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A Case of Primary Autoimmune Myelofibrosis Complicated by Mucormycosis Achieving Treatment Success

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INTRODUCTION

Bone marrow (BM) fibrosis is a histopathological finding that can be associated with a wide variety of conditions, including myeloproliferative disorders and malignant neoplasms. [(1)] ***Autoimmune myelofibrosis (AIMF)*** is a rare entity and considered a diagnosis of exclusion that can be secondary to autoimmune diseases or rarely presents as a primary condition and is often misdiagnosed as ***primary myelofibrosis (PMF),*** the most common form of BM fibrosis. [(2)]

CASE PRESENTATION

- **Clinical data:** A 42-year-old male without relevant medical or surgical history presented with a 3-month history of easy bruising and progressive fatigability.
- **Clinical examination** revealed a purpuric rash with no palpable lymphadenopathy or hepatosplenomegaly.
- **Laboratory investigations** manifested pancytopenia with normal morphology and negative serological and autoimmune markers.
- **Molecular genetics** showed no mutations in the clonal markers JAK2(V617F), MPL, and CALR.
- **Initial BM biopsy** suggested PMF inconsistently with the patient's clinical presentation and laboratory findings hence it was managed as AIMF, and a revision of the biopsy was requested.
- **Initial treatment:** He received packed RBCs, cyclosporine, and dexamethasone, which significantly improved CBC achieving RBC-transfusion independence.
- **Progression of the case:** Two months later, he presented with fever, progressive facial ache, and periorbital swelling that was later complicated by facial palsy, acute cortical venous infarction and blindness. He received Amphotericin B, Filgrastim, Epoetin alfa, Enoxaparin, Levetiracetam and IVIG. He also underwent sinonasal surgical debridement, and a biopsy was taken, which revealed ***mucormycosis***. He completed 15 doses of Amphotericin B since diagnosis.
- **Second BM biopsy** favored AIMF, and the absence of any underlying systemic autoimmune disease suggested primary AIMF.
- **Outcome:** The patient was completely well and off-treatment, with normal CBC 3 months later.

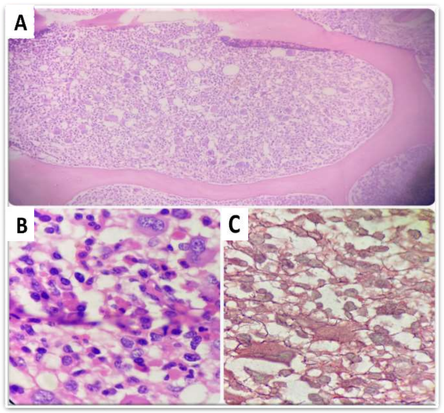


Figure 1: ***Histopathological features of the second bone-marrow biopsy:***

A) BM biopsy (H&E, x200) revealed a hypercellular BM with mild streaming showing normal bony trabeculae, increased granulopoiesis, moderately depressed erythropoiesis, and increased megakaryocytes of normal morphology without signs of atypia, which is better illustrated in (B) (H&E, x400).

C) Reticulin staining showed reticulin fibrosis corresponding to BM fibrosis grade MF-2 (×400).

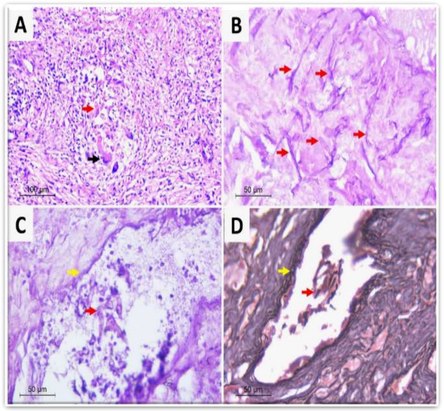


Figure 2: ***Histopathology of the sinonasal biopsy:***

A) Diffuse inflammation with "Langerhans" giant cells (black arrow) around Fungal hyphae (red arrow) (H&E, x200).

B) Wide areas of necrosis with multiple broad non septate branched hyphae (red arrow) favoring mucormycosis (H&E, x400).

C) High power view showing fungal hyphea (red arrow) within a large vascular space (yellow) (H&E, x400) ,which were highlighted by silver stain (D) (GMS, x200).

DISCUSSION

Distinguishing **AIMF** from **PMF** is challenging with often indecisive laboratory and histopathological findings. The following table differentiates between PMF, AIMF [(1)], and our reported case showing that patients don't necessarily need to meet all diagnostic criteria to confirm the diagnosis of AIMF. The patient's immunosuppressed state due to myelofibrosis, combined with the synergistic effect of steroids and cyclosporine, may have led to the development of mucormycosis.

	PMF	AIMF	OUR CASE
Bone Marrow Biopsy			
Megakaryocytes	Proliferation + atypia	Lack of atypia	Normal megakaryocytes
Myeloid dysplasia	Present/absent	Absent	Absent
Lymphocytic infiltration	Present/absent	Present	**Absent**
Osteosclerosis	Present/absent	Absent	Absent
Laboratory			
Anemia	Present/absent	Present/absent	Present
Leucocytosis	Present	Present/absent	Absent
High LDH	Present	Present/absent	Absent
Autoantibodies	Present/absent	Present	**Absent**
Tear drop cells in blood smear	Present	Absent	Absent
Clinical Features			
Constitutional symptoms	Present	Absent	Absent
Splenomegaly	Present	Absent or mild	Absent
Others			
JAK2, CALR, or MPL mutations	Present	Absent	Absent
Response to steroid	Weak response	Good response	Good response
Prognosis	Worst	Favourable	Less favourable

CONCLUSIONS

- Primary AIMF is poorly recognized and often misdiagnosed.
- There is an urge for a clear and comprehensive set of diagnostic criteria.
- Although most AIMF cases tend to show excellent prognosis, it's not always the case.
- AIMF patients should be closely monitored for any opportunistic infections.

REFERENCES

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