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FIBROTIC EXTRAMEDULLARY HEMATOPOIESIS IN INGUINAL LYMPH NODES: A RARE PRESENTATION OF PRIMARY MYELOFIBROSIS

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ABSTRACT Primary myelofibrosis is a rare clonal myeloproliferative neoplasm characterized by progressive bone marrow fibrosis, extramedullary hematopoiesis (EMH), and variable cytopenias. We report a case of an elderly female who presented with anemia, hepatosplenomegaly, and bilateral inguinal lymphadenopathy. Radiological imaging revealed features of skeletal myelosclerosis and EMH. Her bone marrow biopsy showed grade 3 reticulin and collagen fibrosis with atypical megakaryocytes, while an inguinal lymph node biopsy demonstrated extensive fibrosis with trilineage EMH and clusters of dysplastic megakaryocytes, distorting the nodal architecture. This case represents a rare instance of fibrotic EMH in lymph nodes, with only three similar cases reported previously. Awareness of such atypical presentations is vital for accurate diagnosis, especially when lymph node enlargement with associated fibrosis is the primary clinical feature.

KEYWORDS : Megakaryocyte Dysplasia, Myeloid Metaplasia, Lymph Node Fibrosis, Extramedullary Hematopoiesis, Primary Myelofibrosis

INTRODUCTION

Primary myelofibrosis (PMF) is a clonal myeloproliferative neoplasm with characteristic phenotypic features consisting of a leukoerythroblastic blood picture, increased circulating CD34+ cells in the blood, reactive bone marrow fibrosis, dysplastic megakaryopoiesis, splenomegaly and a tendency to form extramedullary fibro-hematopoietic tumors. Patients present with anemia, constitutional symptoms, splenomegaly, and are at risk of developing osteosclerosis as disease progresses. Lymph node involvement with extramedullary hematopoiesis (EMH) and accompanying fibrosis is extremely rare. Here, we describe a case of newly diagnosed PMF in which the lymph node showed infiltration by dysplastic megakaryocytes along with trilineage hematopoiesis and dense fibrosis. Only three such cases have been reported before, one of which showed a novel cytogenetic abnormality del (18) (p11.2-3) previously unreported in this condition [1].

Case Presentation

We report a case of a 65-year-old elderly female, housewife by profession, who presented to the outpatient department with complaints of generalized weakness, significant weight loss, loss of appetite, grade 2 breathlessness, and multiple episodes of giddiness. She also gave a history of vague bony pains since many years. There were no other comorbidities or chronic illnesses, although she had been treated 10 years back for abdominal Koch's disease.

On inspection, the patient appeared poorly built and nourished, with an emaciated look. She had severe pallor, bilateral pitting type of pedal edema which was symmetrical, non-tender and present till the ankles. Bilateral inguinal lymph nodes measuring 2x1 cm were felt which were non-matted and non-tender. Per abdominal examination revealed non-tender mild hepato-splenomegaly of 3 cm and 2 cm below the costal margin respectively. Her laboratory results are presented in table 1.

Table – 1: Laboratory Results *Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) for Tuberculosis

Parameter	Result	Standard Reference Range	Interpretation
Hemoglobin (Hb)	7 g/dL	Males: 13–17 g/dL Females: 12–15 g/dL	Severe anemia
Total Leukocyte Count (WBC)	11,800 cells/μL (or /mm³)	4,000–11,000 cells/μL	Mild leukocytosis
Peripheral blood smear	Leucoerythroblastic blood picture with poikilocytosis, tear-drop cells, and mild polychromasia	Normal smear: no immature cells, no significant poikilocytosis or tear-drop cells	Abnormal (leucoerythroblastic picture + teardrop cells suggest possible myelophthisic process or marrow infiltration)
Lactate dehydrogenase (LDH)	663 U/L	140–280 U/L (most Indian labs)	Elevated
Serum Protein Electrophoresis (SPE)	Faint band in the gamma-globulin region	No discrete (monoclonal) band; gamma region normally polyclonal (0.7–1.6 g/dL)	Abnormal
Tumor Markers	Negative	Negative	Normal
HIV serology	Negative	Negative	Normal
Hepatitis markers	Negative	Negative	Normal
CBNAAT (TB) *	Negative	Negative	Normal

X-ray imaging revealed a solid periosteal reaction with marrow expansion along bilateral femurs and tibial bones along with coarsening of trabeculae and cortical thinning. There was mild sclerosis of lumbar vertebrae, sacrum and the pelvic bones. Ultrasound and contrast enhanced CT scan of the abdomen and pelvis concurred with the X-ray findings, however a lobulated mass was found encasing the main portal vein at the porta hepatis. Multiple, enlarged and diffusely enhancing non-necrotic lymph nodes were confirmed in bilateral inguinal regions along with diffuse sclerosis involving the vertebrae, pelvis, bony rib cage and sternum. These features were suggestive of myelosclerosis with EMH involving the bones, although a neoplastic process such as lymphoma could not be ruled out at this stage.

A bone marrow aspirate and imprint smear resulted in a dry tap with no marrow fragments. However, a trephine biopsy showed decreased cellularity of marrow with Grade-3 collagen and reticulin fibrosis. Special stains were performed; Reticulin and Masson's trichrome stain demonstrated diffuse and dense increase in reticulin and collagen with extensive intersections and coarse bundles of thick fibers corresponding to WHO HAEM5 MF-3, involving >70% of marrow spaces. (Figures 1a-1c).

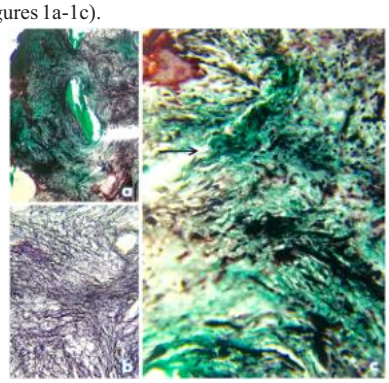

Figure 1: Bone Marrow Biopsy

(a) Masson trichrome stain on bone marrow biopsy demonstrating Grade-3 MF with diffuse and dense increase in collagen in >70% of marrow spaces (100x) and (b) Reticulin stain showing marked reticulin fibrosis- Grade 3 of 3 (100x) (c) Dense bundles of collagen fibers highlighted in green (400x).

There was a streaming effect of hematopoietic cells and alternating hypocellular and hypercellular areas. Occasional clusters of variably sized abnormal megakaryocytes, some bulbous and some small, located in paratrabecular regions suggested a shift from the normal perisinusoidal topography (Figures 2a-2d).

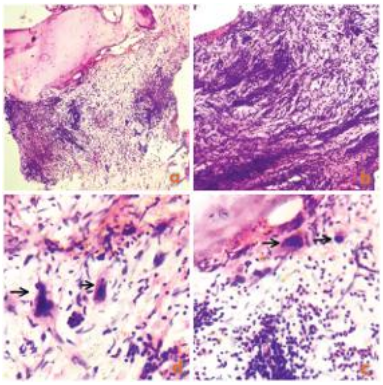

Figure 2: Bone Marrow Trephine Biopsy
(a) H&E stain showing alternating hypo- and hypercellular areas (100x) (b) Fibrosis comprising of spindle shaped fibroblasts in the marrow causing a streaming effect of the hematopoietic cells (400x), (c) Clusters of atypical megakaryocytes marked with black arrows (d) Megakaryocytes clusters showing change in topography adjacent to bony trabeculae. (400x)

While a fine-needle aspiration cytology (FNAC) of the inguinal lymph node revealed scanty amorphous material with occasional neutrophils and lymphoid cells, the biopsy mirrored the marrow findings with extensive fibrosis and spindle cells suggestive of a mesenchymal neoplastic process. Diffusely scattered among them were clusters of dysplastic megakaryocytes, myeloid and erythroid cells suggestive of trilineage EMH. The megakaryocytes were hyperchromatic with bizarre dysplastic nuclei almost similar in morphology to those in the bone marrow (Figures 3a-3d). Molecular testing for driver mutations *JAK2*, *CALR*, and *MPL* and immunohistochemistry was not performed due to financial constraints of the patient. However, the diagnosis was established based on WHO 2022/ICC criteria using clinical, peripheral smear, bone marrow morphology, and histopathology findings.

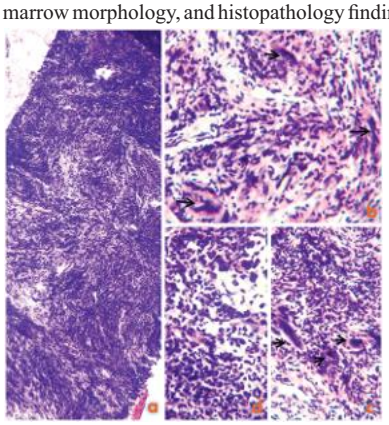

Figure 3: Lymph Node Biopsy
(a) H&E stain on lymph node biopsy showing distortion of nodal architecture and marked fibrosis (100x) (b and c) clusters of immature bizarre dysplastic megakaryocytes marked with black arrows (400x) (d) trilineage hematopoiesis consisting of myeloid and erythroid cells in a background of fibrosis and lymphoid cells (400x)

Thus, after ruling out an array of secondary causes of marrow fibrosis, based on the clinical, radiological and pathological features, a myeloproliferative neoplastic process was favored and a diagnosis of PMF with involvement of the inguinal lymph nodes was made.
Differential Diagnosis considered were

1. Overt Post-Polycythemia Vera Myelofibrosis (Post-PV MF)
2. Lymphocyte depleted Classical Hodgkins Lymphoma (LD-cHL)
3. Myelodysplastic Syndrome with myelofibrosis (MDS-F)

DISCUSSION

The incidence of PMF is rare with 0.44-1.5 cases/100,000 persons per year, usually between an age range of 60-70 years [2]. It is associated with genetic mutations of JAK2 (60%), CALR (25%), or MPL (5%) in 90% of cases. Other mutations related to myeloid neoplasms such as ASXL1, EZH2, IDH1, IDH2, SF3B1, SRSF2, and TET2 may be found in the remainder of cases [3,4].

The diagnosis requires meeting the International Consensus Criteria and WHO 2022 diagnostic criteria of PMF which classifies cases as pre-fibrotic and overt-fibrotic. The major criteria include characteristic bone marrow biopsy findings, genetic mutations as described earlier and the exclusion of other causes of marrow fibrosis. The minor criteria include anemia not attributed to comorbid conditions, leukocytosis ≥11 × 10^9/L, palpable splenomegaly, and an elevated lactate dehydrogenase. Leukoerythroblastosis is an additional minor criterion of Fibrotic PMF [4]. The megakaryocytic alterations are important diagnostically and pathogenically; megakaryopoiesis seen in clusters, frequently around marrow sinuses and paratrabecular location, megakaryocytic nuclear pleomorphism with ballooned or cloud-like nuclei and marked anisocytosis is seen. There may be dysmorphic platelets, bare megakaryocyte nuclei and cytoplasmic fragments in the blood [5,6].

The finding of EMH involving extramedullary organs and tissues occurs most likely via migration and implantation of the clonal neoplastic hematopoietic progenitor cell, and in all probability shares the same neoplastic process as in the BM. Some authors suggest that the scar tissue formation in the marrow disrupts the marrow-blood barrier and stem cells (CD34+) escape the marrow, circulate in peripheral blood to get lodged into tissues with favorable microenvironments [7-9].

Very rarely has EMH in myelofibrosis been associated to present with accompanying fibrosis in the organ involved, and only three cases of myelofibrosis involving the lymph nodes have been published till date. The case published in 2025 by Ding et al was associated with TET2, MPL, and SRSF2 mutations [10]; whereas another similar case in 2019 by Hu et al showed a novel mutation involving del (18) (p11.2-3) [1]. A third case revealed an unbalanced translocation resulting in gain of 1q [11].

CONCLUSIONS

In conclusion, this case highlights the rare occurrence of EMH with accompanying fibrosis in lymph nodes in primary myelofibrosis, an unusual manifestation seen in the spectrum of disease presentation. While the precise mechanisms driving neoplastic stem cell trafficking and seeding remain incompletely understood, disruption of the marrow-blood barrier by fibrosis and subsequent dissemination of CD34+ progenitors likely play a central role. Recognition of such atypical sites of involvement is essential for accurate diagnosis, especially in the absence of classical splenomegaly or when lymph node enlargement with associated fibrosis is the main feature. Further studies are needed to better understand the molecular and microenvironmental factors that facilitate fibrotic extramedullary disease and explore their prognostic and therapeutic implications.

REFERENCES

1. Hu, Y., Zaslav, et al.: Myelofibrosis involving lymph node: a novel cytogenetic abnormality in a mimicker of mesenchymal neoplasm. Journal of Hematopathology. 2009, 2:157-161. 10.1007/s12308-009-0040-1
2. National Cancer Institute. Primary myelofibrosis, NOS (PMF). SEER Hematopoietic and Lymphoid Neoplasm Database. . Accessed: October 9, 2026: https://seer.cancer.gov/seertools/hemelymph/51f6cf57e3e27c3994bd5381/.
3. Tefferi A: Primary myelofibrosis: 2023 update on diagnosis, risk-stratification, and management. Am J Hematol. 2023, 98:801-821. 10.1002/ajh.26857
4. Shao R, Ryder C, Wang L, et al.: A Review of the Pathological and Molecular Diagnosis of Primary Myelofibrosis. Cancers (Basel. 2026, 18:50. 10.3390/cancers18010050
5. Lichtman MA: Is it primary myelofibrosis or chronic megakaryocytic leukemia?. Haematologica. 2022, 107:2779-2781. 10.3324/haematol.2022.280838
6. Ng ZY, Fuller KA, Mazza-Parton A, et al.: Morphology of myeloproliferative neoplasms. Int J Lab Hematol. 2023, 45:59-70. 10.1111/ijlh.14086
7. Amanam I, Otoukesh S, Pullarkat V, et al.: Myelofibrosis-associated extramedullary hematopoiesis: Insights into hepatic, pulmonary, and thrombotic complications. Blood Rev. 2026, 75:101355. 10.1016/j.blre.2025.101355
8. Mohyuddin GR, Yacoub A: Primary Myelofibrosis Presenting as Extramedullary Hematopoiesis in a Transplanted Liver Graft. Case Report and Review of the Literature. Case Rep Hematol. 2016, 2016:9515404. 10.1155/2016/9515404
9. Sonu, R., Y Song, et al.: Extramedullary hematopoiesis associated with myeloproliferative neoplasm manifesting as pleural effusion: case report and review of literature. J Hematopathol. 2012, 5:341-347. 10.1007/s12308-012-0149-5
10. Ding Y, Naresh KN: Primary myelofibrosis involving lymph nodes with the same mutational profile in bone marrow. Blood. 2025, 145:2672. 10.1182/blood.2025028556
11. Yaqoob N, Mansoor N, Naveed H, et al.: Extramedullary hematopoiesis in an inguinal lymph node: an unusual presentation of primary myelofibrosis. World J Surg Oncol. 2022, 20:186. 10.1186/s12957-022-02660-9