CASE REPORT

A Rare Case of T-cell Acute Lymphoblastic Leukemia in Paediatric Patient with Sickle Cell Trait

Swati R Bhutada[1], Vaibhav B Rathod[1], Reshmi Rajan[2], Aishwarya Malwade[1]

Abstract

Background: By definition, the HbS level is less than 50% among sickle cell trait carriers. Patients with sickle cell disease seldom develop hemato-oncological cancers. Adult hemato-oncological cancers with sickle cell characteristics are extremely rare. However, as far as we are aware, this is the first case report of pediatric sickle cell trait patients with acute T-cell lymphoblastic leukemia.

Clinical Description: An 11-year-old boy presented with a two-month history of fever, weight loss, and an enlarging left upper chest swelling. He had notable lymph node enlargement in the neck, armpits, and groin, but no enlargement of the liver or spleen.

Management and Outcome: The child had clinical signs of mild anemia and suspicion of malignancy. Laboratory tests showed a low hemoglobin level (9.1% gm) with a peripheral smear indicating microcytic hypochromic anemia, along with 22% blast cells. The sickling test was positive, confirming sickle cell heterozygosity. CXR imaging revealed mediastinal widening, and chest CT scan indicated soft tissue mass with chest wall infiltration, suggesting a probable lymphoma or thymoma. LDH levels were notably elevated (3089 IU/L). Fine-needle aspiration cytology (FNAC) and biopsy confirmed small round blue cell tumor, consistent with lymphoma. Cytochemistry and immunophenotypic analysis revealed T-cell Acute Lymphoblastic Leukemia (T-ALL). The child received treatment with IV Methotrexate, Folinic acid, 6- Mercaptopurine, and Cytarabine and responded positively.

Conclusion: This case highlights a rare and possibly under-recognized association between sickle cell trait and hematological malignancies, specifically T-cell Acute Lymphoblastic Leukemia. Given this finding, we recommend that patients diagnosed with hematological malignancies— particularly in regions with a high prevalence of hemoglobinopathies—should be routinely screened for sickle cell disease and sickle cell trait. Early identification of coexisting hemoglobinopathies may influence clinical management, risk stratification, and follow-up protocols. At the same time, further research is warranted to explore the prevalence and potential mechanisms linking sickle cell trait to malignancy. Patients with sickle cell disease should be screened for hematological malignancies.

Keywords: T-cell Acute lymphoblastic leukemia, Sickle cell trait, Hematological malignancies.

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Introduction

Hemoglobin S is the consequence of the beta-globin gene's sixth codon's substitution of thymine for adenine, which alters the amino acid generated and causes valine to replace glutamine acid in the beta-globin chain. The Hbs level in sickle trait. Hematooncological cancers, including leukemia, have been linked to homozygous sickle cell disease.[3,5] In the same way, renal medullary cancer has been linked to sickle cell trait individuals. However, in a pediatric child with sickle cell trait, we are reporting T-cell Acute Lymphoblastic Leukemia.

Case Report

Clinical Description

The main complaints of an 11-year, kid who came to the pediatric outpatient department were fever, weight loss, and swelling in the left upper chest that had been present for two months. The infant was pale and had a fever upon physical examination. He was hemodynamic stable. The swelling in left upper chest measured 12 cm by 12 cm, was painful and firm, and had severe inguinal and cervical axillary lymphadenopathy. Hepatosplenomegaly was absent.

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Management and Outcome

Clinical suspicion of mild anemia with malignancy was done. Complete blood count showed Hb 9.1 gm%, WBC 9500/cmm, Platelet count was 428000/cmm, PCV 29%, MCV 58 fL, MCH 17 pg, MCHC 30 gm/dL, RDW 25%. Peripheral smear S/O microcyic hypochromic anemia with target cells with Blast cells 22%.

The sickling test was positive. Hb electrophoresis was S/O sickle cell heterozygous. X-ray chest was S/O mediastinal widening. CECT scan of chest was heterogeneously

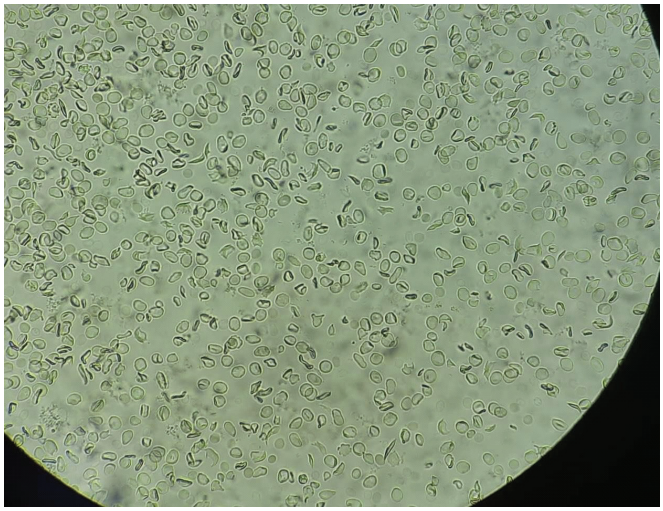

Figure 1: Peripheral blood smear s/o positive sickling test.

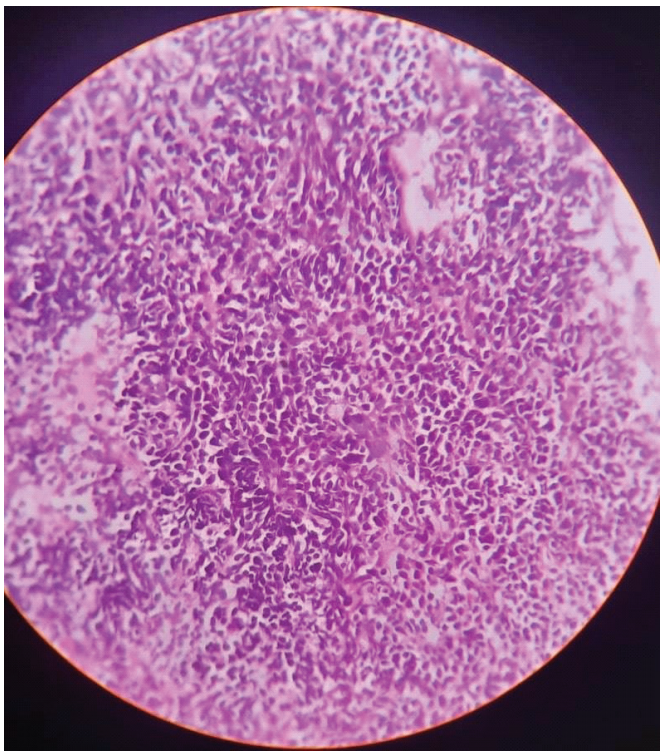

Figure 2: Lymphoproliferative neoplasm.

enhancing soft tissue mass 118 x 46 x 84 mm in anterior mediastinum with lesion abutting costal cartilage anteriorly with chest wall infiltration? Thymoma? Lymphoma. FNAC of lesion was S/O small round blue cell tumor possibility lymphoproliferative neoplasm. Lesion biopsy was S/O small round blue cell tumor? Lymphoma.

In cytochemistry, morphologic and immunophenotypic findings were consistent with T-cell Acute Lymphoblastic Leukemia. USG abdomen was S/O few enlarged para-aortic lymph nodes with mild hilar vascularity. LFT, RFT and Sr Electrolytes were normal. LDH was 3089 IU/L. Sr Ca, Phosphous and Uric acid was normal. Child received IV Methotrexate, Folinic acid, 6-Mercaptopurine, Cytarabine. Responded well to the treatment.

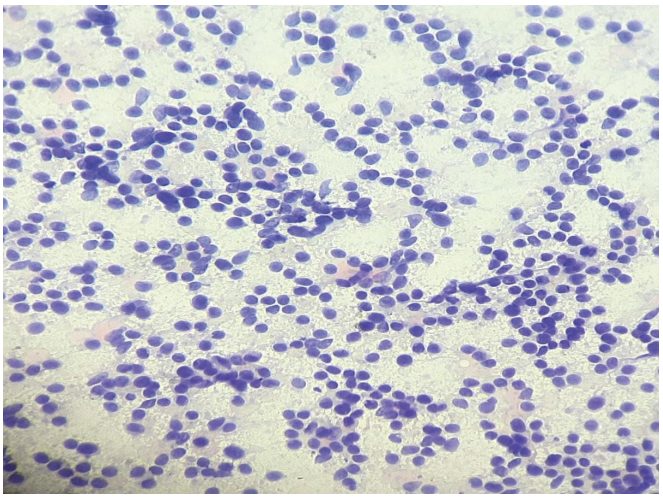

Figure 3: Biopsy suggestive of small round blue cell tumor.

Discussion

More recent research has acknowledged that sickle cell disease patients may also have hematological malignancies. Although the majority of research and case reports have been on people with homozygous sickle cell disease (HbSS), there is growing evidence that people with sickle cell trait—those who are heterozygous for the sickle gene may also be at risk for cancer, although at a lesser risk. Hemoglobin S and normal hemoglobin A are characteristics of sickle cell trait; hemoglobin S levels are usually less than 50%. Even though sickle cell trait carriers frequently show symptoms, in severe circumstances, their red blood cells may still undergo sickling. This pathologic behavior may be linked to inflammation, oxidative stress, and chronic low-grade hypoxia—all of which are linked to the development and spread of cancer. Individuals with sickle cell trait have been shown in multiple studies to have an elevated risk of renal medullary carcinoma.[13] Less research has been done on the connection between sickle cell trait and hematological cancers, including leukemia. Leukemia and sickle cell disease, on the other hand, are more closely associated; research suggests that the risk is 2 to 11 times higher than in the general population.[6-8]

Compared to the general population, sickle cell disease patients had a higher risk of leukemia, according to Brunson *et al*.[9] According to estimates, these individuals have an overall cancer incidence of 1.74 cases per 1,000 patient-years.[4] Up to 8.6% of sickle cell disease patients in certain low-income environments have been documented to have acute leukemia.[5] In our instance, an 11-year-old child who had no past medical history of hemoglobinopathy showed up with a two-month history of fever, weight loss, and a steadily growing lump on his chest wall. His blood work revealed target cells, peripheral blasts, and anemia, which suggested that he had a hemoglobin problem. Sickle cell trait

was confirmed by hemoglobin electrophoresis (hemoglobin A: 60%, hemoglobin S: 24.4%). Immunophenotyping and cytochemistry verified the T-cell acute lymphoblastic leukemia diagnosis. This coincidental discovery suggests that sickle cell trait may be linked to hematologic cancers, particularly T-ALL, which has not been well studied in children. Chronic inflammation, marrow stress from occasional sickling, or unknown genetic susceptibilities could all be part of the pathophysiology. Crucially, the child had no past history of transfusion-related iron overload or hydroxyurea exposure, both of which are known to contribute to leukemogenesis in sickle cell disease.[10-12]

Patients with sickle cell disease now have a far higher chance of survival thanks to hydroxyurea, an inhibitor of DNA synthesis.[10,11] Nonetheless, there is ongoing discussion over its possible involvement in leukemogenesis, particularly in relation to prolonged use.[12] This instance emphasizes the significance of taking sickle cell trait into account as a potential co-factor in pediatric hematological malignancies in light of these findings. Additionally, it backs the suggestion that infants with leukemia undergo comprehensive hematological screening, which includes hemoglobin electrophoresis, especially in populations. Where the sickle gene is very prevalent. To ascertain, whether this link is coincidental or representative of a larger, until unnoticed trend, more thorough epidemiological and cytogenetic research is required. The establishment of this connection may have significant ramifications for at-risk population management and early screening programs. Numerous short series have documented the occurrence of malignancy in both adult and pediatric SCD patients.[1-3] According to one in-situ investigation, there are 1.74 instances of malignancy for every 1,000 patient-years among SCD patients.[4]

Acute leukemia and SCD have even been linked in 8.6% of cases in a low-income nation.[5] Hematologic malignancies are 2-11 times more likely to occur than in the overall population. Three recent epidemiology reports,[6-8] established this. Due to improvements in care, which may be related to the numerous cancer cases that are currently being reported in these patients, the life expectancy of people with SCA has increased recently. When comparing SCD patients to the general population, Brunson *et al.* discovered that they had a higher incidence of leukemia.[9] Long-term fever and mass in the index case raised the risk of cancer, which was verified by Blast-cells on a peripheral smear. Additionally, the presence of target cells on the smear raised the possibility of hemoglobinopathy, which was confirmed by additional research to exhibit sickle cell trait on Hb Electrophoresis. Conservative treatment is given to the great majority of SCD patients. In this context, hydroxyurea has significantly increased SCD patients' survival rates in wealthy nations.[10,11]

As a DNA synthesis inhibitor, HU has the potential to cause a buildup of acquired DNA mutations and ultimately leukemic transformation. One of the main topics of discussion in numerous papers has been whether acute leukemia in SCD patients who have been exposed to HU for an extended period is a coincidental condition or a result of treatment. The length of drug exposure may, in theory, enhance the leukemogenic risk.[12] Although the precise incidence of hematological malignancy in sickle cell disease treated with hydroxyurea over an extended time is unknown, reports of secondary malignancies following long-term hydroxyurea usage have been made.[13] The aforementioned risk factor does not apply to our situation. Patients with sickle cell trait may be at risk for acute lymphoblastic leukemia.[10,11] To identify this, patients with hematological malignancies must undergo a comprehensive evaluation. Additionally, more epidemiological and cytogenetic research on sickle cell anemia patients is required to establish the clue and support the connection between sickle cell disease and hematological malignancy.

Conclusion

An unusual and potentially underappreciated link between sickle cell trait and hematological malignancies specifically, T-cell Acute Lymphoblastic Leukemia is highlighted by this case. In light of this discovery, we advise routine screening for sickle cell disease, and sickle cell trait in patients with hematological malignancies, especially in areas, where hemoglobinopathies are highly prevalent. Clinical care, risk assessment, and follow-up procedures may be impacted by the early detection of concomitant hemoglobinopathies. However, more investigation is necessary to determine the frequency and possible pathways that connect sickle cell trait to cancer. Sickle cell hemoglobinopathies (including disease or trait) should be checked for in patients with hematological malignancies, and vice versa.

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