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Chronic myeloid leukemia with sickle cell trait: rare case report

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Abstract

Hemato- oncological neoplasia are very rare in patient with sickle cell anemia. The term 'sickle cell trait' indicates heterozygosity for sickle cell gene on beta chain. There are very few cases of patients with sickle cell trait who developed Hemato-oncological malignancy including myeloid and lymphoid conditions; however, to best of our knowledge, this is the second case report on sickle cell trait with chronic granulocytic leukemia.

Keywords: Chronic myelogenous leukemia, Sickle cell trait.

Introduction

The term 'sickle cell trait' indicates heterozygosity for sickle cell gene on beta chain. Hematological malignancy is considered to be very rare in sickle cell disease. Patient with hemoglobin SS and AS appear to have normal incidence of Burkett's lymphoma and leukemia. Patient with sickle cell disease or trait can develop malignancy of lymphoid or myeloid origin.[2] This is second case report of adult male patient with sickle cell trait who developed chronic myeloid leukemia.

Case Report

A 55 –year old male reported to medicine OPD, with chief complaints of pain in abdomen since two days, and fever with chills since fifteen days. On physical examination patient was having pallor. Abdominal examination, spleen palpable 16cm below the left costal margin, and liver palpable 4cm below the right costal margin. Complete blood count showed, Hemoglobin 8.4g/dl, the white blood cell count was 2,06,000/cmm, red blood cell count 2.7 million/cmm, platelet count was 5.9lac/cmm, PCV: 21.6%, MCV: 79.5fl, MCH: 31.2pg, MCHC: 39.3g/dl. Considering hematological and clinical findings, bone marrow aspiration done. Peripheral blood smear along with marrow spread, and blood in EDTA for hemolytic profile sent to department of pathology for evaluation of anemia. On peripheral smear, RBCs showed, anisopoikilocytosis, normocytes, moderate hypochomia, microcytes, myeloblast, basophils, three to four nucleated RBC seen per 100 WBC. Total leucocyte count increased. Differential leucocyte count, Blast 2%, Promyelocyte 8%, myelocyte 12%, Metamyelocyte 15%, Band cell 10%, Polymorphs 46%, Lymphocyte 2%, Basophil 5%.[Fig. 1] Bone marrow examination showed, myeloid hyperplasia with erythroid series suppressed. There was no evidence of parasite .Anemia profile done at hematology section. The results took all of us by surprise!. Reticulocyte count was 7%, and early sickling test by sodium meta bisulphate oxygen reduction was negative, But late sickling test was positive, consisting of more than 10% sickle cell.[Fig. 2] Probable diagnosis of chronic myeloid leukemia with sickle cell trait made. In order to confirm the diagnosis, patient subjected to cytogenetic study, and molecular study. Cytogenetic evaluation of peripheral blood sample revealed a karyotype of 46 XY, t(9;22)(q34;q11).[Fig. 3] Florescent insitu hybridization showed BCR-ABL (Philadelphia gene) positive in all cells.[Fig. 3] High performance liquid chromatography (HPLC) showed finding of sickle cell trait. HbS-37.2%, adult hemoglobin 50%, fetal Hb 2%, HbA2 2%. Definite diagnosis of chronic myeloid leukemia with sickle cell trait made. The patient started on imatinib 400mg daily and achieved complete hematological response, and patient is in regular follow up.

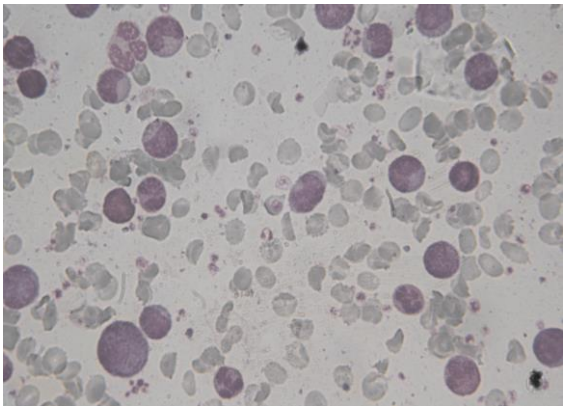

Fig. 1: On peripheral smear, RBCs showed, anisopoikilocytosis, normocytes, microcytes, myeloblast, Promyelocyte, myelocyte, basophils

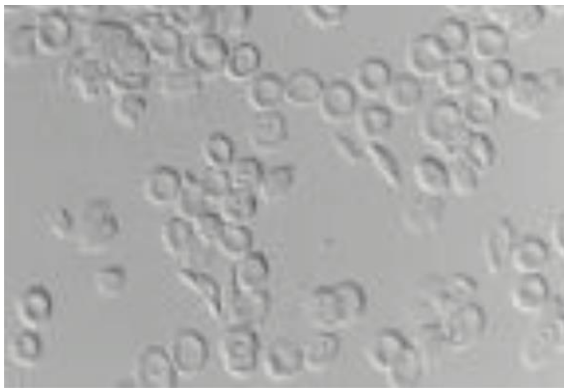

Fig. 2: Sickle cell solubility test, positive for sickle cell

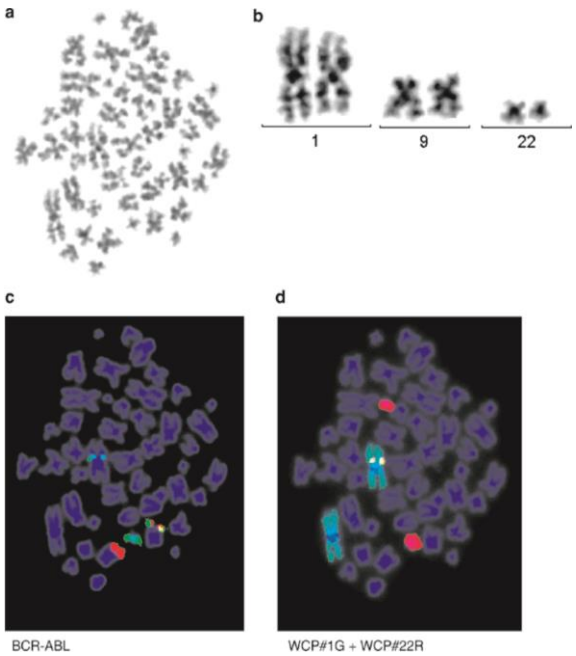

Fig. 3: Cytogenetic evaluation of peripheral blood sample revealed a karyotype of 46 XY, t(9;22)(q34;q11). Florescent insitu hybridization showed BCR-ABL (Philadelphia gene) positive in all cells

Discussion

Hematological malignancies are very rare in Sickle cell disease patients. The first case of Hodgkin's lymphoma occurred in a sickle cell diseases patient.[1] Apart from Hodgkin's lymphoma, other reported hematological malignancy occurring in Sickle cell disease patients are, acute myeloid leukemia (AML), acute lymphoblastic leukemia, multiple myeloma, malignant histiocytosis, B and T-cell non-Hodgkin's lymphomas -T cell lymphoma and chronic lymphocytic leukemia, hairy cell leukemia.[1,2,3] To our knowledge, CML has been reported in 10cases of sickle cell disease. Last case reported by sallam et, al.[4] Of these ten cases, one of which was a case of sickle cell trait.[5] A plausible explanation for rarity of hematological malignancies like, chronic myeloid leukemia in sickle cell anemia is may be due to the short life span of these patient. With advent of modern medical care, average life expectancy of patient with sickle cell disease is increased from 14years to 42years; therefore, we are getting more hematological malignancy in sickle cell disease patient.[6] Risk factors for hematological malignancy in sickle cell disease put foreword; which includes, infection like HIV virus, hepatitis C virus, persistant transfusion related immunomodulation, stem-cell transplantation, and chemotherapeutic agent like hydroxyurea used in treatment of sickle cell disease.[7,2,8] Most common malignancy associated with sickle cell trait is Hodgkin's and non-Hodgkin's lymphoma. Majority of cases, reported in adult with sickle cell disease. Very few cases are there in children with sickle cell disease.

Hydroxyurea treatment has been useful in managing complication in sickle cell disease. It reduces the need for frequent transfusion, and painful crisis in sickle cell disease. Hydroxyurea is ribo-nucleotide reductsae inhibitor. It causes an inhibition of DNA synthesis and increase in F hemoglobin level, thus prevents hemoglobin S polymerization. Exact incidence of hematological malignancy in sickle cell disease treated on long term basis with hydroxyurea is not known, but occurrence of secondary malignancies after long term use of hydroxyurea has been reported.[8]

In our case, there were no such possibilities as mentioned above. This presentation of CML with sickle cell trait, reason for this combination is, due to increased cell turnover. A possible *chromosomal link* between sickle cell disease and leukemia has been described. There might be an associated influence of chronic myeloid leukemia on sickle cell disease, and hence it is desirable to carry out thorough investigations of any patient with a hematological malignancy. We need more epidemiological and cytogenetic studies in the adult sickle cell population to assess the incidence and causative factors of hematological malignancy in these patient. Patient with chronic myeloid leukemia should be screened for sickle cell disease.

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