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CASE REPORT

When bone marrow is Silent: PET/CT detection of splenic lymphoma in persistent pancytopenia

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Abstract:

Background: Chronic pancytopenia in adults presents a broad differential diagnosis and often requires comprehensive evaluation to identify the underlying etiology. **Case Report**: We present the case of a middle-aged man whose initial tests, which included a trephine biopsy and bone marrow aspiration, failed to reveal the cause of his persistent pancytopenia, hepatosplenomegaly, and constitutional symptoms. No cause was found after extensive testing for infections, autoimmune diseases, and dietary deficiencies. Eventually, ^18F-FDG PET/CT showed that the spleen was diffusely hypermetabolic, which led to the suspicion that the patient had primary splenic lymphoma. Histopathological analysis and splenectomy confirmed the diagnosis. The patient unfortunately passed away before treatment could be initiated. **Conclusion**: This case study demonstrates the limitations of traditional marrow-based diagnostics in some hematologic malignancies and emphasizes the critical need for sophisticated imaging, specifically PET/CT, in detecting hidden lymphomas when regular investigations provide inconclusive results.

Key Words: Bone Marrow Biopsy, Pancytopenia, PET/CT Scan, Splenic Lymphoma

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Introduction

Primary splenic lymphoma (PSL) is a rare extranodal lymphoma, which amounts to around 1-2% of all lymphomas when narrowly defined as a disease involving only the spleen and its hilar lymph nodes (1).

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Due to its rarity, combined with non-specific systemic findings like fever, weight loss, and malaise, its diagnosis is usually delayed. A lack of peripheral lymphadenopathy and a non-diagnostic bone marrow examination add further complexity to the diagnostic challenge, especially in early or localized disease.

Bone marrow aspiration and biopsy remain essential first-line investigations in patients with unexplained cytopenias and suspected hematologic malignancy(2-4). However, their sensitivity is limited in scenarios where lymphoma is confined to the spleen or demonstrates patchy marrow involvement, creating a diagnostic blind spot. Conventional imaging modalities, including ultrasound and contrast-enhanced computed tomography (CT), can reliably detect

splenomegaly and large focal lesions but cannot assess metabolic activity. In contrast, ^{18}F-FDG PET/CT provides a combined anatomical and metabolic assessment, enabling the detection of hypermetabolic splenic lesions that may be morphologically subtle or radiologically occult on CT (5).

Here, we report a diagnostically challenging case of T-cell/histiocyte-rich large B-cell lymphoma presenting with primary splenic involvement, where repeated evaluations of the bone marrow were non-diagnostic.

Case Presentation

A 50-year-old man came to the hospital in early May 2025 with progressive tiredness, pallor, low-grade fever, and dark urine. Rectal bleeding had been noted by the patient two months back, which had initially attributed to haemorrhoids, and he has been self-medicating with unregulated herbal preparations ("Hakeem" medicines). The history of past illnesses was haemorrhoids of eight-year duration and chronic usage of herbal medications. Examination findings: pallor and mild splenomegaly without hepatomegaly or lymphadenopathy. Laboratory examination on initial workup showed recurrent pancytopenia on three different complete blood counts (Hb 7.4 g/dL, WBC 2.4 × 10^9/L, platelet 93 × 10^9/L), normocytic red cells (MCV 94 fL), and increased red cell distribution width (RDW 17.8%). Urinalysis: dark yellow urine, bilirubin (+++), urobilinogen, no hematuria. C-reactive protein (CRP) positive, malaria, tuberculosis, and Hepatitis B/C screening negative.

Aspiration and biopsy on 14 May 2025 showed 60% cellularity with active trilineage hematopoiesis, megaloblastic changes in erythroid precursors, large abnormal myeloid forms, active megakaryocytes, absent iron stores, and no granuloma, lymphoma, or metastatic tumor. This was compatible with combined vitamin B12 and folate deficiency with iron deficiency. He was started on vitamin B12 injections, oral folate, and iron supplementation. Iron and folate levels normalized by the end of May, and vitamin B12 levels were increased secondary to supplementation. Carcinoembryonic antigen (CEA) and stool calprotectin were within normal limits.

In June 2025, the patient reported persistent fever (up to 103°F), productive cough with white sputum, and progressive weight loss of 12 kg over three months. Colonoscopy showed normal mucosa with only external hemorrhoids, confirming a likely source of chronic gastrointestinal blood loss. Repeat laboratorytesting demonstrated elevated CRP (43.50 mg/L), reduced total iron-binding capacity (210 µg/dL), and low transferrin saturation (24.83%). Hepatitis B and C ELISA testing remained non-reactive. Contrast-enhanced CT of the chest, abdomen, and pelvis on 21 June revealed moderate hepato splenomegaly with multiple hypodense splenic lesions (largest 6.2 × 6.2 cm) and mild perihepatic ascites (Figure. 1). Splenic biopsy was planned but deferred due to technical limitations.

By July 2025, the patient's symptoms had continued with aggravating sign and symptoms.CBC on 28 July demonstrated worsening pancytopenia (hemoglobin 7.0 g/dL, WBC 1.9 × 10^9/L, platelets 82 × 10^9/L). Ferritin was significantly high (20,368 ng/mL), LDH was increased (312 U/L), and

fibrinogen was low-normal (205 mg/dL).

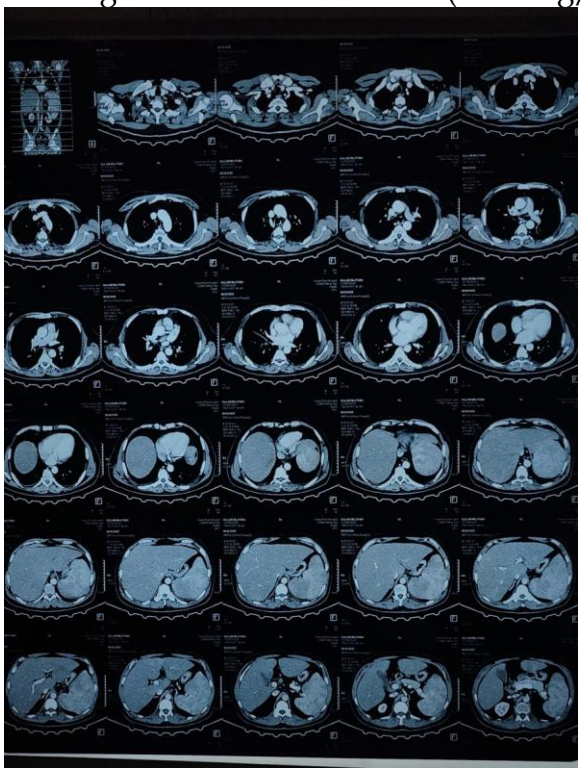

Figure1.Moderately enlarged hepatosplenomegaly. Multiple hypo densities in spleen biopsy correlation is needed.

Extensive infectious workup came back negative except for CMV DNA PCR, which identified active viremia (viral load 4,440 IU/mL). Imaging verified persistent hepatosplenomegaly with multiple splenic lesions and no indication of portal hypertension. Hematology and infectious disease teams contemplated secondary hemophagocytic lymphohistiocytosis (HLH) and recommended additional evaluation.

PET/CT on 24 July 2025 demonstrated hepatosplenomegaly with diffuse uptake in the liver, multiple hypermetabolic lesions in the spleen (SUVmax of up to 13.7), some hypermetabolic lymph nodes in the abdomen, and multifocal skeletal uptake compatible with early marrow involvement. Ultrasound-guided Tru-Cut biopsy of the spleen, on 28 July 2025, produced multiple intact cores, and histopathology on 5 August confirmed T-cell/histiocyte-rich large B-cell lymphoma (CD20+, PAX5+, CD79a+, CD3+ background T cells, negative for EBER, Ki-67 moderate). Bone marrow examination on 7 August demonstrated hypercellular marrow containing active trilineage hematopoiesis, mild mega blastoid change, and no lymphoma infiltration. At diagnosis, the disease had only involved the spleen and lymph nodes in the abdomen, consistent with primary extranodal splenic involvement. The patient had undergone multiple diagnostic investigations from different laboratories, including Aitzaz Lab and Diagnostic Center (Mandi Bahauddin), Pakistan Kidney and Liver Institute and Research Center (Lahore), and Shaukat Khanum Memorial Cancer Hospital and Research Centre (Lahore).

The initial differentials were nutritional deficiencies (vitamin B12, folate, and iron), substantiated by initial bone marrow findings, as well as chronic gastrointestinal bleeding secondary to hemorrhoids and the potential toxic marrow suppression by unregulated herbal medications. Hemolytic anemia was also in the differential secondary to dark urine and indirect hyperbilirubinemia, though the direct antiglobulin test was negative. Infectious causes such as malaria, tuberculosis, HIV, viral hepatitis, CMV, and EBV were thoroughly examined, with only CMV viremia identified. The autoimmune and inflammatory causes, such as secondary hemophagocytic lymphohistiocytosis (HLH), were also suspected owing to markedly elevated ferritin, prolonged febrile course, and cytopenias present. Ultimately, infiltrative or neoplastic causes such as aplastic anemia, myelodysplastic syndrome, leukemia, and lymphoma were in the differential after imaging identified multiple

splenic lesions. The lack of diagnostic marrow findings presented a clinical blind spot, eventually unraveled by PET/CT-guided splenic biopsy, establishing the diagnosis of T-cell/histiocyte-rich large B-cell lymphoma.

Supportive care with transfusions of blood, antimicrobial treatment, and nutritional support was continued; yet disease-directed chemotherapy could not be initiated due to the swiftly progressive state of the patient. The patient unfortunately passed away a short time after diagnosis was confirmed. The outcome reveals to what extent delay at diagnosis can significantly detract from therapy opportunities.

Discussion

The diagnostic evaluation of persistent pancytopenia is fundamentally difficult, given its broad differential diagnosis encompassing hematologic malignancies, marrow failure syndromes, autoimmune diseases, chronic infections, and nutritional deficiencies(6). Clinically, the aspiration and biopsy of the bone marrow are the definitive diagnostic tools of hematologic malignancies(7).

This case highlights the importance of a multimodal diagnostic workup. Although standard imaging (ultrasound, CT) can detect splenomegaly, it is frequently insensitive to lesions that are metabolically active but morphologically mild. ^18F-FDG PET/CT, on the other hand, offers both metabolic and anatomical information, allowing detection of hypermetabolic splenic involvement that would otherwise be missed (5). PET/CT in our patient noted intense FDG uptake within the spleen, which led the clinical team towards splenectomy and histopathological confirmation of lymphoma.

This case presents three major diagnostic lessons. First, refractory pancytopenia with constitutional symptoms justifies sustained diagnostic initiative, despite the lack of first-line diagnostic findings. Second, a non-diagnostic marrow does not rule out lymphoma, especially among patients with unexplained splenomegaly. Third, PET/CT ought to be incorporated sooner in the diagnostic pathway in those with a high clinical index of suspicion but indeterminate marrow studies, because PET/CTscan localize the disease, direct site-specific biopsies, and shorten diagnostic delay.

Lastly, early splenic lymphoma diagnosis requires a high index of suspicion, selective use of adjunctive imaging, and a second examination of negative results. This case illustrates PET/CT's role, specifically, at the diagnostic turning point when the bone marrow was silent.

Conclusion

This case demonstrates the profound diagnostic challenges posed by primary splenic lymphoma presenting with persistent pancytopenia and inconclusive marrow studies.Early integration of PET/CT into the diagnostic pathway may not only facilitate timely diagnosis but also provide patients with the opportunity to receive appropriate treatment before the disease becomes fatal.

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Note: Consent details and related documents were given by brother of the deceased patient to be published as case report.

References

1. Sinit RB, Dorer RK, Flores JP, Aboulafia DM. Rare causes of isolated and progressive splenic lesions: challenges in differential

diagnosis, evaluation, and treatment of primary splenic lymphomas. *Clin Med Insights BloodDisord*.2020;13:1179545X20926188.
2. Bedu-Addo G, Amoako YA, Bates I. The role of bone marrow aspirate and trephine samples in haematological diagnoses in patients referred to a teaching hospital in Ghana. *Ghana Med J*. 2013;47(2):74–78.
3. Khan MI, Ahmad N, Fatima SH. Haematological disorders: analysis of haematological disorders through bone marrow biopsy examination. *Prof Med J*.2018;25(6):823-3. DOI:10.29309/TPMJ/18.4500
4. Munir AH, Qayyum S, Gul A, Ashraf Z. Bone marrow aspiration findings in a tertiary care hospital of Peshawar. *J Postgrad Med Inst*. 2015;29(4): 297-300.
5. Salem AE, Shah HR, Covington MF, Koppula BR, Fine GC, Wiggins RH, et al. PET-CT in clinical adult oncology: I. Hematologic malignancies. *Cancers (Basel)*.2022;14(23):5941. https://doi.org/10.3390/cancers14235941
6. Gnanaraj J, Parnes A, Francis CW, Go RS, Takemoto CM, Hashmi SK. Approach to pancytopenia: diagnostic algorithm for clinical hematologists. *Blood Rev*. 2018;32(5):361–67.
7. Syed NN, Moiz B, Adil S, Khurshid M. Diagnostic importance of bone marrow examination in non-hematological disorders. *J Pak Med Assoc*. 2007;57(3):123–25.

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