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Case Report

Beta Thalassemia Major and Chronic Myeloid Leukemia in a Young Adult Male: A Rare Combination

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Abstract

Beta-thalassemia major (β-TM) is a severe hereditary haemoglobinopathy that is rarely associated with hematological malignancies. Though isolated case reports of association with acute lymphoblastic leukemia, acute myeloid leukemia is known. Only a few case reports of the association of β-TM and chronic myeloid leukemia (CML) are known. We present a case of a 25-year-old male with β-TM who later developed CML. The patient's management involved a multidisciplinary approach, incorporating hematological, molecular, and genetic assessments. This report indicates that malignancies should be suspected and kept in mind in patients with β-thalassemia syndromes presenting with proposed signs and symptoms including unexplained lymphadenopathy, leukocytosis, and splenomegaly. This case highlights the importance of comprehensive evaluation and tailored therapeutic strategies in complex hematological disorders.

Keywords: Chronic Myeloid Leukemia (CML); Beta Thalassemia

Introduction

Thalassemia and myeloproliferative neoplasms (MPNs) are recognized as two separate diseases. The coexistence of thalassemia and myeloproliferative neoplasia are rarely reported [1,2]. Thalassemia is a hereditary hemolytic disease which results in the deficiency of globin chain production [3]. MPNs are a group of clonal hematologic malignancies morphologically characterized by expansion of terminally differentiated myeloid cells of these CML is the commonest [4]. CML is characterized by the Philadelphia chromosome (Ph), resulting from a reciprocal translocation between chromosomes 9 and 22 [4]. This results in the generation of the BCR/ABL fusion gene which possesses tyrosine kinase activity and can be targeted by Tyrosine kinase inhibitors [5]. The incidence of CML is Incidence: 10 - 20 cases per million/year and ratio of is M: F = 1.2 ~ 1.7:1. It is a disease of the elderly the mean age. of diagnosis being 65 years [6,7]. β-TM is occasionally complicated by cancer, especially that of the liver while the coincidence of thalassemia with hematological malignancies is very rare [1,8]. The coexistence of CML and β-TM is exceedingly rare [2,9] with only three cases reported in the literature.

Case Report

A 23-year-old male presented with fatigue, malaise, and intermittent bone pain, to the outpatient department. He had been diagnosed with beta thalassemia major shortly after birth due to failure to thrive, pallor, and easy fatiguability. Genetic testing confirmed homozygosity for beta thalassemia mutations. Throughout childhood and adolescence, he remained transfusion-dependent, receiving 2-3 packed red blood cell transfusions per month to maintain adequate hemoglobin levels. At the age of 14, he underwent

splenectomy due to increasing transfusion requirements and iron overload. The serum ferritin at this time was 2484.20ng/mL and he had features of growth retardation. Splenectomy-histopathology revealed features of fibro congestive splenomegaly.

On presentation at our centre he had severe anemia hemoglobin: 10.7 g/dL (normal range-13-16.5 mg/dL), thrombocytosis (platelet count: 566 × 10^9/L (normal range: 1.5-4.5lacs/mm^3), and hyperleukocytosis White blood cell count blood cell count: 555 × 10^9/L (normal range: 4000-12000/mL). Leishman Giemsa-stained peripheral blood smear demonstrated showed microcytic, hypochromic red blood cells with occasional basophilic stippling, marked leukocytosis with granulocytic left shift and basophilia, myelocyte bulge, 4 nucleated RBCs/100 white blood cells (WBCs), and 08% circulating blasts; Figure 1 (A). There was polychromasia and corrected reticulocyte count was 6.7%. Serum lactate dehydrogenase (LDH) was elevated (428 U/L) (normal range: 100 to 250 U/L).

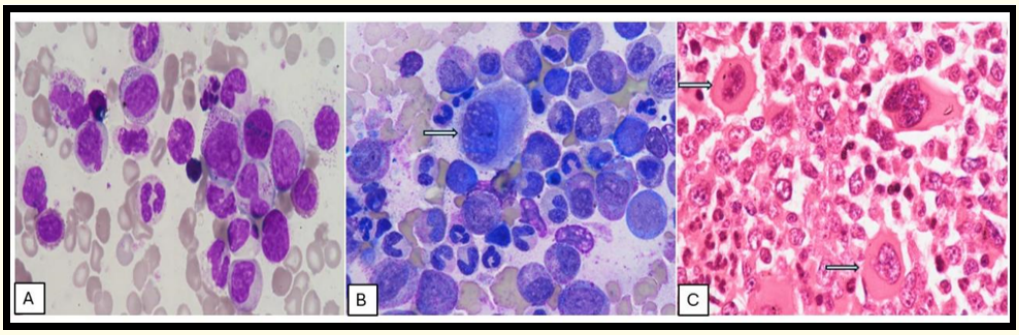

Figure 1: (A) Peripheral blood smear picture: Neutrophilic leukocytosis with myelocyte bulge, basophilia and 08% circulating blasts (Leishman-Giemsa stain, 100x). 2(B) Bone Marrow Aspirate smear: Myeloid preponderance and dwarf megakaryocytes as shown by arrow (Leishman-Giemsa stain, 100x). 3(C) Bone Marrow Biopsy: Hypercellular bone marrow biopsy with marked myeloid preponderance, prominent megakaryocyte with numerous dwarf megakaryocytes as shown by the arrow (Hematoxylin and Eosin, 100x).

Bone marrow aspirate smears revealed a hypercellular marrow with myeloid hyperplasia and myelocyte bulge with myeloid to erythroid ratio being 15:1. Megakaryocytes were prominent with hyposegmentation with dwarf morphology as depicted in Figure 1(B). The bone marrow biopsy revealed hyper cellularity with similar findings of dwarf megakaryocytes. Figure 1(C). However, no reticulin or collagen fibrosis was seen, and scattered interstitial immature cells were noted. In view of 08% blasts on peripheral smear, multiparametric flow cytometry was carried out and these blasts were positive for cMPO (cytoplasmic Myeloperoxidase) CD13, CD33, CD117, and negative for CD19 and CD10 and were consistent with a myeloid lineage. Molecular testing revealed the presence of the Philadelphia chromosome and BCR-ABL1 fusion gene rearrangement thereby confirming the diagnosis of CML. The patient was initiated on treatment with a first-line tyrosine kinase inhibitor (TKI), imatinib mesylate, at a dose of 400 mg daily. Close monitoring of hematological parameters and molecular response was performed according to established guidelines [5]. Response assessment at three months showed a significant reduction in leukocytosis and basophilia, with normalization of platelet counts. Molecular testing for BCR-ABL1 transcript levels revealed a major molecular response. Regular follow-up visits were scheduled to monitor treatment response and manage adverse effects. Concurrent management of beta thalassemia included periodic blood transfusions; however, the frequency of transfusions has drastically been reduced to once in a month and iron chelation therapy accordingly.

Discussion

The coexistence of beta thalassemia major and chronic myeloid leukemia presents a complex clinical scenario, characterized by the interplay of chronic anemia, iron overload, oxidative stress and leukemogenesis [1]. Beta thalassemia major, characterized by severe hemolytic anemia, ineffective erythropoiesis, and chronic transfusion dependency, predisposes individuals to iron overload second-

ary to repeated blood transfusions [10-12]. Iron overload, in turn, contributes to end-organ damage, including growth retardation, hypogonadism, and hepatosplenomegaly [13]. Splenectomy, performed to alleviate complications of hypersplenism and reduce transfusion requirements, may further exacerbate iron overload, and alter the bone marrow microenvironment, potentially influencing the development of hematological malignancies [14,15].

The occurrence of chronic myeloid leukemia in this patient, although rare, suggests a possible interplay between genetic predisposition, chronic inflammation, and the effects of long-standing anemia and iron overload [16]. It underscores the need for comprehensive hematological evaluation and multidisciplinary management. The presence of the Philadelphia chromosome and BCR-ABL1 fusion gene confirms the diagnosis of CML, necessitating targeted therapy with tyrosine kinase inhibitors (TKIs) such as imatinib. Imatinib, a tyrosine kinase inhibitor targeting the BCR-ABL1 fusion protein, represents the standard of care for CML and has been shown to induce durable responses and improve overall survival in affected individuals. However, the optimal management of CML in the setting of beta thalassemia remains uncertain, necessitating careful consideration of treatment-related toxicities, including myelosuppression and cardiotoxicity, in the context of pre-existing hematological abnormalities and iron overload. Long-term follow-up is essential to assess the response to therapy, monitor for disease progression, and manage potential complications, including infections, iron overload-related organ damage [17].

Conclusions

This case illustrates the complex interplay between beta thalassemia major and chronic myeloid leukemia in a young adult male, emphasizing the importance of a multidisciplinary approach to diagnosis and management. Further research is needed to elucidate the underlying mechanisms linking these two conditions and optimize therapeutic strategies to improve outcomes in affected individuals.

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