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Homozygous Sickle Cell Disease Presenting As Acute Pulmonary Infection: A Case Report

Poonam Singal[1], Yasmeen Singh[2], Mohanvir Kaur[3]

[1]Senior Resident, Department of Pathology, Government Medical College, Patiala.
[2]Junior Resident, Department of Pathology, Government Medical College, Patiala.
[3]Assistant Professor, Department of Pathology, Government Medical College, Patiala.

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ABSTRACT

Sickling syndromes are characterized by the presence of HbS which imparts sickle shape to red cells in a state of reduced oxygen tension. Cases of homozygous state sickle cell anemia have mainly HbS in their red cells and is the most severe form of disease. The sickle gene confers increased susceptibility to infections especially to certain bacterial pathogens which is a significant contributor to the morbidity and mortality in sickle cell disease. Respiratory tract infections in patients with sickle cell disease are common and vary in severity from mild upper respiratory tract infections to moderately severe uncomplicated pneumonia which may progress to acute chest syndrome (ACS) which is a serious and potentially fatal complication. We report a case of 46 years old female admitted for chest pain, fever and jaundice in which sickle cell anemia was diagnosed. Patient's electrophoresis led to research similar cases in the family. The mother was first to be analysed, who was ultimately diagnosed with sickle cell trait having previously been ignored. This case would be a form with few symptoms and diagnosed in middle age because the patient does not describe painful crisis in childhood or adolescence.

Keywords: Sickle cell disease, Acute chest syndrome, Homozygous state.

INTRODUCTION

Sickle cell anemia is an inherited single gene disorder that results from amino acid substitution in the gene encoding the β globin subunit. Polymerization of deoxygenated sickle hemoglobin leads to decreased deformability of red blood cells. It is prevalent in Africa, mediterranean countries and India.[1] Patients of sickle cell disease are susceptible to infections that act as a significant contributor to morbidity and mortality in sickle cell disease.[2] Respiratory infections are particularly important and if left untreated, may progress to acute chest syndrome. Acute chest syndrome presents with clinical symptoms similar to pneumonia and is clinically described as the combination of hypoxia, fever and new infiltrates on chest X-ray.[3]

CASE REPORT

A 46 year old female, migrant of Jharkhand currently residing in Sunam, Punjab presented to Medicine OPD at Rajindra Hospital, Patiala with chief complaints of chest pain, fever, jaundice and breathlessness for 7 days. Fever was intermittent and was relieved after medication. She also complained of generalized bodyaches and weakness. On examination, mild splenomegaly was observed which was later confirmed by ultrasonography. Chest X-ray was conducted which showed pulmonary infiltrates. Further investigations were carried out. CBC showed Hb- 7g/dl, TLC-15,800/cumm, DLC- Neutrophils 75%, Lymphocytes 24%, Eosinophil 01%, Platelet count-4,20,000/cumm, MCV-102 fl, MCH- 39.1 pg and MCHC- 36.8 g/dl, reticulocyte count- 10% and ESR-6 mm in first hour. On PBF, RBC picture showed marked degree of anisopoikilocytosis, microcytes, many target cells and sickle cells. Mild polychromasia and 10NRBCs/100WBCs were also seen. To confirm the presence of sickle cells, Sodium metabisuphite sickling test was done which showed immediate sickling. Other investigations showed S. bilirubin-2.9 mg/dl (direct-1.0mg/dl and indirect-1.9mg/dl), TSP- 6.8 gm% (Albumin-3.8gm% and Globulin- 3.0 gm%), RBS-88mg%, Na+- 150 meq/L, K+- 4.8 meq/L, B. urea- 40 mg/dl, S. creatinine- 1.0 mg/dl, WIDAL- negative. Urine for urobilinogen showed positive results. Hb electrophoresis was advised to confirm sickle cell anemia. High performance liquid chromatography (HPLC) showed HbA- 22.8%(↓), HbF- 8.7%(↑),

Name & Address of Corresponding Author
Dr. Yasmeen Singh
Junior Resident,
Department of Pathology
Govt. Medical College, Patiala.

HbS- 63.9%(↑), HbA2- 2.4% (normal). The results led to the further questioning of the patient in search of a family history of sickle cell disease and painful episodes in childhood or adolescence. She gave history of similar episodes of chest infection, abdominal pain, generalized weakness, repeated blood transfusions and recurrent hospitalization in the last three years for chest infection. According to the patient, similar complaints were also seen in her mother. The Hb electrophoresis of her mother was carried out, which showed sickle cell trait.

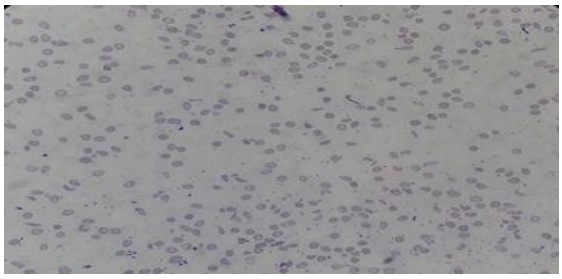


Figure 1: PBF showing sickled cells (arrows)

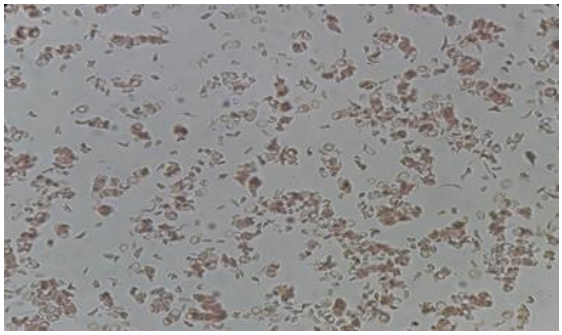


Figure 2: Photomicrograph showing sickled cells with Sodium metabisulphite sickling test (arrows)

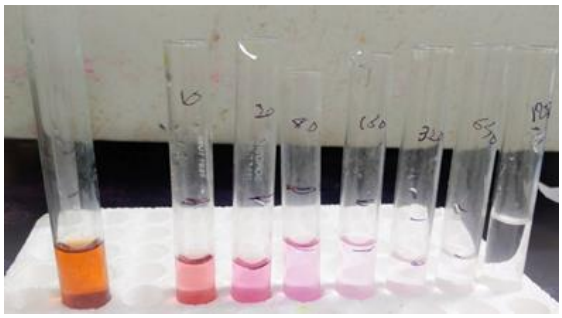
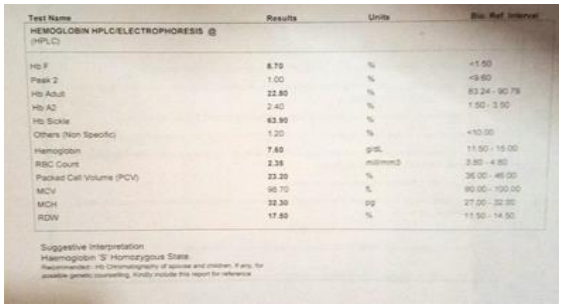


Figure 3: Photograph showing positive Ehrlich's aldehyde test for urobilinogen in urine.Test positive till1:1280 dilutions



Test Name	Results	Units	Bio. Ref. Interval
HEMOGLOBIN HPLC/ELECTROPHORESIS @ (HPLC)			
Hb F	8.70	%	<1.50
Peak 2	1.00	%	<3.50
Hb Adult	22.80	%	83.24 - 90.79
Hb A2	2.40	%	1.50 - 3.50
Hb Sickle	63.90	%	
Others (Non Specific)	1.20	%	<10.00
Hemoglobin	7.60	gm%	11.50 - 15.00
RBC Count	2.38	million/cmm	3.80 - 4.80
Packed Cell Volume (PCV)	23.20	%	36.00 - 46.00
MCV	96.70	fL	80.00 - 100.00
MCH	32.30	pg	27.00 - 32.00
RDW	17.60	%	11.50 - 14.50

Suggestive Interpretation
Haemoglobin 'S' Homozygous State.
Recommended : Hb Chromatography of spouse and children, if any, for possible genetic counselling. Kindly include this report for reference

Figure 4: photograph showing HPLC report

DISCUSSION

Sickle cell anemia is an inherited single gene disorder. The highest frequency of sickle cell disease is seen in tropical regions, particularly sub-Saharan Africa, tribal regions of India and the Middle-East.[4] According to a survey conducted by ICMR, prevalence of Sickle cell gene varies from 5 to 34% amongst different tribal groups of India.[5] In India, cases of sickle cell anemia are common in the state of Gujarat, Maharashtra (Nandurbar and Gadchiroli district), Chhattisgarh, Madhya Pradesh, Orissa, Andhra Pradesh and Tamil Nadu tribal area.[6] According to another study, sickle cell disease is common in ethnic groups of central India that share a genetic link with African communities,[7] where the prevalence varies from 9.4 to 22.2% especially in the endemic areas of Madhya Pradesh, Rajasthan and Chhattisgarh.[8] Our case is a migrant from Jharkhand (part of central India) which probably explains its genetic link.

In our case, as the patient does not describe painful crisis in childhood or adolescence, it was diagnosed at an unusual age. Patient had history of recurrent chest infections and generalized weakness with repeated blood transfusions and jaundice which should have alerted the physicians to previous chronic hemolysis.

Many genetic factors are involved in regulating the intensity of clinical features. One of the best known and most studied of these is fetal hemoglobin (HbF). High HbF is slightly associated with reduced rate of acute painful episodes, fever, leg ulcers and longevity.[9] Fetal hemoglobin inhibits the polymerization of HbS and thereby reduces the complications of the disease.[10] The value of 8.7% of HbF for this patient is relatively higher than normally seen, and may have played a role in delaying the onset and intensity of clinical features.

Also it has been suggested that despite same underlying genetic mutation, the range in severity of phenotype is striking, with some patients disabled by frequent crisis and long term complications while others live virtually normal lives. This suggests phenotype is multigenic.[11] Since many unlinked genes are involved in underlying pathological processes in sickle cell disease, variation in alleles at multiple foci may modify outcome.[12]

This patient presented with recurrent respiratory tract infections treated with routine antibiotics. It was only when she was referred to a tertiary care centre, with allied symptoms of weakness and jaundice, that a PBF was advised by physician. PBF showed sickle cells and the diagnosis was ultimately confirmed on Hb electrophoresis.

One of the serious and potentially fatal complications of respiratory tract infections in patients with SCD is ACS, hence every case of repeated chest infection requires a close monitoring.[12] The initial insult, which may be

pulmonary infection causes a fall in alveolar oxygenation tension, which causes HbS polymerization. This in turn, leads to decreased pulmonary blood flow that exacerbates vaso-occlusion, producing more severe hypoxia such that a vicious cycle of hypoxia, HbS polymerization, vaso-occlusion and altered pulmonary blood flow ensues.[13] The most common bacterial organism identified in adults is Chlamydophila pneumoniae and in children is Mycoplasma pneumonia.[13] The clinician must carefully consider the antimicrobials prescribed which should provide coverage against atypical bacteria.[13] It is therefore imperative that sickle cell disease patients with acute or chronic infections of the lungs must be closely monitored with blood gas analyzers so as to detect and correct hypoxia and its deleterious effect on red cell sickling.[14]

CONCLUSION

The unusual diagnosis of sickle cell disease (SCD) in a middle-aged adult who had few symtopms in childhood or adolescence including uneventful pregnancies illustrates the probability of genetic involvement in the onset of disease manifestations. Also the history of recurrent chest infections with fever, jaundice and repeated blood transfusions should not be overlooked and should guide the physician to rule out an underlying chronic hemolytic process.

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