Primary bone marrow diffuse large B-cell lymphoma with secondary myelofibrosis: A case report

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Abstract. Primary bone marrow (BM) diffuse large B-cell lymphoma (PBM-DLBCL) is an extremely rare and highly aggressive subtype of extranodal lymphoma. Its non-specific clinical manifestation, often presenting with pancytopenia, poses significant diagnostic challenges, frequently leading to misdiagnosis as other hematological disorders. In April 2023, a 70-year-old man was hospitalized in the Department of Hematology of The First Affiliated Hospital of Jishou University (Jishou, China). The patient presented to the hospital with fever, malaise and severe pancytopenia. An initial BM biopsy indicated a T-cell lymphoproliferative disorder accompanied by myelofibrosis (MF), for which empirical immunosuppressive therapy was administered without clinical benefit. A total of 10 months later, a repeat BM biopsy demonstrated a distinct population of $CD20^+$ and $CD79a^+$ large B-cells, establishing a definitive diagnosis of PBM-DLBCL with secondary MF. The patient declined further therapeutic interventions and was lost to follow-up thereafter. The present case report underscores the diagnostic challenges of PBM-DLBCL, which can mimic other marrow pathologies. The report highlights the critical importance of repeat BM biopsies in cases of refractory or unexplained pancytopenia. The potential mechanisms linking DLBCL with secondary MF are also discussed, emphasizing the need for heightened clinical vigilance to prevent misdiagnosis.

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Introduction

Lymphomas can originate in almost all tissues and organs, and may subsequently infiltrate peripheral tissues, distant tissues and bone marrow (BM) (1,2). Primary BM lymphoma (PBM) is a rare entity defined by lymphoma confined to the BM without evidence of nodal or extranodal involvement at diagnosis. Diffuse large B-cell lymphoma (DLBCL) is the most common histological subtype of PBM, yet it accounts for <1% of all DLBCL cases and is typically associated with an aggressive clinical course and poor prognosis (3). Patients often present with constitutional symptoms (fever, night sweats and weight loss) and peripheral blood cytopenias, which can mimic a wide spectrum of benign and malignant hematological diseases, frequently resulting in diagnostic delay or error (4). Diagnosis requires strict exclusion of systemic involvement (no lymph node/organ enlargement confirmed by physical examination and imaging) and is easily misdiagnosed as lymphoma of secondary BM involvement. Peripheral blood lymphocyte counts and morphology are usually unremarkable (5).

Myelofibrosis (MF) is a clonal myeloproliferative neoplasm (MPN) of the BM caused by an abnormal clone of hematopoietic stem cells (6). MF can be classified into primary MF (PMF), a Philadelphia chromosome (Ph)-negative MPN, and secondary MF, which refers to reactive MF induced by a variety of underlying diseases or conditions. Accurate differentiation between the two is critical for determining appropriate therapeutic strategies and requires an integrated assessment of clinical presentation, laboratory findings, BM histopathology and molecular genetics (7). The pathophysiological association between DLBCL and MF is considered to involve cytokine-mediated activation of fibrotic pathways (for example, JAK/STAT and SMAD). Profibrotic factors such as transforming growth factor-β (TGF-β) and platelet-derived growth factor (PDGF), secreted by lymphoma cells, lead to collagen deposition and subsequent extramedullary hematopoiesis. Clinically, cytopenias, hepatosplenomegaly and systemic symptoms predominate, with a median survival time of ~6 years (8).

The present study reports a rare and diagnostically challenging case of primary BM-CLBCL (PBM-DLBCL) that was initially misdiagnosed as a T-cell lymphoma with associated MF based on initial BM histopathology and clinical presentation. The diagnosis of PBM-DLBCL was established following

two BM aspirates and biopsies. The diagnosis and therapeutic timeline over the course of the patient's two hospitalizations is summarized in Table I. The present case illustrates the potential diagnostic pitfalls and emphasizes the necessity of repeated and comprehensive BM histopathological assessment in patients with persistent cytopenias.

Case report

Patient presentation. A 70-year-old man with no significant past medical history was admitted to the Department of Hematology of The First Affiliated Hospital of Jishou University (Jishou, China) in April 2023, presenting with a 2-day history of fever and profound malaise. Physical examination revealed marked pallor, without evidence of lymphadenopathy, hepatosplenomegaly or hemorrhagic manifestations.

Initial laboratory investigations demonstrated severe pancytopenia, with a white blood cell count of $2.36x10^9$/l (normal range, 4-10$x10^9$/l), hemoglobin count of 52 g/l (normal range, 120-160 g/l) and platelets count of $37x10^9$/l (normal range, 100-400$x10^9$/l). C-reactive protein was markedly elevated at 137.15 mg/l (normal range, 0-8 mg/l). Iron studies, vitamin B12, folate levels and immunoglobulin profiles were within normal limits. Lactate dehydrogenase (LDH) was elevated at 450 U/l, exceeding the reference range of 120-250 U/l. Serological tests for common viruses, including HBV, HCV, HIV and EBV, were negative. Contrast-enhanced computed tomography (CT) of the chest and abdomen revealed no lymphadenopathy or organomegaly. A positron emission tomography (PET)-CT scan was not performed due to the patient's clinical status and logistical constraints.

BM aspirate and biopsy were performed. The aspirate demonstrated an elevated lymphocyte ratio (40%). Flow cytometric analysis (Fig. 1) revealed a predominant T-cell population (79.54%; CD4:CD8 ratio of 1.70) with monoclonal T-cell receptor (TCR)-γ gene rearrangement. Immunoglobulin heavy chain gene rearrangement was not assessed in the initial sample. No aberrant B-cell or NK-cell populations were detected. The core biopsy (Fig. 2) revealed a hypercellular marrow with marked collagen fibers proliferation, multifocal lymphocytic aggregates (reticulin staining confirmed persistent grade 2 MF), and megakaryocytes without significant atypia. Immunohistochemistry (IHC) revealed focal CD3 positivity (~30% of nucleated cells). The initial integrated interpretation favored a T-cell lymphoproliferative disorder complicated by secondary MF.

The initial administration of cyclosporine (50 mg twice daily) represented an empirical therapeutic trial, aligned with the Chinese Society of Clinical Oncology (CSCO) diagnosis and treatment guidelines for malignant lymphoma 2021 (English version) (9). This strategy aimed to suppress a potential aberrant T-cell clone or immune-mediated marrow suppression prior to establishing a definitive diagnosis. Immunosuppressive therapy is a considered option under such circumstances per guidelines including those from CSCO. This was not a bypass of standard lymphoma treatment regimens but rather a supportive care attempt aimed at the most life-threatening issue, pancytopenia, at a time when a definitive lymphoma diagnosis had not been established. However, after several months of treatments, the patient's cytopenias and clinical symptoms showed no improvement. A subsequent empirical course of methylprednisolone (16 mg daily) initiated in June 2023, was also ineffective.

In March 2024, the patient was readmitted presenting with worsening pancytopenia (hemoglobin, 35 g/l) accompanied by recurrent fever. Repeat imaging with CT and ultrasonography again revealed no evidence of lymphadenopathy or splenomegaly. A second BM biopsy proved decisive. The aspirate (Fig. 3) demonstrated a marked lymphocytosis (74% total lymphocytes; 30.02% T-cells; and 43.96% NK-cells). Flow cytometry failed to detect the previously identified clonal T-cell population, or any aberrant B-cell clone. However, the core biopsy revealed a diffuse infiltrate of large lymphoid cells. IHC confirmed B-cell lineage, with strong CD20 and CD79a expression, and a Ki-67 proliferation index of ~30%. CD3 highlighted a residual background population of T-cells. Reticulin staining confirmed persistent grade 2 MF. Collectively, these findings established a diagnosis of DLBCL. A definitive diagnosis of PBM-DLBCL with secondary MF was established, in accordance with the World Health Organization classification of hematolymphoid tumors (2022) (10), owing to the absence of extramedullary involvement.

The patient and their family declined the recommended immunochemotherapy (R-CHOP regimen) and further diagnostic tests, including molecular testing for JAK2, CALR and MPL mutations or FISH for MYC/BCL2 rearrangements. The patient was subsequently lost to follow-up, and the ultimate outcome remains unknown.

Methods

Flow cytometric analysis. Immunophenotyping of bone marrow samples was performed using multicolor flow cytometry. A comprehensive antibody panel targeting lineage-associated antigens for lymphoid and myeloid leukemias/lymphomas was employed for surface and/or intracellular staining. Briefly, the staining protocol was as follows: In total, ~$1x10^6$ cells were incubated with pre-titrated antibody cocktails at room temperature for 15-20 min in the dark. Subsequently, red blood cells were lysed using a lysing solution, followed by two washes with phosphate-buffered saline. The cells were then resuspended in fixation buffer prior to acquisition.

Data acquisition was conducted on a BD FACSymphony A5 flow cytometer (BD Biosciences). The acquired data were analyzed using FlowJo™ software (version 10.8; BD Biosciences).

For data analysis, target lymphocyte populations and other nucleated cell subsets were precisely gated based on forward scatter and side scatter properties, combined with CD45 expression. To eliminate spectral overlap in multicolor detection, fluorescence compensation was applied using single-stained compensation beads. Positive thresholds for specific antibody expression were determined using isotype controls and/or fluorescence-minus-one controls.

The antigens investigated, along with their corresponding fluorochromes, catalog numbers and suppliers, are detailed in Table II. All antibodies were purchased from BD Biosciences and used according to the manufacturer's recommended concentrations.

Histological staining protocol. Bone marrow biopsy specimens were fixed in 10% neutral buffered formalin at

Table I. Timeline of key clinical events, interventions, and diagnostic findings.

Date	Event/intervention	Key diagnostic findings/outcome
2023-04	Initial admission	Presented with fever, malaise. Found to have severe pancytopenia (hemoglobin, 52 g/l).
	First bone marrow biopsy	Flow cytometry: 79.54% T-cells (CD4:CD8=1.70), monoclonal TCR-γ rearrangement. Biopsy: Collagen fiber proliferation, multifocal lymphocytic infiltrates (30% $CD3^+$). Suspected T-cell lymphoma with MF.
2023-04 to 06	Cyclosporine therapy	No significant improvement in blood counts or symptoms.
2023-06	Methylprednisolone therapy	Started 16 mg/day. No response observed.
2024-03	Second admission	Worsening pancytopenia (hemoglobin, 35 g/l) and fever.
	Second bone marrow biopsy	Flow cytometry: No abnormal clone detected. Biopsy and IHC: $CD20^+$, $CD79a^+$ large B-cells (Ki-67 30%+). Diagnosis: Primary bone marrow diffuse large B-cell lymphoma with secondary MF.
	Post-diagnosis	Immunochemotherapy recommended but refused by the patient. and family
2024-06 (Manuscript preparation)	Outcome	Lost to follow-up. Final outcome unknown.

MF, myelofibrosis; TCR-γ, T-cell receptor γ; IHC, immunohistochemistry.

room temperature (22-25˚C) for 12-24 h. Following fixation, tissues were processed through standard dehydration, clearing and paraffin embedding procedures. Consecutive sections were cut at a 3-μm thickness using a rotary microtome and mounted on charged glass slides.

For hematoxylin and eosin staining, deparaffinized and rehydrated sections were stained with hematoxylin solution (room temperature, 8 min), blued in running tap water and counterstained with eosin ethanol solution (room temperature, 3 min). Sections were then dehydrated through graded ethanol, cleared in xylene and mounted with neutral balsam.

Reticular fiber staining was performed using Gomori's methenamine silver method. The procedure included treatment of deparaffinized sections with 0.5% periodic acid (room temperature, 10 min) for oxidation, followed by impregnation in freshly prepared methenamine silver working solution (room temperature, 20-30 min). Subsequent steps involved toning with 0.2% gold chloride and nuclear counterstaining with nuclear fast red.

All staining procedures were conducted at room temperature following standard protocols, with detailed information on staining reagents provided in Table III. All sections were examined, evaluated and imaged using an Olympus BX43 light microscope (Olympus Corporation).

IHC staining protocol. Bone marrow biopsy specimens were fixed in 10% neutral buffered formalin at room temperature for 40 min, followed by routine dehydration and clearing before embedding in paraffin. Tissue blocks were sectioned at a 3-μm thickness and mounted on glass slides. After deparaffinization and rehydration, endogenous peroxidase activity was blocked by incubation with 3% hydrogen peroxide at room temperature for 8 min. The antibodies used in this study and their corresponding specifications are listed in Table III. Sections were subsequently incubated with primary antibodies. Following thorough washing, the sections were treated with appropriate secondary antibody detection systems. Diaminobenzidine was employed as the chromogenic substrate, followed by counterstaining with hematoxylin, dehydration, clearing and final mounting. All stained sections were examined under an Olympus BX43 light microscope, with representative images captured at x40 and x100 magnification.

Discussion

The present case report illustrated the substantial diagnostic challenges posed by PBM-DLBCL. The initial presentation characterized by pancytopenia and BM fibrosis and the presence of a clonal T-cell population, initially suggested a T-cell lymphoproliferative disease. The second biopsy revealed a proliferation of medium-to-large lymphocytes that had not been detected in the initial fibrotic sample. Crucially, IHC demonstrated that these large cells were strongly positive for CD20 and CD79a (B-cell markers), with an elevated Ki-67 index, confirming a dominant monoclonal B-cell process. T-cell populations were present but merely constituted a background component. The markedly different finding on the second BM biopsy underscores the pivotal role of repeat marrow evaluation in patients with refractory cytopenia or a progressive clinical course.

The initial clonal T-cell population represented an enigmatic finding. Its absence on the second BM evaluation suggests it may have reflected an incidental clonal T-cell expansion of uncertain clinical significance or a reactive process that was subsequently overtaken by the more aggressive DLBCL

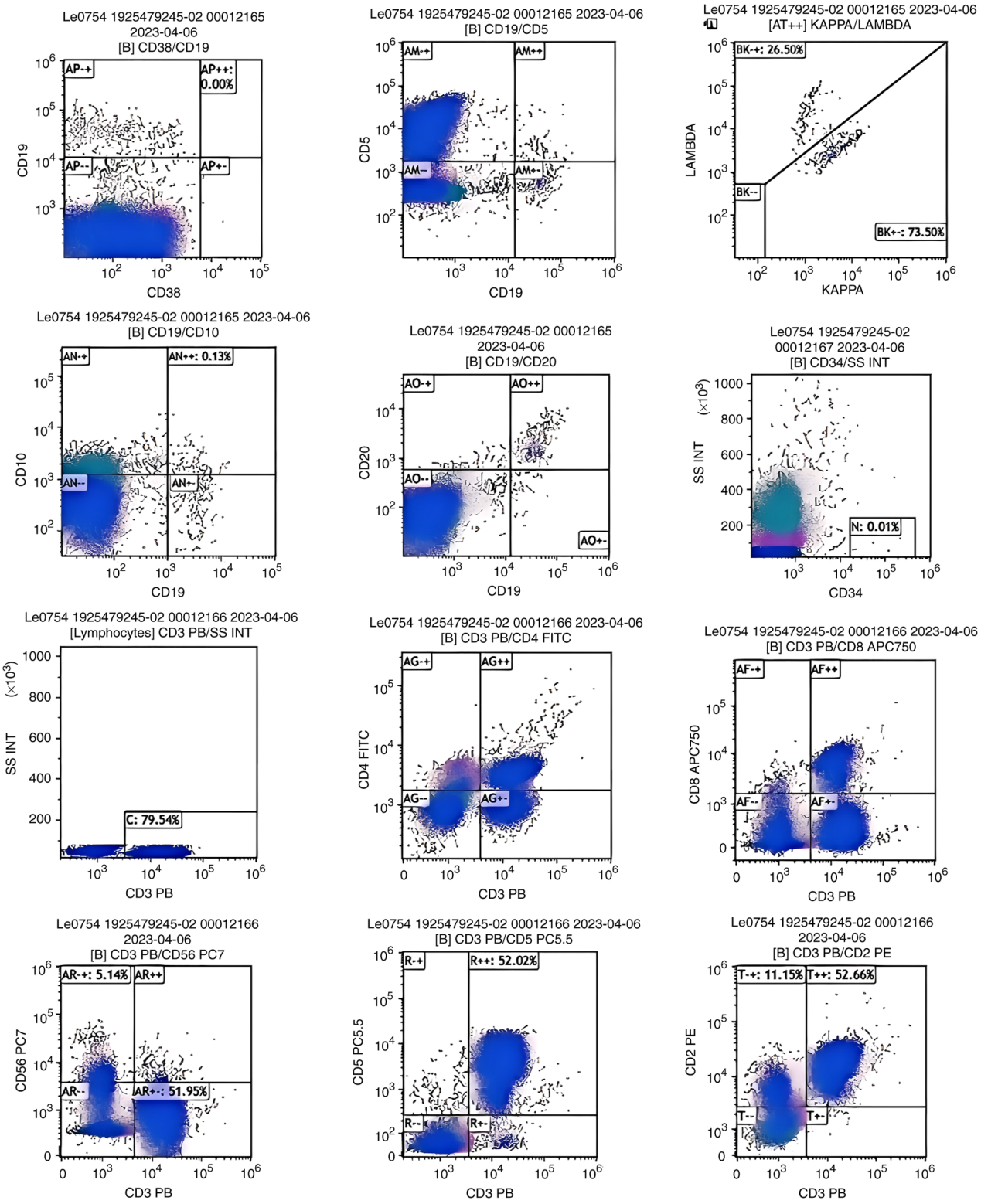

Figure 1. Flow cytometric analysis of surface marker expression. Representative flow cytometry plots gated on relevant lymphocyte populations. The analysis shows the expression profiles and co-expression of various B-cell markers, including CD19, CD20 and CD3, among others, as indicated on the axes. Percentages within the quadrants indicate the proportion of cells positive for the respective markers. Samples were acquired from peripheral blood. The specific sample identifier is Le0754 1925-079245-02, with an acquisition date of 2023-04-06.

clone. Although the presence of a true composite lymphoma is conceivable, it appears less likely. Comparative TCR-γ gene rearrangement analysis or more comprehensive molecular profiling on the second sample were not performed due to patient refusal, leaving this question unresolved.

The patient received supportive care and regular monitoring in an outpatient setting. Following the initial biopsy, the working diagnosis was a T-cell lymphoproliferative disorder with associated MF. However, the patient failed to respond to first-line immunosuppressive therapy (cyclosporine)

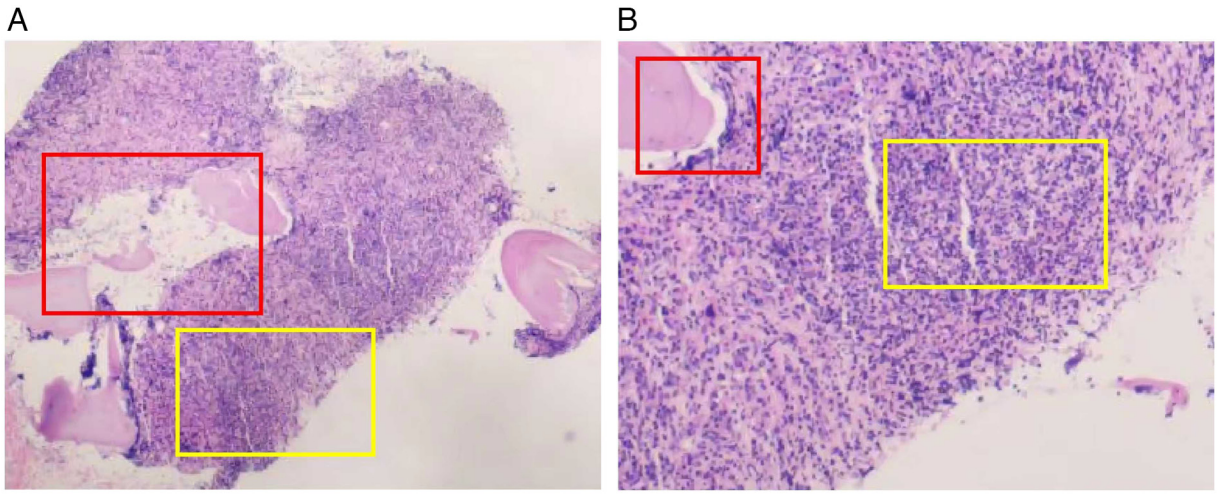

Figure 2. Initial bone marrow biopsy (April 2023). Morphological analysis of hematoxylin and eosin-stained sections revealed myeloproliferative changes with dense infiltration of small-to medium-sized lymphocytes (red-marked areas). Combined reticulin staining demonstrated prominent stromal fibrosis in the bone marrow (yellow-marked areas), confirming the presence of densely branched reticular fibers consistent with Grade 2 myelofibrosis (OLYMPUS BX43 microscope). (A) x40 magnification and (B) x400 magnification.

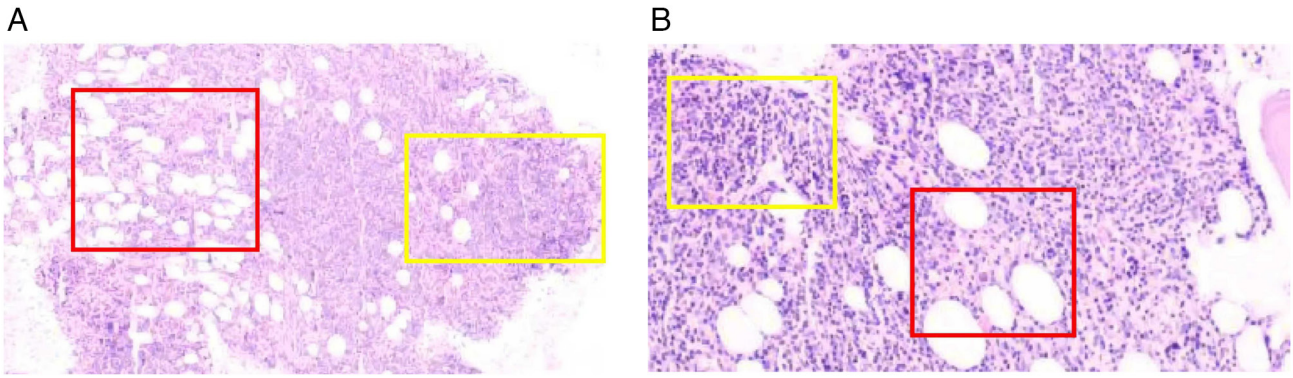

Figure 3. Second bone marrow biopsy (March 2024). Microscopic analysis of hematoxylin and eosin-stained sections revealed prominent lymphocytic hyperplasia with moderately enlarged cells (red-marked areas). Reticulin staining identified focal collagen fiber proliferation within the bone marrow stroma (yellow-marked areas), confirming the presence of densely branched reticular fibers consistent with Grade 2 myelofibrosis (OLYMPUS BX43 microscope). (A) x40 magnification and (B) x400 magnification.

and subsequent glucocorticoid treatment, a finding that fundamentally challenged the initial diagnostic impression. Glucocorticoid resistance is highly unusual in classical T-cell lymphomas and effectively ruled out steroid-responsive conditions such as autoimmune cytopenia or certain forms of aplastic anemia. Treatment failure thus became the key catalyst prompting re-evaluation and a definitive second BM biopsy. In effect, the lack of treatment response served as the most critical 'diagnostic test' at this stage, directing investigation toward a more aggressive underlying pathology.

Lack of response to glucocorticoids is characteristic of high-grade lymphomas, including DLBCL. Although glucocorticoids exhibit lympholytic effects and are commonly used in combination chemotherapy (for example, R-CHOP), they are largely ineffective as long-term monotherapy in DLBCL. Their action primarily induces apoptosis in mature lymphocytes, but aggressive malignant clones such as DLBCL rapidly develop resistance (11). Thus, the persistent clinical and hematological deterioration despite glucocorticoid therapy was inconsistent with an indolent T-cell disorder or immune-mediated cytopenia and instead aligned with the profile of an aggressive lymphoma such as DLBCL. This clinical course provided critical corroborative evidence for the ultimate diagnosis and reinforced the histopathological findings of the second biopsy.

Secondary MF is frequently a reactive process to an underlying malignancy, analogous to the MF observed in metastatic cancer (12). However, its occurrence in the rare context of PBM-DLBCL generates a complex clinical scenario that can obscure the underlying diagnosis. In the present case, the secondary MF was hypothesized to be cytokine-mediated. The DLBCL cells likely secreted profibrotic cytokines such as TGF-β and PDGF, which subsequently activated the JAK/STAT and SMAD pathways in BM stromal cells, ultimately leading to collagen deposition and marrow fibrosis, as confirmed by the reticulin staining. This cytokine-driven remodeling of the BM microenvironment represents a plausible central mechanism (13,14). According to the 2024 CSCO guidelines for PMF, diagnosis requires the presence of all three major criteria, including megakaryocyte hyperplasia with atypia, grade ≥2

Table II. Flow cytometric analytes and fluorochromes.

Antigen	Fluorochrome	Clone	Catalog number	Supplier
CD45	V500	HI30	560777	BD Biosciences
CD45	PerCP-Cy5.5	HI30	560777	BD Biosciences
CD45	APC-H7	2D1	560178	BD Biosciences
CD3	FITC	UCHT1	561806	BD Biosciences
CD3	PerCP-Cy5.5	SK7	340916	BD Biosciences
CD4	FITC	SK3	340133	BD Biosciences
CD8	APC	SK1	561953	BD Biosciences
CD19	PE	HIB19	561741	BD Biosciences
CD19	V450	HIB19	561297	BD Biosciences
CD20	PE-Cy7	L27	560734	BD Biosciences
CD5	APC	L17F12	561896	BD Biosciences
CD5	PE-Cy7	UCHT2	561899	BD Biosciences
CD7	PE	M-T701	561603	BD Biosciences
CD2	APC	RPA-2.10	561765	BD Biosciences
CD10	APC	HI10a	561003	BD Biosciences
CD38	Brilliant Violet 711	HB-7	563438	BD Biosciences
CD56	PE	NCAM16.2	562751	BD Biosciences
Kappa	FITC	TB28-2	556867	BD Biosciences
Lambda	PE	1-155-2	556874	BD Biosciences
CD34	V450	581	561204	BD Biosciences
CD117	PE	104D2	561199	BD Biosciences
HLA-DR	PerCP-Cy5.5	L243	552764	BD Biosciences
CD33	PE	P67.6	561816	BD Biosciences
CD71	APC	M-A712	561775	BD Biosciences
CD41	PE	HIP8	561433	BD Biosciences

reticulin fibrosis and JAK2/CALR/MPL mutation, along with at least one minor criterion (for example, splenomegaly, anemia or increased serum LDH level). By contrast, establishing a diagnosis of secondary MF requires the exclusion of PMF or other MPNs with differentiation by BM pathology and mutation analysis for JAK2/CALR/MPL (15). In the last decade, two targeted therapies have been approved for the treatment of MF, both JAK2 inhibitors, namely ruxolitinib and fedratinib (16). While the majority of patients with DLBCL present with advanced-stage disease at diagnosis, >60% can be cured with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) immunochemotherapy (11). In the present case report, the clear evidence of a B-cell lymphomatous process supports the classification as secondary MF. Although molecular testing for JAK2, CALR and MPL mutations would have been invaluable to formally exclude an underlying MPN, the patient's refusal precluded this analysis, presenting a significant limitation.

The review by Zamò *et al* (17) demonstrated that molecular characterization of rare hematological malignancies necessitates multicenter collaboration to accrue sufficient sample sizes. For PBM-DLBCL with secondary MF, further studies can be conducted in the following aspects: i) Molecular mechanisms: Delineating the microenvironmental differences between patients with PBM-DLBCL with versus without MF by single-cell sequencing or spatial transcriptomics to identify fibrosis-driving factors. ii) Prognostic impact: Evaluating whether the presence of MF exacerbates BM failure or contributes to treatment resistance in PBM-DLBCL requires long-term follow-up data support. iii) Clinical management: Assessing the feasibility and efficacy of combined therapeutic approaches, including immunochemotherapy (for example, R-CHOP), targeted agents (JAK inhibitors) and antifibrotic interventions (for example, TGF-β inhibitors).

Currently, the efficacy of conventional DLBCL regimens (for example, R-CHOP) in PBM- DLBCL with secondary MF remains uncertain. Although using rituximab markedly improves the prognosis of patients with CD20-positive B-cell lymphomas, its efficacy has not been rigorously validated in PBML due to the lack of randomized controlled clinical trials (18,19). The potential utility of incorporating a JAK inhibitor (for example, ruxolitinib) to target the fibrotic morrow microenvironment in this setting remains unexplored and warrants future investigation. In conclusion, the extreme rarity of PBM-DLBCL with MF creates substantial gaps about its pathophysiology and optimal therapeutic strategies. In the future, cases could be collected through international registry systems (for example, NIH or ESMO rare tumor databases) and combined with multi-omics analyses to facilitate personalized treatment approaches. The patient's refusal of treatment precluded any assessment of therapeutic response and resulted in a loss of valuable prognostic data.

Table III. Staining reagents and conditions for bone marrow biopsy.

A, Immunohistochemistry

Target/stain	Supplier	Catalog no.	Dilution	Incubation temperature, ˚C	Incubation duration, min	Conjugate
Primary antibodies						
CD10	Jiangsu Calt Biotechnology Development Co., Ltd.	CTB062V6	1:50	37	30	/
CD20	Fuzhou Maixin Biotechnology Development Co., Ltd.	Kit0001	1:200	37	30	/
CD23	Fuzhou Maixin Biotechnology Development Co., Ltd.	RMA0504	1:100	37	30	/
CD3	Fuzhou Maixin Biotechnology Development Co., Ltd.	MAB0740	1:100	37	30	/
CD34	Zhongshan Aoquan Biotechnology Development Co., Ltd.	NCL-L-END	1:150	37	30	/
CD5	Zhongshan Aoquan Biotechnology Development Co., Ltd.	RTU-CD5-4C7-QH	1:150	37	30	/
CD56	Zhongshan Medical Technology Development (Guangzhou) Co., Ltd.	ZM0057	1:150	37	30	/
CD61	Zhongshan Aoquan Biotechnology Development Co., Ltd.	NCL-L-CD61	1:100	37	30	/
CD79a	Zhongshan Medical Technology Development (Guangzhou) Co., Ltd.	ZA0293	1:150	37	30	/
E-cad	Zhongshan Aoquan Biotechnology Development Co., Ltd.	RTU-ECAD-QH	1:100	37	30	/
Ki-67	Jiangsu Calt Biotechnology Development Co., Ltd.	CTB004V6	1:150	37	30	/
Cyclin-D1	Jiangsu Calt Biotechnology Development Co., Ltd.	CTB026V6	1:100	32	35	/
Secondary antibodies						
CD10	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:200	37	15	DAB
CD20	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:1,000	37	15	DAB
CD23	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:500	37	15	DAB
CD3	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:500	37	15	DAB
CD34	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:1,000	37	15	DAB
CD5	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:1,500	37	15	DAB

Table III. Continued.

A, Immunohistochemistry

Target/stain	Supplier	Catalog no.	Dilution	Incubation temperature, ˚C	Incubation duration, min	Conjugate
CD56	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:8,000	37	15	DAB
CD61	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:1,000	37	15	DAB
CD79a	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:1,000	37	15	DAB
E-cad	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:5,000	37	15	DAB
Ki-67	Zhongshan Aoquan Biotechnology Development Co., Ltd.	7600	1:4,000	37	15	DAB
Cyclin-D1	Jiangsu Calt Biotechnology Development Co., Ltd.	CTBK11-1	1:750	32	12	DAB

B, Hematoxylin and eosin staining

Target/stain	Supplier	Catalog no.	Dilution	Incubation temperature, ˚C	Incubation duration, min	Conjugate
Hematoxylin	Zhuhai Besso Biotechnology Co., Ltd	BA-4097	RTU	22-25	8-10	/
Eosin	Zhuhai Besso Biotechnology Co., Ltd	BA-4098	RTU	22-25	1-3	/

C, Reticular fiber staining

Target/stain	Supplier	Catalog no.	Dilution	Incubation temperature, ˚C	Incubation duration, min	Conjugate
Periodic acid	Sinopharm Chemical Reagent Co., Ltd.	10024118	0.5% (aq)	22-25	10	/
GMS	Shenzhen DAKEWE Bio-engineering Co., Ltd.	D02013	RTU	22-25	20-30	MS
Gold chloride	Shanghai Aladdin Biochemical Technology Co., Ltd.	G112803	0.2% (aq)	22-25	22-25	/
Nuclear fast red	Shanghai Macklin Biochemical Co., Ltd.	R817461	0.1% (aq)	22-25	5	/

DAB, 3,3'-diaminobenzidine; RTU, ready-to-use; (aq), aqueous solution; GMS, methenamine silver solution; SM, metallic silver.

PBM-DLBCL represents a diagnostically challenging malignancy, underscoring the importance of heightened clinical awareness. PBM-DLBCL should be considered in patients presenting with unexplained pancytopenia.

The present case report has several limitations, primarily due to the patient's refusal of further testing. The lack of PET/CT imaging precludes definitive exclusion of occult extramedullary disease, though it was not detected on available CT scans. Additionally, the absence of molecular data (JAK2/CALR/MPL and MYC/BCL2 analysis by FISH) and an extended IHC panel (for example, MUM-1, BCL-2, BCL-6 and C-MYC) hampers accurate prognostic stratification for both the MF and the DLBCL. The 11-month interval between the initial steroid-refractory presentation and the second BM biopsy, although ultimately leading to a definitive diagnosis, represents a potential delay; however, it was the progression of symptoms and cytopenias that necessitated the repeat procedure. In conclusion, accurate diagnosis of PBM-DLBCL requires a comprehensive clinical and laboratory evaluation, the utilization of appropriate diagnostic modalities in cases of unexplained cytopenia, and a meticulous clinical approach to ensure optimal patient safety and outcomes. PBM-DLBCL is a diagnostic chameleon capable of mimicking T-cell malignancies, aplastic anemia and other causes of marrow failure. The present case report highlights that the presence of a clonal T-cell population does not necessarily confirm a T-cell lymphoma diagnosis and may represent a misleading secondary finding. Unexplained and persistent pancytopenia, especially when accompanied with systemic symptoms and elevated LDH, warrants a low threshold for repeat BM evaluation. Moreover, the complex interplay between lymphoma and the marrow microenvironment, leading to fibrosis, represents a critical avenue for further research to elucidate pathogenesis and identify potential therapeutic targets. Overall, this case underscores the diagnostic challenges and the imperative for thorough and at times, repeated diagnostic assessment.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JY, SKT, HP, YYP, ML and KS conceived and designed the study. JY, SKT, HP and YYP collected and interpreted all relevant clinical and laboratory data. JY, SKT, HP, YYP, ML and KS prepared the manuscript. ML and KS revised the manuscript. All authors have read and approved the final manuscript. JY, SKT, HP, YYP, ML and KS confirm the authenticity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Competing interests

The authors declare that they have no competing interests.

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