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CASE REPORT ON SICKLE CELL HEMOGLOBINOPATHY AND CEREBRAL VENOUS THROMBOSIS

General Medicine

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ABSTRACT

CVT is a rare type of stroke usually affecting young individuals, especially women. Risk factors include primarily inherited and acquired hypercoagulable states and drugs like oral contraceptive pills. Hematological conditions like sickle cell disease have also been associated with CVT but not as widely studied. Here we describe two such cases of CVT with sickle cell hemoglobinopathy as the predisposing factor.

KEYWORDS

Cerebral venous thrombosis, Sickle cell disease, stroke

INTRODUCTION:

Sickle cell anemia (SCA) is an autosomal recessive disease caused due to transversion mutation (A>T) on the 6th codon of the β-globin gene leading to the change of amino acid from glutamic acid to valine.[1] In hypoxic condition, valine exposed to the surface forms a hydrophobic bond with the nearest valine of other β-globin chain and forms a polymer impelled internally to change a normal RBC into a sickle-shaped RBC (SRBC).[2] Sickle RBC becomes sticky, rigid, irreversible, irregular shaped, and with activated platelet, leukocyte, and endothelial membrane can get stuck into small blood vessels, which can slow down or block blood flow to different parts of the body leading to vaso-occlusion at that site. In SCA, clinical presentation varies from asymptomatic to severe symptoms affecting many organs and even premature death. The vaso-occlusive crisis (VOC) episodes are the most common complication, requiring medical attention.

Sickle cell disease is one of the most common hemoglobinopathies worldwide affecting 20-25 million people. Cerebrovascular complications are commonly seen, and SCD is a cause of stroke in children. The most important cause is large vessel occlusion caused by abnormal adhesive properties of the RBC which produce inflammation, endothelial damage and thrombosis. Incidence of cerebral complications is 5-10%.[3] In 11% cases stroke usually occurred by the age of 20 mainly infarction in middle cerebral artery and Internal carotid arteries.[4]

The incidence of sickle cell disease is very high in this geographical region, and the occurrence of pediatric stroke is common. Here we report 2 cases of adult patients with sickle cell disease who developed cerebral venous thrombosis.

Case presentation:

Case 1:

A 42 year old male presented with a history of sudden onset headache and weakness in his right upper limb for one day. There was no associated history of fever, seizures or loss of consciousness. He presented to the emergency room when he realised that the weakness in his right arm was getting worse and he was unable to lift his hand or hold any objects with it. He did not have a history of hypertension, diabetes, smoking or alcohol use.

On admission his BP was 136/80 mm Hg, pulse rate 88min, respiratory rate of 20/ min and temperature of 98.6 degrees F. Neurological examination showed a power of 2/5 in his right upper limb with depressed deep tendon reflexes in that limb. Rest of the examination was normal.

He was subjected to CT scanning the same day of admission. CT did not show any parenchymal abnormality. However the weakness and headache persisted. The next day an MRI was performed. MRI with venogram showed thrombosis of the right transverse and sigmoid sinuses.

His HB was 10.6 g/dl. Thrombophilia testing was negative for Protein C, Protein S and Antithrombin deficiency. Because of the high prevalence of sickle cell disease in this region, we tested for sickle cell disease. Hb electrophoresis showed presence of sickle cell trait in the patient. In the absence of any other risk factors for CVT, sickle cell trait was identified to be the predisposing factor in this case. He was started on anticoagulants and physiotherapy and he made an uneventful recovery.

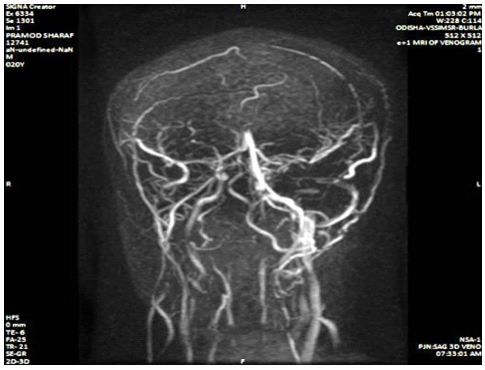

Figure 1: MR venogram showing thrombosis of right transverse and sigmoid sinus

Case 2:

An 18 year old female presented with seizures. She did not have history of prior seizures. It was followed by a loss of consciousness. There was no preceding fever, history of trauma or altered behaviour. She had a history of sickle cell disease which was detected during her childhood but was not on any medication. She was admitted to the emergency department and administered lorazepam for seizures and stabilised. The following day she remained drowsy but no further episodes of seizure occurred.

She had a blood pressure of 100/70 mm Hg, pulse rate of 110/min and respiratory rate of 25/ min with temperature of 99.6 degree F. Neurological examination showed an extensor plantar response on the right with a power of 0/5 on the right upper and lower limb. Examination of other systems was unremarkable.

MRI was done the next day which showed a hemorrhagic infarction, in the left frontoprietal region. MR venogram was subsequently performed which showed thrombosis of the superior saggital sinus. She was started on intravenous mannitol. Her haemoglobin was 8.6 mg/dl. Urine pregnancy test was negative. She was tested for thrombophilias (Protein C, Protein S and Antithrombin) which were negative. She was also tested for ANA and lupus anticoagulant which came out to be negative. On testing for sickle cell disease, her Hb electrophoresis showed SS pattern, with HPLC showing 73% of HbS. She was subsequently started on anticoagulation and hydroxyurea and discharged from the hospital after a period of three weeks at the time of which she was able to walk with support.

DISCUSSION:

Association between SCD and cerebral thromboembolic events has been investigated in several studies. Alli et al reported the presence of skull bone infarction crisis and deep vein thrombosis in a boy with homozygous sickle cell anemia.[5] In individuals with sickle cell trait (SCT) cerebral infarction and stroke is rare and there are few case reports related to the incidence of stroke in these individuals. Few studies from Mediterranean countries reported the occurrence of CVST and stroke in SCD patients. Sidani et al have reported the existence of venous and sinus thrombosis and stroke in a Lebanese young homozygous sickle cell patient.[6] In this patient the presence of proteins C, S, antithrombin III, factor V Leiden (FVL), and prothrombin mutations as well as anticardiolipin antibodies were negative. Also, a 25-year-old French SCD patient with cerebral vein thrombosis and bilateral thalamic infarcts has been reported.[7] In addition, Radhakrishnan et al reported the presence of stroke in two young adult sickle cell trait individuals from Libya.[8]

Other causes of hemorrhagic stroke in sickle cell patients have also been reported. Lenticulostriate and intraventricular hemorrhages in adults were associated with carotid stenosis and abnormal capillary networks in the Virshow–Robin spaces, similar to hemorrhagic forms of Moyamoya disease Moreover, the development of compensatory vascular pial anastomoses can lead to SAH (seen in one patient). Aneurysm was the more classical cause of SAH. Aneurysms occurred during childhood in association with stenotic vasculopathy but were symptomatic mainly during adulthood

Conclusion:

Sickle cell hemoglobinopathy is an important cause of neurological manifestations in adults as well as pediatric population. Cerebral venous thrombosis is more common than previously expected and in high prevalence region like ours, sickle cell disease should be ruled out as a predisposing factor in patients.

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