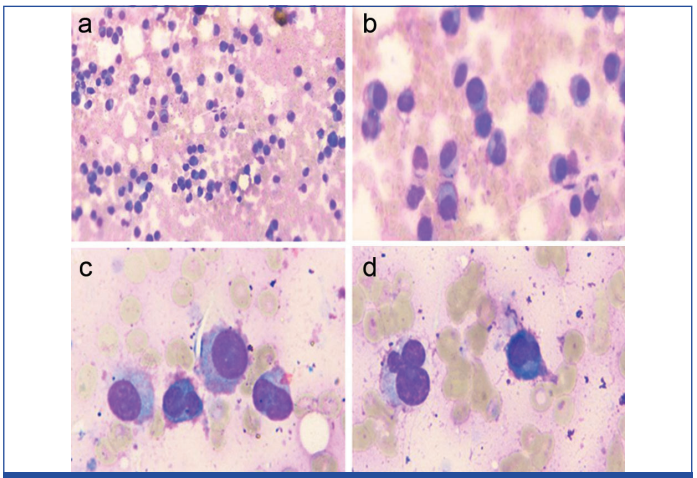
Bone marrow aspiration and trephine biopsy were subsequently performed. Aspiration smears showed hypercellular marrow with 69% plasmacytoid lymphocytes and 21% plasma cells, along with 10% residual haematopoietic cells [Table/Fig-2,3]. The plasmacytoid cells exhibited eccentric nuclei, coarse chromatin, perinuclear clearing, and nuclear budding, mimicking plasma cells. The trephine biopsy revealed preserved bony trabecular architecture, which is effaced by diffuse infiltration of small round blue cells with plasmacytoid morphology, displaying eccentric nuclei and occasional binucleation. [Table/Fig-4].



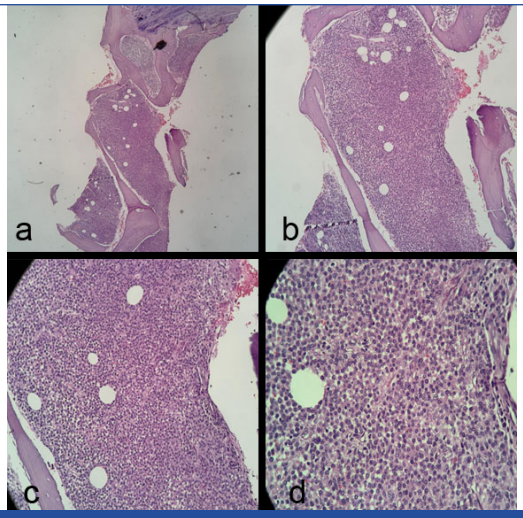
[Table/Fig-1]: (a) Computed Tomography (CT) image showing a lytic lesion in the sacrum; (b) Positron-Emission Tomography-CT (PET-CT) image showing corresponding hypermetabolic activity in the same region (Radiological correlation demonstrating sacral involvement).

Cell Type	Percentage (%)
Plasma cells	21%
Plasmacytoid lymphocytes (with nuclear budding)	69%
Other haematopoietic cells	10%

[Table/Fig-2]: Bone marrow differential count showing increased proportion of plasma cells and plasmacytoid lymphocytes.



[Table/Fig-3]: Bone marrow aspiration smear, Wright stain: (a) Plasma cells and plasmacytoid cells (40×); (b) Plasma cells with eccentric nuclei (100×); (c) Plasmacytoid lymphocytes (100×); (d) Plasmacytoid lymphocytes with nuclear budding (100×).



[Table/Fig-4]: Trephine biopsy, Haematoxylin and Eosin (H&E) stain: (a) Overall marrow cellularity (4×); (b) Diffuse infiltration by atypical lymphoplasmacytoid cells and normal bony trabeculae (10×); (c) Sheets of plasmacytoid cells (20×); (d) Round blue cells with plasmacytoid morphology (40×).

Morphological overlap: The marrow displayed features shared by both LPL and plasma cell neoplasm- an admixture of mature plasma cells and plasmacytoid lymphocytes with eccentric nuclei and prominent perinuclear Hof formation. The lack of classical "sheet-like" plasma cell proliferation typical of myeloma, however, introduced diagnostic ambiguity.

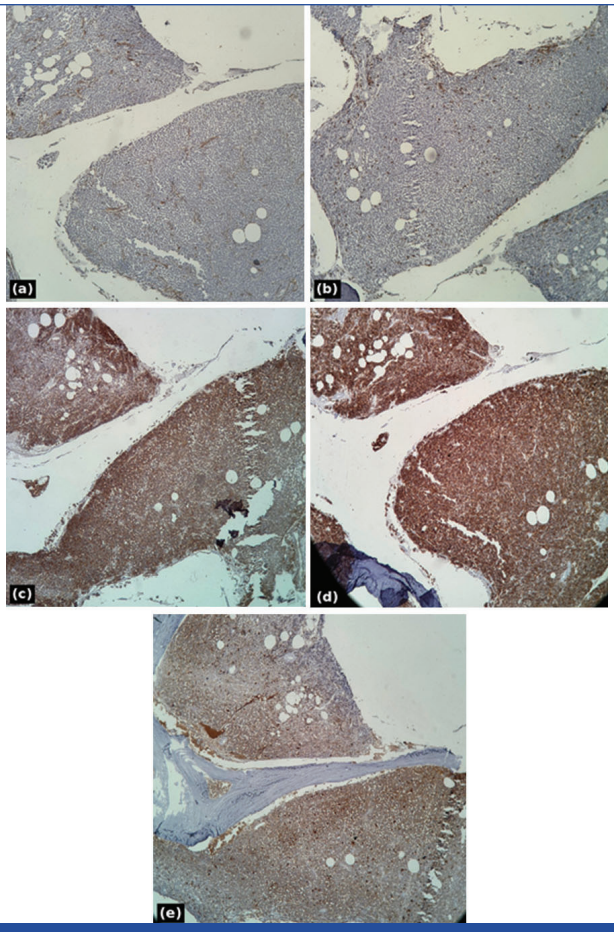
A provisional diagnosis of a low-grade B-cell lymphoma with plasmacytic differentiation was thus considered. The key differentials included LPL, plasma cell myeloma, and marginal zone lymphoma with plasmacytic differentiation.

Since morphology alone could not delineate these entities, an extended IHC work-up was performed to establish lineage and clonality.

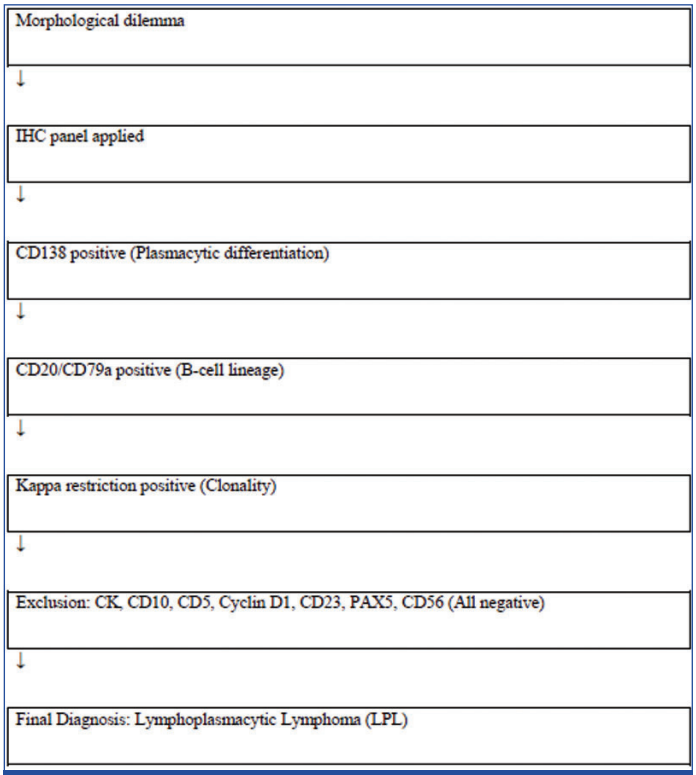
An extended IHC panel was performed to confirm lineage, establish clonality, and differentiate between plasma cell neoplasm and LPL [Table/Fig-5-7]. The neoplastic cells showed CD20 and CD79a positivity, indicating B-cell lineage, while CD138 positivity highlighted plasma cell differentiation. CD45 positivity confirmed haematolymphoid origin. Kappa light-chain restriction established monoclonality, supporting a neoplastic proliferation. Cytokeratin (CK) was negative, excluding epithelial malignancy. The absence of CD10, CD5, Cyclin D1, CD23, and PAX5 helped rule out other small B-cell lymphomas, including follicular lymphoma, mantle cell lymphoma, and Chronic Lymphocytic Leukaemia/Small Lymphocytic Lymphoma (CLL/SLL). CD56 was also negative, which aided in excluding plasma cell myeloma, as CD56 expression is commonly associated with myeloma cells.

Marker	Interpretation in this case	Utility in differentiation
CD138	Positive	Confirms plasma cell differentiation
CD45	Positive	Supports haematolymphoid origin
CD20, CD79a	Positive	Indicates B-cell lineage → favours LPL
Kappa restriction	Positive (monoclonal)	Confirms clonality, essential for neoplastic diagnosis
CK	Negative	Excludes epithelial malignancy
CD10	Negative	Excludes follicular lymphoma
CD5	Negative	Excludes mantle cell lymphoma/CLL
Cyclin D1	Negative	Excludes mantle cell lymphoma
CD23	Negative	Excludes CLL
PAX5	Negative	Excludes other mature B-cell neoplasms
CD56	Negative	Excludes plasma cell myeloma

[Table/Fig-5]: Immunohistochemistry (IHC) profile demonstrating positive and negative markers used in differentiating plasma cell neoplasm from Lymphoplasmacytic Lymphoma (LPL).



[Table/Fig-6]: Immunohistochemistry (IHC): (a) CD10 negative (×20) showing absence of membranous staining; (b) CK negative (×20) showing absence of cytoplasmic staining; (c) CD138 positive (×20) showing strong membranous and cytoplasmic positivity; (d) CD20 positive (×20) highlighting diffuse membranous staining in B-lymphoid cells; (e) Kappa light chain restriction (×20) showing diffuse cytoplasmic positivity.



[Table/Fig-7]: Flowchart demonstrating the diagnostic approach followed to confirm Lymphoplasmacytic Lymphoma (LPL).

The overall IHC profile- CD20$^+$, CD79a$^+$ B-cells, CD138$^+$ plasma cells, kappa restriction, and negative staining for CD56, Cyclin D1, CD10, CD5, CD23, and PAX5- confirmed the diagnosis of LPL with plasmacytic differentiation rather than plasma cell myeloma.

The patient was initially managed elsewhere with a provisional diagnosis of multiple myeloma and received one cycle of anti-myeloma therapy. However, due to inadequate clinical response and persistent cytopenias, further evaluation was undertaken at our centre. Thus, based on the combined morphological, immunohistochemical and radiological findings, the diagnosis was revised to LPL. The patient was subsequently initiated on a rituximab-based regimen, following which there was symptomatic improvement. At six months of follow-up, the patient remains clinically stable and is under regular monitoring.

DISCUSSION

The LPL is an indolent B-cell neoplasm characterised by a mixture of small lymphocytes, plasmacytoid lymphocytes, and plasma cells, and is usually associated with an IgM monoclonal paraprotein. Plasma cell neoplasms, by contrast, are clonal proliferations of terminally differentiated B cells that secrete monoclonal immunoglobulins, with multiple myeloma being the most common clinical entity [1].

The worldwide incidence of multiple myeloma is low, estimated at about two cases per 100,000 individuals, with regional variation ranging from 0.54 to 5.3 per 100,000 [2]. LPL/Waldenström macroglobulinaemia is even rarer, and Indian case series have documented only small numbers of patients over extended periods, underlining its infrequency in the local population [3].

Morphologically, LPL demonstrates marrow infiltration by small lymphocytes, plasmacytoid lymphocytes, and plasma cells in varying proportions, while plasma cell neoplasms typically form sheets of plasma cells with eccentric nuclei, producing a uniform infiltrate without lymphoid admixture [4]. The principal diagnostic challenge lies in distinguishing LPL from plasma cell neoplasms, as both may display overlapping plasmacytoid morphology and share partial immunophenotypic features [5]. In the present case, this overlap was particularly evident within the plasmacytoid component, making diagnosis difficult and necessitating careful correlation of marrow findings with IHC.

The cell of origin in LPL is believed to be a post-germinal centre B cell lacking active somatic hypermutation [6]. A major molecular breakthrough was the identification of the MYD88 L265P mutation in Waldenström macroglobulinaemia, detected in more than 90% of cases, which is now recognised as a key diagnostic marker distinguishing LPL from plasma cell myeloma and other indolent B-cell neoplasms. Subsequent studies have reinforced its significance: Zheng L and Guo Z demonstrated MYD88 mutations in both IgM and non-IgM LPL, showing its relevance across subtypes [7]; Johansen S et al., described a lymphoplasmacytic variant of multiple myeloma, emphasising the morphological and immunophenotypic overlap with LPL [5]; and Kumar V et al., highlighted that unusual plasma cell morphologies can further complicate diagnosis, necessitating integrated molecular and immunophenotypic assessment [6]. Collectively, these observations confirm the critical role of MYD88 mutation testing in resolving diagnostic uncertainty, particularly in cases with plasmacytoid overlap.

While plasma cell neoplasms typically produce monoclonal immunoglobulins [1], monoclonal protein production may also occur in B-cell lymphomas, including LPL [2,3]. Bone marrow evaluation helps in distinction: a uniform clonal plasma cell infiltrate with residual polyclonal B cells supports plasma cell myeloma, whereas a clonal B-cell population with admixed plasma cells is more consistent with lymphoma [4]. When both monoclonal B cells and plasma cells with identical light-chain restriction co-exist, the findings favour lymphoma with plasmacytic differentiation [5,6]. In such circumstances, morphology alone cannot reliably exclude a concurrent plasma cell neoplasm, underscoring the importance of integrated immunophenotypic and molecular evaluation [7-9].

In summary, this case illustrates the diagnostic dilemma posed by overlapping plasmacytoid morphology. Reports in the literature note that plasma cell neoplasms may occasionally show atypical features such as CD138 negativity or irregular nuclear contours, further obscuring the distinction from lymphoid malignancies [10,11]. More recent studies emphasise that evolving classifications mandate integration of morphology, immunophenotype, molecular studies, and cytogenetics to achieve definitive diagnosis [12]. Our findings reinforce the necessity of a comprehensive multimodal approach, particularly in resource-limited settings, and add to the growing evidence that precise separation of these entities is crucial for effective patient management and prognostication.

CONCLUSION(S)

This case underscores the diagnostic challenge of differentiating LPL from plasma cell neoplasms when plasmacytoid morphology is prominent. Accurate classification is crucial, as it directly impacts therapeutic decisions and prognosis. While plasma cell neoplasms require anti-myeloma regimens, LPL typically responds well to B-cell–directed therapies such as rituximab-based combinations, leading to improved outcomes and disease control.

A multimodal diagnostic approach- integrating morphology, IHC, and molecular testing such as MYD88 mutation analysis- is vital to resolve overlapping features and ensure appropriate management. Continued reporting of such diagnostically challenging cases will enhance recognition of this entity and guide optimal treatment strategies for better patient prognosis.

REFERENCES

[1] Mansour AT, Shandiz AE, Zimmerman MK, Roth TD, Zhou J. Concomitant lymphoplasmacytic lymphoma and plasma cell myeloma, a diagnostic challenge. Am J Blood Res. 2017;7(2):10-17.
[2] Kumar V, Rajkumar V, Kyle RA. Worldwide incidence of multiple myeloma: A review. Oncologist. 2020;25(5):e640-e648. Doi: 10.1634/theoncologist.2019-0730. PMID:32335971.
[3] Narayanan G, Suresh Babu MC, Sreedharanunni S, Nair RA, Prem S, Sukumaran R, et al. Clinical characteristics and treatment outcome of Waldenström macroglobulinaemia: Experience from a tertiary cancer centre in India. Asian Pac J Cancer Care. 2024;9(1):59-65. Doi: 10.31557/APJCC.2024.9.1.59.
[4] Wang MH, Wu CC, Cho SF. Diagnostic challenges in plasma cell myeloma with lymphoplasmacytic lymphoma-feature. Kaohsiung J Med Sci. 2023;39(8):853-54. Doi: 10.1002/kjm2.12717.
[5] Johansen S, Gjelberg HK, Reikvam H. Lymphoplasmacytic variant of multiple myeloma. eJHaem. 2022;3(2):437. Doi: 10.1002/jha2.437.
[6] Kumar S, Ahmed F, Mundada M, Kondandapani S, Kumar P. Surprising visit: The rare plasma cell variant. Blood Sci. 2025;7(1):e00218. Doi: 10.1097/BS9.0000000000000218.
[7] Zheng L, Guo Z. A case report of lymphoplasmacytic lymphoma with paraprotein IgA and IgM. Med Case Rep Study Protoc. 2021;2:e0045. Doi: 10.1097/MD9.0000000000000045.
[8] Baloush R, Reddy V. Plasma cell myeloma with lymphoplasmacytic morphology and negative CD138 expression: Case report and differential diagnosis. Ann Intern Med Clin Cases. 2022;1:e220691. Doi: 10.7326/aimcc.2022.0691.
[9] Itchaki G, Jarhovsky O, Castillo JJ, Hassan H, Gatt ML, Leiba M, et al. Lymphoplasmacytic lymphoma and multiple myeloma coexisting in the same patient: A case series and literature review. Leuk Lymphoma. 2024;65(6):01-08. Doi: 10.1080/10428194.2024.2332499.
[10] Hosoi H, Tane M, Sogabe M, Iwamoto R, Minoura N, Murata S, et al. Flower-shaped plasma cells in multiple myeloma with morphological heterogeneity. Diagnostics (Basel). 2024;14(20):2285. Doi: 10.3390/diagnostics14202285.
[11] Mahajan V, Vishwaroop S, Khodaiji S. Unusual plasma cell morphology: A diagnostic dilemma. Indian J Hematol Blood Transfus. 2023;39(2):353-55. Doi: 10.1007/s12288-022-01614-1.
[12] Fend F, Dogan A, Cook JR. Plasma cell neoplasms and related entities- evolution in diagnosis and classification. Virchows Arch. 2023;482(2):163-77. Doi: 10.1007/s00428-022-03431-3.

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