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Case Report

Burkitt Leukemia in a Child with Beta Thalassemia Major

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ABSTRACT

Due to the advances in the treatment of patients with beta thalassemia major, their lifespan has increased, and hence, they are exposed to various morbidities including malignancies. In this study, a 4-year-old male child with beta thalassemia major who received regular blood transfusions every four weeks at thalassemia center is described. As he complained of abdominal pain, abdominal ultrasound was performed. The results showed ileocolic intussusception. He underwent surgery by a general surgeon, but there was no follow-up and the patient did not revisit the surgeon. Two months later, a pediatric hematologist-oncologist visited the patient who exhibited symptoms of fever, pallor, weakness, abdominal pain, and abdominal distension. Bone marrow aspiration was done under local anesthesia because the patient suffered from bone pain, anemia, and thrombocytopenia. It was found that bone marrow was infiltrated with more than 90% vacuolated lymphoblast, which confirmed Burkitt leukemia (ALL L3). Flow cytometry analysis also confirmed this diagnosis.

Keywords: Thalassemia major, Burkitt Leukemia, Malignancy

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Introduction

Beta thalassemia (β-thalassemia) major is an inherited hemoglobin disorder that severely reduces synthesis of beta globin chain. Patients with this disorder are dependent on blood transfusions and, because of the iron overload in various tissues, many complications occur such as cardiomyopathy, which is the most common cause of death in these patients. Iron chelators such as deferoxamine, deferasirox, and deferiprone are used to reduce excess iron in these patients (1, 2). Regular blood transfusion and use of iron chelators improve survival of the patients and increase their lifespan. Increased life expectancy in these patients has led to other complications, including malignancies (3, 4). Malignancies reported in various studies in patients with β-thalassemia major and β-thalassemia intermedia include hematologic malignancies such as acute lymphoblastic leukemia (ALL), chronic myelogenous leukemia (CML), Hodgkin lymphoma, non-Hodgkin lymphoma and non-hematologic cancer including thyroid cancer, hepatocellular carcinoma, seminoma, renal cell carcinoma, and meningioma (4, 5). Here, a 4-year-old male child with thalassemia major and Burkitt leukemia is described. The concurrence of Burkitt leukemia and β-thalassemia major was not reported before.

Case Report

The patient was a 4-year-old male child with β-thalassemia major who underwent regular blood transfusions every four weeks and used Defrasirox at a dose of 375 mg daily. Thalassemia major was diagnosed using hemoglobin electrophoresis at 9 months of age (HbA=2%, HbF=98%). He was the sixth child of the family. His 8-year-old brother, the fourth child of the family, was diagnosed with β-thalassemia major at five months of age. The patient underwent abdominal ultrasound two months previously due to abdominal pain. The results indicated ileocolic intussusception. He underwent surgery by a general surgeon. Unfortunately, there was no follow-up and the patient did not visit the surgeon again. Two months after the operation, a pediatric hematologist/oncologist examined him because he complained of fever, weight loss, pallor, weakness and lethargy, inability to walk, pain and abdominal distension. The surgical scar was seen in the right lower quadrant (RLQ) during the physical examination of the abdomen (Figure 1), and the mass was tender to the touch in the same region. The patient was hospitalized and laboratory tests were performed as follows.

The complete blood count was as follows: White blood cell: $16\times10^3/mm^3$, lymphocyte: 86%, hemoglobin: 6 gr/dl, MCV: 82 fL, Platelet: $28\times10^3/mm^3$. Erythrocyte sedimentation rate (ESR) was 68 mm/hr and lactate dehydrogenase (LDH) was 4850 IU/L. The levels of blood urea nitrogen, creatinine, liver function tests, and alkaline phosphatases were within normal limits.

Bone marrow aspiration was performed because of anemia and thrombocytopenia. The bone marrow was infiltrated by lymphoblasts with darkly basophilic and vacuolated cytoplasm confirming Burkitt leukemia (ALL L3, 90% blasts) (Figure 2). Flow cytometry analysis (positive for CD10, CD19, CD20, negative for TDT) confirmed the diagnosis. The t (8; 14) by RT-PCR was positive. The cerebrospinal fluid (CSF) analysis was normal, and there was no evidence of lymphoblast. The patient then underwent chemotherapy with LMB-96 protocol.

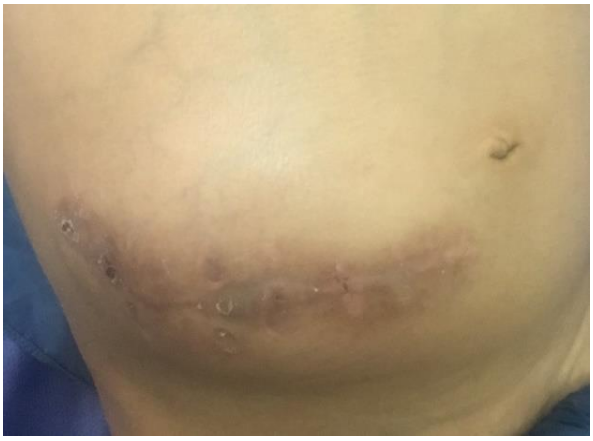

Figure 1. Surgical scar and mass in the right lower quadrant of the abdomen

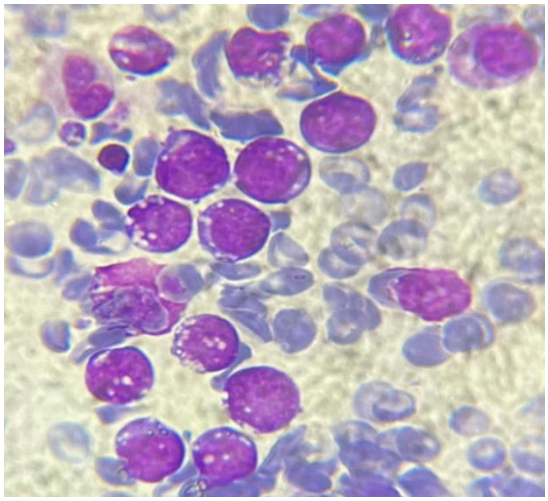

Figure 2. Vacuolated lymphoblasts and cytoplasmic basophilia shown in bone marrow smear

Discussion

In the present study, the occurrence of Burkitt leukemia in a child with β-thalassemia major is described. Based on previous studies, environmental or genetic factors, or a combination of the two, may play a role in the development of malignancies in these patients or may just cause the concurrence of these two diseases (3, 6). Factors such as iron overload and oxidative damages resulting from it, infection with the hepatitis C virus in a number of patients, immunosuppression caused by blood transfusion and viruses transmitted through blood can increase the risk of malignancy in patients with thalassemia (4). However, there are few reports from different countries on the occurrence of malignancies in patients with thalassemia, and some researchers believe these malignancies are more likely to be caused by factors that make these patients susceptible to malignancies (7).

Various studies have reported lymphoma (3, 4, 7), chronic myelocytic leukemia (3, 7), acute lymphoblastic leukemia (4, 7), hepatocellular carcinoma (4, 8), thyroid cancer (4), breast cancer and brain tumor (4), and osteosarcoma (7) in patients with β-thalassemia major and β-thalassemia intermedia. Concurrence of β-thalassemia major with hematologic malignancies was reported to be 0.24% in a multicenter study (7) and 9.5% in another study (9) conducted in Iran. In a cohort study in Taiwan, there was a 5.32-fold increase in the risk of hematologic malignancies in patients with thalassemia; this increase in risk was 9.32-fold in patients receiving blood transfusions (10).

In another study in the Italian Thalassemia Center in Milan, it was reported that six thalassemia patients who were not dependent on blood transfusions developed malignancies (11).

Hodroj MH *et al.* (12) also suggested that patients with thalassemia were at greater risk of malignancies and, although the precise mechanism of the malignancy development was unclear, there were potential predisposing factors.

Given the advances in treating and taking care of patients with thalassemia major, which have led to increased survival and lifespan of these patients, and considering the risk factors that make them susceptible to malignancies, it is recommended to screen them for different cancers. In addition, any signs and symptoms such as worsening of anemia, thrombocytopenia, splenomegaly, abdominal mass, soft tissue mass, and lymphadenopathy in these patients must be a warning to examine them carefully for malignancies and must not be justified just in the context of underlying diseases.

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Author's Contributions

Ghasem Miri-Aliabad: Study concept, and literature search.

Majid Naderi: Manuscript editing.

Hossein Izadi-Nia: Manuscript editing.

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none

Conflicts of interests

The authors declare that there is no conflict of interests.

Informed Consent

Written informed consent was obtained from the patient's parents.

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