MAR Oncology & Hematology (2023) 6:3

Research Article

Myeloproliferative Hypereosinophilic Syndrome - Chronic Eosinophilic Leukemia

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Received: 28 August 2023

Published: 08 September 2023

Abstract

The presented article summarizes a case report of a 43 year old male, diagnosed with Myeloproliferative HES. The report highlights the clinical course, diagnostic challenges, treatment strategies & outcomes of the patient's journey. MP HES is a rare hematological disorder associated with persistent eosinophilia, organ involvement & absence of other causative factors. The report underscores the complex interplay of genetic, molecular & immunological factors contributing to disease pathogenesis. The patient's initial symptoms were itching, cough, Malena & weight loss. Thorough hematologic workup revealed abnormal blood counts & genetic testing by FISH confirmed PDGFR-A mutation. The discussion delves into the rarity of blood hypereosinophilia & outlines diagnostic criteria for chronic eosinophilic leukemia (CEL), highlighting the role of FIP1L1 -PDGFRA fusion gene . The patient was managed with steroids & later oral Imatinib, targeting the fusion gene, leading to improvement in symptoms & blood counts. The conclusion stresses the importance of thorough evaluation, timely intervention, & the potential effectiveness of imatinib in managing MP HES. Overall, the case report provides valuable insights into diagnosis, treatment & outcomes of this rare hematologic disorder.

Introduction

A very uncommon type of hypereosinophilia that's called myeloproliferative hypereosinophilic syndrome is identified by a persistent and noticeable eosinophilia, organ involvement, and lack of any other hypereosinophilia causes including parasitic infections, allergic reactions, or reactive diseases. The disorder belongs to the class of clonal neoplasms known as myeloproliferative neoplasms, which develop from hematopoietic stem cells.

Myeloproliferative hypereosinophilic syndrome is characterized by complex interplay of genetic, molecular & immunological factors that contribute to the pathogenesis of the disease. Its rarity & variable clinical presentation, often leads to diagnostic challenges, warranting a thorough evaluation & differentiation from other eosinophilic disorders, myeloproliferative disorders & related malignancies.

The identification of specific gene mutations, such as PDGFRA & PDGFRB, has provided valuable insights into molecular mechanisms underlying pathogenesis of MP HES, leading to more targeted therapeutic approaches. However, the heterogeneity of genetic alterations & diverse clinical manifestations ,continue to pose challenges in both diagnosis & management.

In this case report, we present a detailed account of a 43 year old male, diagnosed with MP HES, highlighting the intricate clinical course, diagnostic journey ,therapeutic strategies & outcomes.

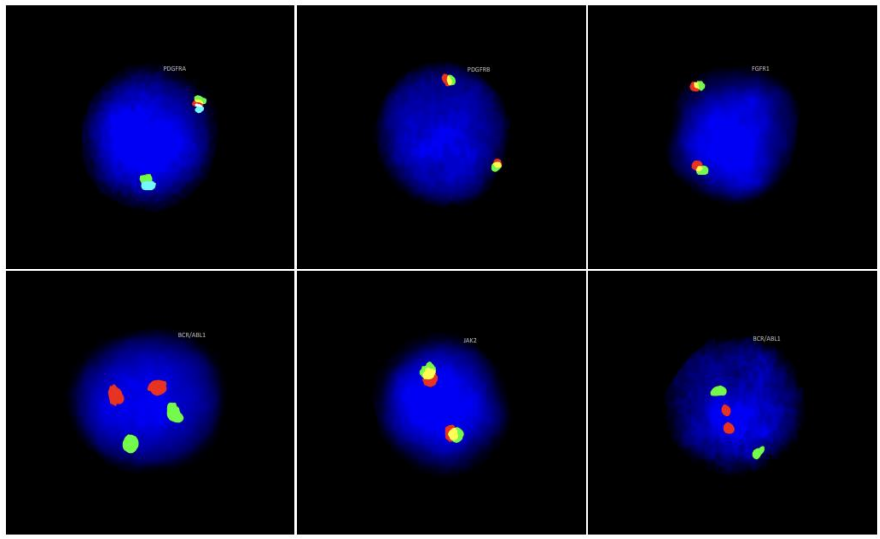
Case Report

A 43 year old male, came to medical oncology OPD with complaints of itching on the neck and thigh for 1 year , cough since 6 months which was intermittent, non progressive, nonproductive. 2 episodes of malena in the last 1 week . He has given h/o weight loss of 6 kgs in the last 6 months. On examination,there was pallor , supraclavicular lymphadenopathy ,hepatomegaly and non-tender splenomegaly .

On hematologic workup: CBC- Hb - 6.6; TLC -18400, PLT - 69000 ; Eosinophils - 70%, ESR- 14; Peripheral smear -s/o normocytic normochromic anemia, with eosinophilic leukocytosis & thrombocytopenia. Filarial antibody, stool for parasite,ova,cyst and Recombinant K-39 antigen for kala azar were negative .FNAC from supraclavicular lymph nodes revealed reactive lymphoid cells. Chest X ray was unremarkable.UGI scopy, for melena,was s/o with multiple erosions in the first part of duodenum. Bone Marrow Aspiration – Differential Count Blasts - 0%, Promyelocyte - 0%, Myelocyte - 4%, Metamyelocyte - 5% , Band forms - 9%•with no haemoparasites, atypical cells, granulomas or metastatic deposits.BM biopsy -reduced trilineage haematopoiesis with markedly increased number of eosinophils,along with foci of clusters of blasts ? CEL.In view of the possibility of CEL, FISH for MPN panel was done which revealed a positive PDGFRA mutation in 80% cells, negative for BCR - ABL, PDGFR B & JAK2 mutations. 2d echo done was normal. Sr.vit B12 was borderline elevated.

Referral Reason: FISH for MPN Panel

Test: FISH was performed on interphase nuclei using MPN probe panel PDGFRA[Cutoff value-5.6%(11 cells)], PDGFRB[Cutoffvalue-4.1%(8 cells)], FGFR1[Cutoff value-4.9%(10 cells)] , JAK-2[Cutoff value-5.6%(11 cells)], BCR/ABL1[Cutoffvalue-5.6%(11 cells)] from Metasystems Germany.



Number of interphase nuclei analyzed: 200/probe **Metaphases:**

Result:

Abnormal signal pattern for PDGFRA(2G2B1R) in 80% of cell population,normal signal pattern for others in 98% of cells.nuc ish(FIP1L1X2, CHIC2X1,PDGFRAX2)[160/200], nuc ish(PDGFRB)X2[196/200], nuc ish(FGFR1)X[196/200], nuc ish(JAK-2)X2[196/200],nuc ish(BCR/ABL1)X2[196/200] ISCN 2020.

Impression:

POSITIVE for PDGFRA rearrangement in 80% of cell population.
NOTE: Normal for BCR,ABL1,PDGFRB,FGFR1& JAK-2 probes.

Then a diagnosis of CEL was made based on clinical, laboratory & molecular studies. Patient was initially started on steroids & tapered.Later patient was started on oral Imatinib 400 mg OD .Patient was reviewed a week later ,he was better symptomatically CBC done a week after starting oral Imatinib revealed Hb -8.7 ,TLC -4.9,AEC -100,PLATELETS -80K

Discussion

Mild blood eosinophilia, as defined by an absolute eosinophil count (AEC) between 0.5 and 1.0 × 109/L, is common, occurring in 3% to 10% of individuals, usually seen in atopy,asthma,drug hypersensitivity & strongyloides infection.In contrast,blood hypereosinophilia ,defined as AEC of ≥1.5 × 109/L, is rare & warrants thorough evaluation. HES is very rare & its true prevalence is relatively unidentified. In one study using SEER data base, the estimated prevalence was between 0.36 to 6.3 per 100,000. Most patients are between 20-50 years.It is usually seen in males.

Simplified criteria for the diagnosis of chronic eosinophilic leukemia include the following:

Eosinophil count of at least 1500/μL Peripheral blood blast count of > 2% and bone marrow blast cell count > 5% but < 19% of all nucleated cells.

Criteria for atypical CML, chronic myelomonocytic leukemia, and chronic granulocytic leukemia (BCR-ABL–positive CML) are not met Myeloid cells are demonstrated to be clonal (eg, by detection of clonal cytogenetic abnormality or by demonstration of a very skewed expression of X chromosome genes)

Some of the cytogenetic abnormalities that have been described in chronic eosinophilic leukemia include t(5:12) and t(8:13), and molecular genetic abnormalities include the FIP1L1-PDGFRA fusion gene and ETV6-PDGFRβ.

The fusion gene FIP1L1-PDGFRA (F/P) is the most common clonal event identified in hypereosinophilic syndrome (HES).According to the World Health Organization (WHO) classification of myeloproliferative neoplasms, this variant of HES is now considered a chronic eosinophilic leukemia (CEL) in which eosinophil proliferation is directly related to enhanced kinase activity of PDGFRα induced by the fusion gene.Male predominance, cardiac involvement, and hepatosplenomegaly are common findings in F/P+ CEL. HE of any etiology, is associated with several complications -cardiac failure, thromboembolism & neurological involvement. Consequently, the decision to initiate urgent therapy depends on both the acuity and severity of the clinical presentation and the perceived risk of rapid progression.

Originally developed for the treatment of chronic myelogenous leukemia (CML),6 imatinib targets different tyrosine kinases, including FIP1L1-PDGFRα, whose constitutive kinase activity is 100-fold more sensitive as a target for imatinib than BCR-ABL.

Thus, imatinib has revolutionized the therapy F/P+ CEL . However,the dose of Imatinib is still a matter of debate ,concerning the initial dose (100mg/d vs 400mg/d) & safety of reducing maintenance dose(100mg /week).The imatinib regimen was defined as follows: the first dose of imatinib received by the patient until the first change in dosage was considered as the initial dose (ID). All doses after the ID were recorded as maintenance doses (MDs). To assess treatment efficacy, the following criteria were used: CHR was defined as a decrease in the absolute eosinophil count below the normal range (<500/mm3). CMR was defined as a negative RT-PCR and/or RQ-PCR assay for the F/P rearrangement. Hematologic relapse was defined as absolute eosinophil count beyond the upper normal range not explained by any other cause.

Conclusion

This case has been reported due to rarity of its incidence and to emphasize on the importance of thorough evaluation of a patient presenting with raised eosinophil count. High index of suspicion is required in such cases as timely intervention can prevent progression of the disease and reduce the mortality and morbidity associated with the condition. Timely initiation of Imatinib in such patients has proven to be effective in this case.

Reference

1. Bain B et al. Chronic eosinophilic leukemia & the hypereosinophilic syndrome. In: Jaffe ES, Harris NL, Stein H, Vardiman JW(Eds). World Health Organisation Classification of Tumors

2. Kodjovi Messie, Ahoefa Vovor, "Clonal Hypereosinophilic Syndrome: Two Cases Report in Black Men from Sub-Saharan Africa and Literature Reviews", International Scholarly Research Notices, vol. 2011, Article ID 974609, 6 pages, 2011.

3. Legrand F, Renneville A,French Eosinophil Network. The Spectrum of FIP1L1-PDGFRA-Associated Chronic Eosinophilic Leukemia: New Insights Based on a Survey of 44 Cases. Medicine (Baltimore). 2013 Sep;92(5):e1-e9. doi: 10.1097/MD.0b013e3182a71eba. PMID: 23982058; PMCID: PMC4553979.

4. Jason Gotlib, Jan Cools, James M. Malone III,the FIP1L1-PDGFRα fusion tyrosine kinase in hypereosinophilic syndrome and chronic eosinophilic leukemia: implications for diagnosis, classification, and management.Blood journal by ASH .103 (8): 2879–2891.

5. Kasturi K, Vanajakshi S. Chronic eosinophilic leukemia -NOS,specified transformation into AML. J Appl Hematol 2015;6;125-9

6. Lambert F, Heimann P, Herens C, Chariot A, Bours V. A case of FIP1L1-PDGFRA-positive chronic eosinophilic leukemia with a rare FIP1L1 breakpoint. J Mol Diagn. 2007 Jul;9(3):414-9.

7. Hafsa Shabeer, Chethana Mannem, Gayathri Bilagali Ramdas, Persistent Eosinophilia: A Diagnostic Dilemma, Annals of Pathology and Laboratory Medicine, Vol. 7, Issue 5, May, 2020, C70-C73

8. Ashutosh Kumar, Swasti Sinha, Anil Kumar Tripathi. Chronic eosinophilic leukemia: a case report and review of literature, Indian J. Hematol. Blood Transfus 23(3–4):112–115