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Sickle Cell Disease presenting as Young Stroke: A case report

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Abstract

Sickle cell disease is an inherited condition, with a clinical and hematologic phenotype caused by an assortment of genotypes of which Sickle cell Anemia (SCA), defined as homozygosity for the sickle hemoglobin mutation, is the most common genotype. This leads to polymerization of hemoglobin in deoxygented states causing vaso-oclusion and tissue infarction.

A 22 year old right handed male patient, presented with acute onset, non progressive weakness of left upper and lower limb with Upper Motor neuron (UMN) facial palsy. He had history of recurrent jaundice since childhood and painful swelling of right ankle joint 2 months back, for which he took treatment intermittently from local physician, but wasn't evaluated for the same. On general examination, vitals were stable, pallor and icterus was present. MRI Brain was suggestive of acute infarct in Right MCA territory. Blood Investigations revealed Hemolytic Anemia with Indirect Hyperbilirubinemia. Peripheral Smear showed Sickle cells and Hb electrophoresis confirmed the same, with HbS of 52.9%, HbF 11.4% and HbA2 2.3%. CT Abdomen and pelvis revealed splenic atrophy.

Patient was given prbc transfusions, iv antibiotics and fluids, hydroxyurea, L glutamine , folic acid, antiplatelets and statins. Vaccination against capsulated organisms and regular physiotherapy was advised. On 3 month follow up, patient showed clinical improvement.

Hence, prompt diagnosis and integrated management involving hematologist and neurologist would be a cornerstone in managing Cerebrovascular Accident (CVA) in Sickle cell disease. New drugs under trial are a ray of hope for preventing and managing these devastating complications.

Keywords: Acute chest syndrome, Blood transfusion, Antibiotics.

Introduction

Sickle Cell Disease (SCD) is an autosomal recessive hemoglobinopathy, characterized by point mutation in the sixth codon of the β gene, thereby encoding valine instead of glutamic acid in the sixth position of β globin chain of haemoglobin[1]. SCD includes all mutations in the β-globin gene that precipitate the same clinical

syndrome, of which Sickle Cell Anemia (SCA) (homozygosity of the beta-S (βS) allele) is the most common form[2]. The myriad of clinical manifestations that occur in SCD is attributed to four pathophysiological processes; polymerization of Sickle Hemoglobin(HbS), vaso-occlusion, and hemolysis mediated endothelial dysfunction and sterile inflammation[3].

Neurological manifestations in SCD range from neurocognitive dysfunction to Cerebrovascular Accident (CVA), due to the widespread vasculopathy and hypercoagulability[4]. CVA is a cataclysmic complication that affects 6% to 17% of children and young adults[1].

We present a patient, case of stroke in young with a concealed diagnosis of SCA that unfolded as the etiology.

Case Description

A 22 year old male, right handed, presented to the emergency with complaints of acute onset non progressive weakness of left upper and lower limb since 12 hours, deviation of angle of mouth to right associated with drooling of saliva and slurring of speech since 6 hours.

There was no history of fever, headache, vomiting, seizures and no history suggestive of any other cranial nerve involvement. He had history of recurrent jaundice since childhood, for which he wasn't evaluated. He gives history of painful swelling of right ankle joint 2 months back for which he received treatment from a local physician, that subsided over 3 days. No history of similar episodes in the past.

Personal and Family history were non-contributory.

On General Physical Examination, patient was febrile, had heart rate of 106/min, regular. Respiratory rate was 16 cycles/min, Blood Pressure was 132/78mmHg, Spo2 was 99% on room air. Pallor and Icterus was present.

On Neurological Examination, patient was conscious, co-operative and well oriented, GCS was E4V5M6. Slurred speech was present and comprehension was intact, left UMN facial palsy and left hemiparesis was present Meningeal signs were negative.

Other systemic examination was fair.

On investigations,

ECG -Sinus Tachycardia.

There was Anemia, Neutrophilic leukocytosis and indirect hyperbilirubinemia.

Peripheral Smear was suggestive of sickle cells, macrocytosis, anisopoikilocytosis and target cells (Figure 1).

Sickling test was positive.

Viral markers-HbSAg, Anti HCV, HIV was non reactive.

Iron profile and VitB12 was normal. Folate was low (1.5ng/ml) and LDH was elevated (>1995 U/L).

Urine Routine and CSF Analysis was normal.

To rule out any other co-existent prothrombotic state Lupus Anticoagulant, Anti Cardiolipin Ab, Protein C and S, factor V leiden mutation, Serum Homocysteine levels were evaluated and found to be non contributory.

MRI Brain was suggestive of acute infarct in right MCA territory (Figure 2).

Usg Abdomen and Pelvis showed hepatomegaly, spleen couldn't be visualized.

CT Abdomen and Pelvis revealed splenic atrophy and Calcification (Figure 3).

Hb Electrophoresis was sent, HbS 52.9%, HbF 11.4%, HbA 33.4%, HbA2 2.3%, Homozygous Sickle cell Disease, HbA could have been attributed to the blood transfusion that was given prior to the electrophoresis.

Patient was started on T.Hydroxyurea 750mg once daily L-Glutamine 5g (1 packet) twice daily, Folic acid 1mg/day, antiplatelets, statins, DVT prophylaxis, IV Antibiotics and fluids, prbc transfusion was given.

On day 3 of treatment, patient desaturated (spo2 90% on room air), respiratory examination was suggestive of fine end inspiratory crepitations in right mammary, infra-axillary and infra-scapular areas. CBC showed increased leukocytosis (neutrophil predominant) with fall in hemoglobin (Hb). D-dimer was negative. Sputum and blood cultures were sent, which did not yield any growth. CXR was normal, HRCT was suggestive of pleural based fibrotic strands in lateral basal segment of right lower lobe; well defined soft tissue masses in left 6^{th}, 9^{th} and 10^{th} intercostal spaces, no evidence of any calcification; ?rib infarct.

Suspecting Acute Chest Syndrome clinically, antibiotics were escalated, supplemental O2 and iv fluids as per hydration status were provided, low dose steroids were added, prbc transfusions were given, incentive spirometry and regular physiotherapy was advised. Patient showed symptomatic improvement and was discharged on day 7 with necessary medications, vaccination against capsulated organisms and advise on chronic transfusions. Advise on family screening and molecular studies to assess β globin gene mutation was given. During 3 month follow up patient showed clinical improvement with the power being 4/5 in left upper and lower limb. Patient was then referred to hematologist for further management.

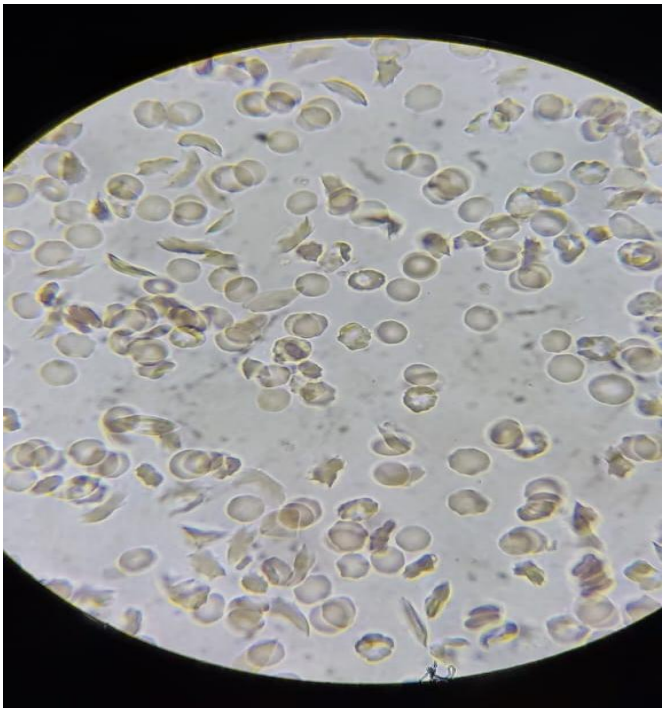

Figure 1: Positive sickling test

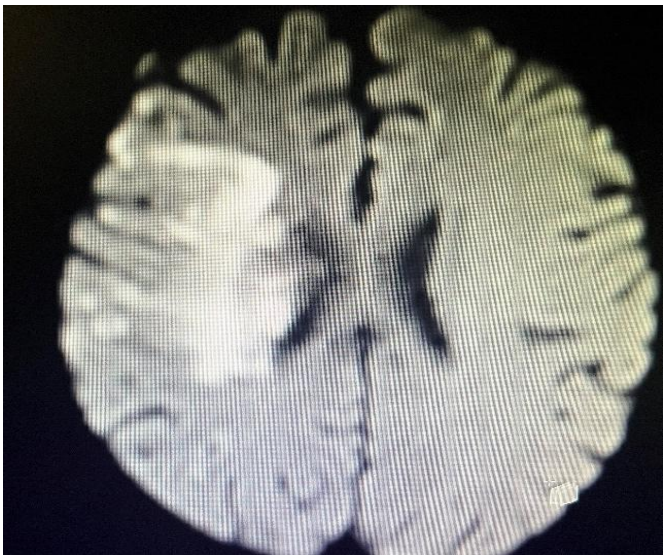

Figure 2: DWI showing acute infarct in Right MCA territory

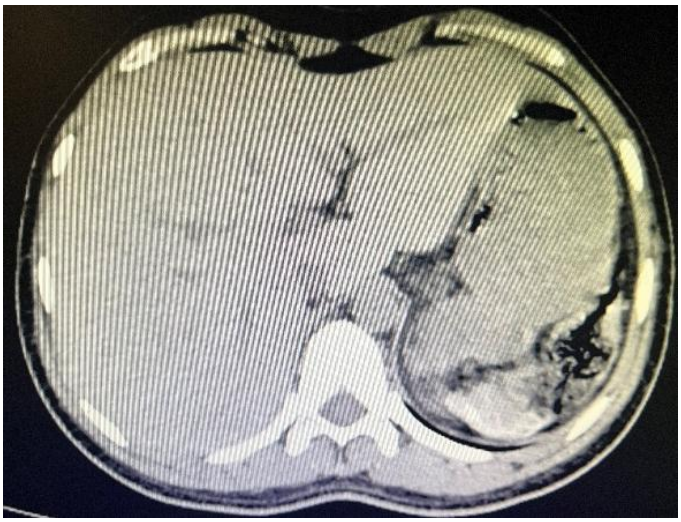

Figure 3: CT Abdomen and Pelvis showing splenic atrophy and calcification

Discussion

The risk of CVA in SCD increases after the age of 2 (due to the loss of protective effect of fetal hemoglobin), and is highest with HbSS. The type of CVA varies according to the age, with ischemic variant being predominant during the first decade and after >30 years, hemorrhagic being common during 20's[5].

Transcranial Doppler ultrasound (TCD) has emerged as a keystone in primary prevention of CVA in SCD, and hence is recommended for routine screening[6]. TCD measures the time-averaged mean maximum velocity (TAMMV), a value ≥200 cm/s is considered abnormal[7,8].This was utilized in a landmark Randomized control trial, Stroke Prevention Trial in Sickle Cell Anemia (STOP) and its successor study STOP 2, where the treatment arm (based on the abnormal TCD) received chronic prbc transfusions, every 4 weeks to maintain a Hb of 9 g/dl and HbS<30% which resulted in a remarkable 93% reduction in relative risk of CVA[9,10].

Our patient has surpassed the stage of primary prevention and presented with a disabling complication of SCD, which is CVA. Had he been evaluated for recurrent jaundice and painful swelling of his right ankle joint, which probably was a vaso-occlusive crisis, this complication could have been prevented.

The primary aim in management of CVA in SCD is to maintain a HbS<30%, which can be achieved through exchange or simple transfusion, the former being better[11]. Chronic transfusions also serve as a way through in preventing subsequent strokes over and above hydroxyurea[12].

L-Glutamine is essential for the synthesis of antioxidants like NAD, glutathione and glutamate, thereby reducing oxidative stress in sickle cells. However, it is under clinical trials for evaluation on mortality and end organ dysfunction[13].

Folic acid supplementation showed mixed results [14].

Drugs like Voxelotor and Crizanlizumab are under clinical trials, and considering the occurrence of CVA, our patient becomes an indication to be evaluated for Hematopoietic stem cell transplantation (HSCT) and hence was referred to a Hematologist.

Conclusion

Stroke in Young is a devastating condition that needs a meticulous search for an underlying Haematological disorders, malignancies and pro-thrombotic state. Considering SCD, an adept clincal acumen and swift measures utilizing the chronic transfusion and the era of HSCT would prevent any other fatal complications.

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