Acute Lymphoblastic Leukemia in β-Thalassemia: A Case Report

M. Taalab MD, PhD[1] and N. El Menshawy MD, PhD[2]
1.Internal Medicine Department, Faculty of Medicine, Mansoura University, Mansoura City. Egypt.
2.Clinical Pathology Department, Faculty of Medicine, Mansoura University, Mansoura City, Egypt.

Introduction

Thalassemia syndromes are hematological disorders characterized by a reduced or absent production of one or more normal globin chains. These syndromes are categorized into two primary phenotypic groups: transfusion-dependent thalassemia (TDT) and non-transfusion-dependent thalassemia (NTDT). The association of acute lymphoblastic leukemia (ALL) with thalassemia is considered rare and has predominantly been documented through individual case reports.

Aim

We present a patient with β-thalassemia who was subsequently diagnosed with ALL after experiencing thrombosis following a splenectomy.

Background

Thalassemia is a complex inherited blood disorder that presents in different clinical forms, each with distinct pathological features. The condition is characterized by an imbalanced ratio of α- to β-globin chains, resulting in ineffective erythropoiesis, chronic hemolysis of red blood , and an accumulation of iron in the body. These factors can lead to potential damage in multiple organs[1].

ALL is a hematologic malignancy characterized by the proliferation and accumulation of lymphoid progenitor cells in the bone marrow and other tissues. The incidence of ALL demonstrates a bimodal distribution, with an overall age-adjusted rate of 1.7 cases per 100,000 individuals.[2].

The etiology of ALL is considered to be multifactorial. It encompasses a range of influences, including both exogenous and endogenous exposures, genetic predisposition, and random chance[3].

Case Report

A 25-year-old female patient with known NTDT transitioned to TDT in 2023 due to severe anemia, resulting in an increase in the transfusion requirement to 2 units of packed red blood cells every 4 weeks. The patient exhibited pallor, jaundice, and splenomegaly extending 20 cm below the left costal margin. The patient underwent splenectomy after receiving the necessary pre-splenectomy vaccinations. A complete blood count (CBC) at the time of discharge revealed a total leukocyte count (TLC) of 9.03 × 10^9/L, hemoglobin (Hb) of 9.3 g/dL, and platelets (PLT) of 254 × 10^9/L. The differential leukocyte count demonstrated no abnormalities. One month later, the patient experienced pain and swelling in the left lower limb, which was diagnosed as lower limb deep venous thrombosis. A follow-up CBC showed TLC of 215 × 10^9/L, Hb of 9.1 g/dL, and PLT of 314 × 10^9/L. The blood film demonstrated 90% blast cells.. A bone marrow examination accompanied by multiparameter flow cytometry (MFC) showed 88% of TLC are abnormal lymphoblasts that express CD19, cCD79a, CD34, and HLADR, but are negative for: CD10, CD20, CD5, CD3 cCD3, CD4, CD8, MPO, CD117, CD33, CD13 and CD14, confirming the diagnosis of precursor B-cell ALL (B-ALL), while the cytogenetic analysis was negative for the Philadelphia chromosome. The patient initiated pre-phase treatment with vincristine and dexamethasone, subsequently followed by the hyper fractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (hyper-CVAD) regimen, along with anticoagulant therapy. The cerebrospinal fluid cytospin and MFC showed clear evidence of central nervous system (CNS) involvement. The treatment comprised intrathecal chemotherapy and cranial irradiation. Following the completion of course 1, the patient achieved a complete response. The patient continued the treatment regimen and subsequent maintenance therapy, given the absence of a fully matched sibling donor.

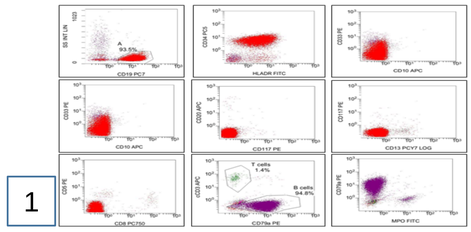


Figure 1: The flow cytometry indicated abnormal lymphoblasts expressing CD19, cCD79a, CD34, and HLADR. However, they were negative for CD10, CD20, CD5, CD3, cCD3, CD4, CD8, MPO, CD33, CD13, and CD14.

Summary

A 25-year-old woman with NTDT transitioned to TDT in 2023 developed post-splenectomy lower limb thrombosis. A follow-up CBC indicated 90% blast cells. Bone marrow examination and flow cytometry showed 88% abnormal lymphoblasts confirming B-ALL, negative for the Philadelphia chromosome. She began treatment with vincristine and dexamethasone, followed by the hyper-CVAD regimen and anticoagulants. CNS involvement was noted, leading to intrathecal chemotherapy and cranial irradiation. After the first course, she achieved a complete response and continued maintenance therapy due to the absence of a matched sibling donor.

Discussion

The association between thalassemia and hematologic malignancies has been highlighted in two significant cohort studies[4,5], both indicating an increased risk among affected individuals compared to the general population. Although several potential risk factors are identified, the mechanisms behind cancer development in thalassemia patients remain unclear, necessitating further research for improved early diagnosis and management.

References

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