Case Report

Neoplastic hypereosinophilia syndrome: When to suspect?

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ABSTRACT

Chronic eosinophilic leukemia and myeloid neoplasms with FIP1-like 1 – Platelet-Derived Growth Factor Receptor Alpha (*FIP1L1-PDGFRA*) rearrangements are rare clonal disorders. In resource-limited settings, distinguishing these from reactive eosinophilia (allergic or parasitic) is challenging but critical, as targeted therapy can prevent irreversible organ damage. This 27-year-old male presented with recurrent vomiting and a high total leukocyte count of 33,000/mm^3 with absolute eosinophilia (60%). The patient was diagnosed with a Myeloid Neoplasm with tyrosine kinase fusion (per World Health Organization/International Criminal Court 2022) and achieved rapid clinical improvement on imatinib 400 mg. This case highlights that molecular screening should be prioritized over exhaustive allergy/infectious work-ups in patients with unexplained eosinophilia and splenomegaly, even when morphology appears mature. Early identification of the *FIP1L1-PDGFRA* mutation is life-saving and cost-effective, as it allows for highly successful, targeted treatment with imatinib while preventing irreversible end-organ damage.

Key words: Early identification, Eosinophilia, Leukemia

Eosinophilia is an uncommon hemogram finding. In roughly 95% of cases, the cause is reactive, most often allergic and parasitic, while malignant causes account for fewer than 5% [1]. Beyond this distinction, the workup for eosinophilia is extensive, and in resource-constrained settings, the question remains how far and in which direction to investigate. Identifying neoplastic eosinophilia early allows timely management and can prevent complications from cytokines released by eosinophils, as well as transformation to more aggressive variants like acute myeloid leukemia (AML) [2].

This case highlights the clinical clues and diagnostic approach relevant to suspected neoplastic hypereosinophilia syndromes.

CASE REPORT

A 27-year-old male daily-wage laborer was referred to our center with a 1-month history of recurrent vomiting. Further history-taking revealed loss of appetite and early satiety for 2 months. There was no history of allergy, atopy, altered bowel habits, or diarrhea.

Examination showed moderate splenomegaly of 10–11 cm; the rest of the systemic examination was unremarkable. Routine metabolic parameters were within normal limits.

Baseline complete blood count showed leukocytosis with absolute eosinophilia (25,000/mm^3 with 30% eosinophils). Hemogram showed hemoglobin 13 g/dL, total leukocyte count 33,000 with 60% eosinophils, and platelet 2.3 L/mm^3. Peripheral smear showed absolute eosinophilia >1500 with mature eosinophils and no atypical cells (Fig. 1) (Table 1). Stool microscopy was negative for pathogens, and serum immunoglobulin E (IgE) levels were within a normal range. Given his splenomegaly, a suspicion of hematolymphoid malignancy with clonal eosinophilia was raised.

Bone marrow aspiration and biopsy were performed, with aspirate sent for karyotyping and fluorescence *in situ* hybridization (FISH) eosinophilia panel. Bone marrow aspirate and biopsy showed hypercellularity with an increased M: E ratio 15:1; the myeloid series showed an increase in both mature cells and eosinophilic precursors, with blasts under 1% and no evidence of fibrosis (Figs. 2 and 3). The erythroid and megakaryocyte series showed normal maturation, and the karyotype was normal (46,XY). FISH was positive for FIP1-like 1 – Platelet-Derived Growth Factor Receptor Alpha (*FIP1L1-PDGFRA*) fusion at the cysteine-rich hydrophobic domain 2 (CHIC2) locus in 84% of eosinophilic cells. An myeloproliferative neoplasm

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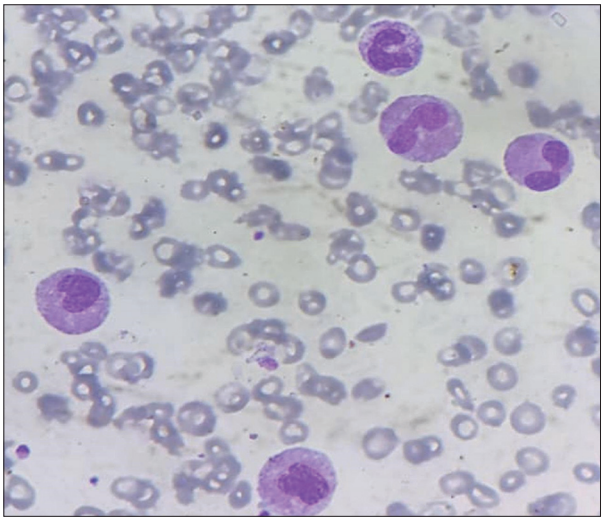


Figure 1: Peripheral smear (×40) (Wright-Giemsa/Lesihamnn stain): Red blood cell with mild anisocytosis, normochromic; leukocytosis with mature eosinophils with no atypical features, normal platelet range

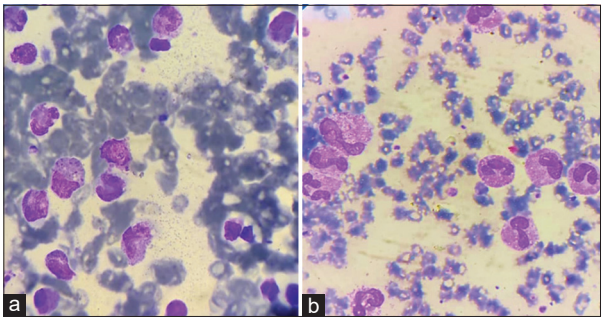


Figure 2: (a and b) Bone marrow aspirate (a-×40, b-×100) (Wright-Giemsa/Lesihman stain) hypercellular bone marrow with a population of large mononuclear cells having moderate purple cytoplasm and round bilobed/indented nuclei with clumped chromatin, mixed with mixture of normal appearing erythroid/lymphoid cells

Table 1: Investigations with patients value versus reference ranges

Parameters	Patients value	Reference range
Hemoglobin	13 g	13–16 g%
Red blood cell count	3.65	3.5–4.5/mm^3
Total leukocyte count	33000	4000–11000/mm^3
Neutrophils	7000	7000–8000/mm^3
Lymphocytes	6100	4000–5000/mm^3
Basophils	100	40–400/mm^3
Eosinophils	19,800	400–1100/mm^3
Platelet	2.3 L	1.5–3.5 L/mm^3
Serum immunoglobulin E	120	100–200 mcg/mL

(MPN) reflex from peripheral blood, performed to rule out other MPN-related mutations, was negative for Breakpoint Cluster Region - Abelson (BCR-ABL), Janus Kinase 2 (JAK2), Myeloproliferative Leukemia Virus Oncogene (MPL), and Calreticulin (CALR). Serum vitamin B12 and Tryptase were not measured, which is a limitation, though the molecular diagnosis was independently confirmed by FISH. Baseline cardiac and pulmonary function evaluation was normal. He was classified as a myeloid neoplasm with a TK fusion per the World Health Organization/International Criminal Court (WHO/ICC 2022) criteria and started on oral imatinib 400 mg and low-dose prednisone 10 mg per the National Comprehensive Cancer Network guidelines.

A tentative plan of assessing response clinically, splenic size, and repeat molecular testing at monthly intervals was made and discussed with the patient. He followed up after 1month with improvement in clinical symptom; however, thereafter he defaulted therapy and did not follow-up. The clinical timeline is shown in Fig. 4.

DISCUSSION

Chronic eosinophilic leukemia is a rare MPN characterized by clonal expansion of eosinophilic precursors; unlike reactive eosinophilia, it behaves aggressively, potentially transforming into AML [3]. Our patient met the WHO/ICC 2022 criteria for a myeloid neoplasm with tyrosine kinase fusion: eosinophilia sustained beyond 4 weeks, a myeloproliferative marrow, and exclusion of both reactive causes (normal IgE, negative stool microscopy, no history of atopy) and other MPN drivers (negative BCR-ABL, JAK2, MPL, and CALR) [4,5].

In our patient, the peripheral smear showed only mature eosinophils, with no dysplastic features and blasts under 1%, a picture which, in isolation, would typically be reassuring for a reactive process. This is precisely the pitfall this case illustrates: Neoplasm driven by *FIP1L1-PDGFRA* characteristically lacks the overt dysplasia seen in other myeloid leukemias, so morphology alone could not exclude malignancy here [6]. What prompted us to proceed to marrow evaluation despite this bland morphology was clinical clues rather than the smear itself – splenomegaly of 10–11 cm, 2 months of early satiety and loss of appetite, and the magnitude and persistence of the eosinophilia. We did not measure serum vitamin B12 or tryptase, which have been proposed as inexpensive surrogate markers favoring a myeloproliferative process when molecular diagnosis is delayed or unavailable [6,7]; this is a limitation of our workup. In our patient, the diagnosis was instead established directly by FISH, which demonstrated *FIP1L1-PDGFRA* fusion at the CHIC2 locus in 84% of eosinophilic cells – a high clonal burden consistent with a disease driver rather than a passenger mutation. This finding reclassified the presentation from a generic hypereosinophilic syndrome to a specific, molecularly defined myeloid neoplasm with eosinophilia, a distinction that mattered clinically because this driver predicts an excellent response to low-dose imatinib [6,7].

Given the striking male predominance of *FIP1L1-PDGFRA*-associated disease (approximately 17:1), we would argue that a young male with unexplained, persistent eosinophilia and any degree of splenomegaly should proceed for marrow studies and molecular screening once reactive causes have been reasonably excluded by history and basic serology, rather than routed through an exhaustive allergy and infectious workup first.

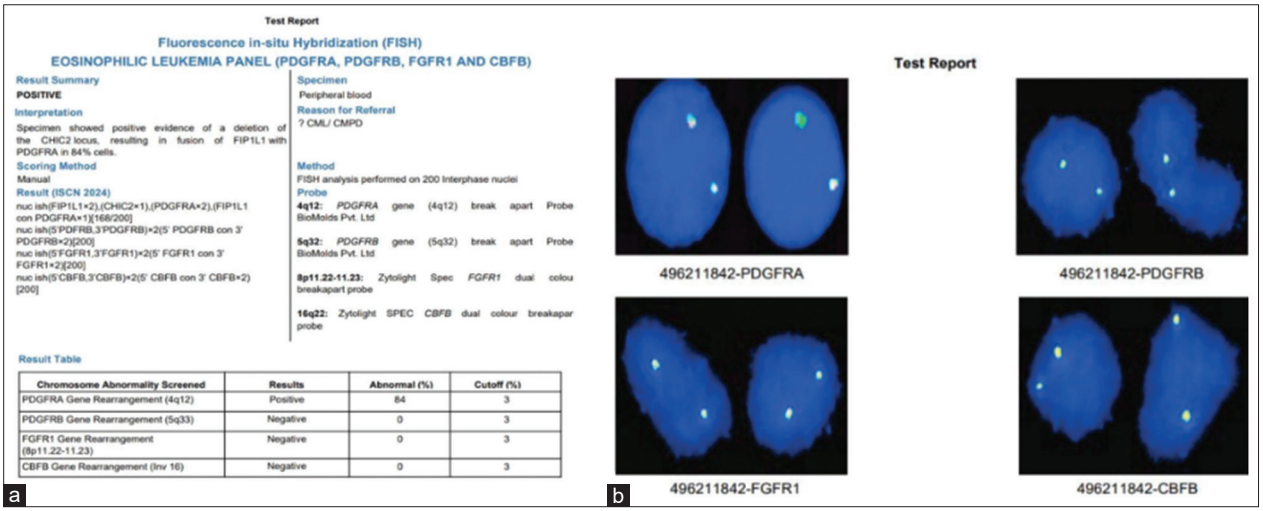


Figure 3: (a and b) Fluorescence *in situ* hybridization report showing positive forplatelet-derived growth factor receptor alpha positive in 84% cells

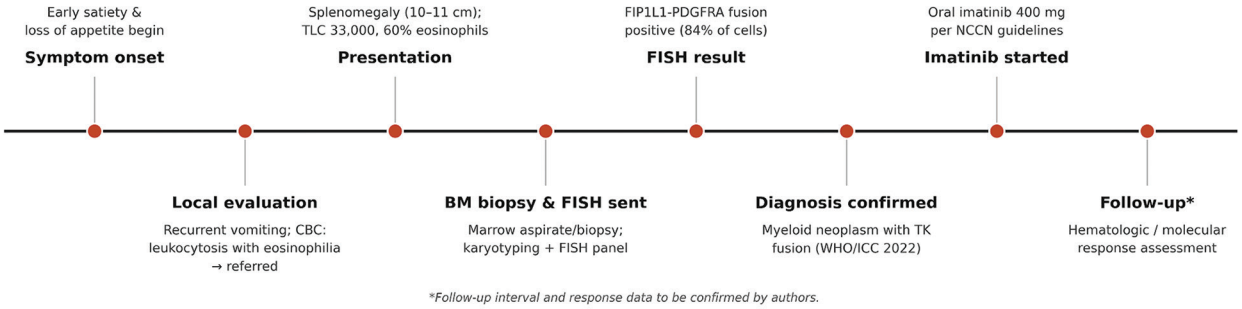


Figure 4: Clinical timeline from symptom onset to treatment initiation

In a resource-limited setting, this sequencing avoided a battery of expensive, low-yield tests while the patient remained at risk of irreversible endomyocardial fibrosis from ongoing eosinophil-mediated organ damage [8,9].

Once the molecular diagnosis was confirmed, imatinib was the natural choice of therapy given its established efficacy in PDGFRA-rearranged disease, in contrast to the aggressive chemotherapy required for other myeloid leukemias. Treatment response and follow-up in our patient are detailed in the case summary; sustained hematological and molecular monitoring will determine whether the response is durable or not.

CONCLUSION

This case highlights that molecular screening should be prioritized over exhaustive allergy/infectious work-ups in patients with unexplained eosinophilia and splenomegaly, even when morphology appears mature. Early identification of the *FIP1L1-PDGFRA* mutation is life-saving and cost-effective, as it allows for highly successful, targeted treatment with imatinib while preventing irreversible end-organ damage.

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