Case Report

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Radiology Section

Moyamoya Syndrome with Recurrent Stroke in a Splenectomised Patient with Beta-Thalassaemia Major: A Case Report

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ABSTRACT

Moyamoya Syndrome (MMS) is a progressive disease with typical angiographic 'moyamoya' alterations. Here, the authors discuss a case of 16-year-old male patient who developed MMS after being diagnosed with β-thalassaemia major. This patient was detected with heterozygous mutations in the β-globin gene and underwent splenectomy at the age of 12 years. Four years postsplenectomy he presented with paresis of the right upper limb. Magnetic Resonance Imaging (MRI) showed infarction and stenosis of the internal carotid artery with the collateral vessel's formation. Recurrence of stroke and progression of the vasculopathy were seen. Till now, only a few cases of MMS have been linked to thalassaemia major.

Keywords: Endothelial proliferation, Hypercoagulopathy, Splenectomy

CASE REPORT

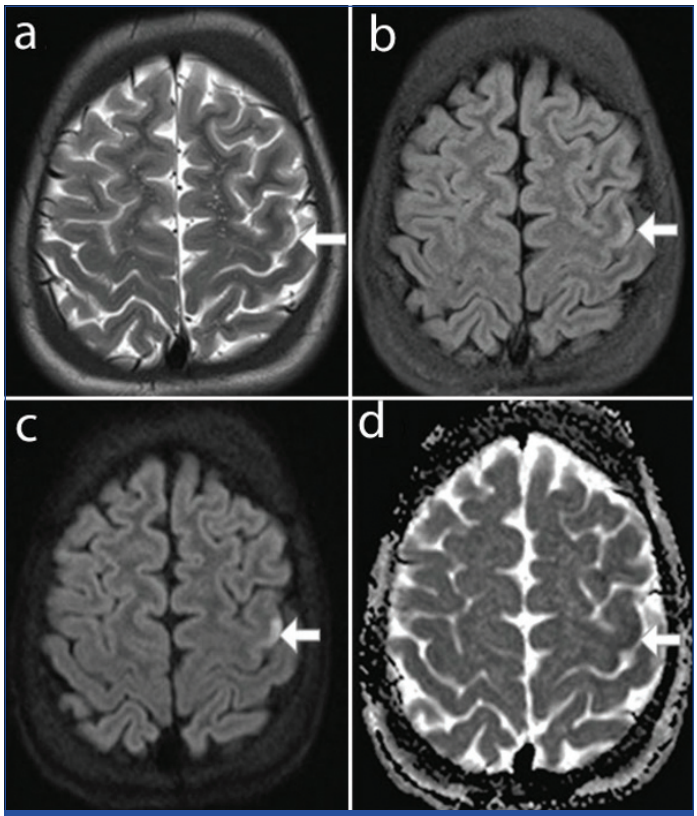
A male patient of age 16-year-old, diagnosed with transfusion dependent β-Thalassaemia major, complained of acute onset of right upper limb weakness associated with slurring of speech and deviation of angle of mouth. No previous history of neurological deficits, epilepsy or psychiatric manifestations was present. No conventional risk factor for other vascular diseases was present. Family history was non significant. Neurologic examination revealed reduced muscle power in the right upper limb (3/5) with brisk deep tendon reflexes and spasticity. Examinations of other systems showed pallor and hepatomegaly.

The results of peripheral blood analysis showed haemoglobin was 8.6 g/dL, serum ferritin was 697 mg/L, mean corpuscular volume was 74.5 fL, total bilirubin was 3.78 mg/dL (Indirect and direct bilirubin was 2.28 mg/dL and 1.67 mg/dL, respectively). Molecular genetic test for Hemoglobin Subunit Beta (HBB) (β-Globin) gene showed heterozygous pathogenic variants c.47G>A and c.92+5G>C in HBB gene consistent with the diagnosis of β-Thalassaemia major.

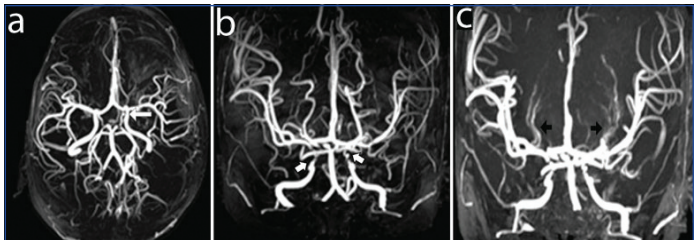
Patient had been dependent on blood transfusions since he was nine-year-old, requiring transfusions once or twice a month. He was splenectomised when he was 12-year-old. After that, blood transfusions were reduced to once every 3-4 months.

Magnetic Resonance Imaging (MRI) was performed and revealed acute infarct in the left precentral gyrus in the left high frontal region [Table/Fig-1] and cystic encephalomalacia with surrounding gliosis in the left frontal centrum semiovale region. Magnetic Resonance Angiography (MRA) depicted bilateral supraclinoid Internal Cerebral Arteries (ICA) narrowing with mild narrowing of the M1 segment of left Middle Cerebral Artery (MCA) with extensive bilateral collaterals suggestive of Moyamoya pattern. Lenticulostriate arteries in bilateral basal ganglia were prominent [Table/Fig-2]. Dilated collateral vessels were seen as multiple punctate prominent vessels in the basal ganglia and thalamic region on Susceptibility Weighted Imaging (SWI) [Table/Fig-3] and flow voids on T2 Weighted Image (T2WI). The patient was managed conservatively and discharged.

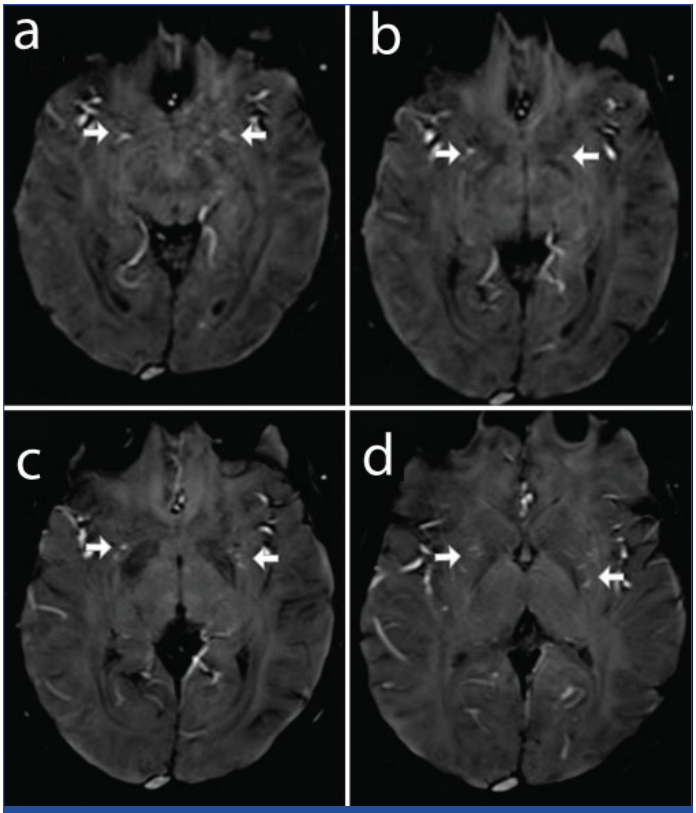
The patient presented after three months with complaints of left lower limb weakness and a follow-up MRI was performed which revealed acute infarct in the right high parietal parasagittal and left



[Table/Fig-1]: MRI Brain: a) Axial T2 weighted image; b) Axial Fluid Attenuated Inversion Recovery (FLAIR); c) Diffusion Weighted Imaging; d) Apparent diffusion coefficient showing acute infarct in the left frontal lobe in precentral gyrus appearing hyperintense on T2WI and FLAIR showing restricted diffusion on DWI with low ADC values.

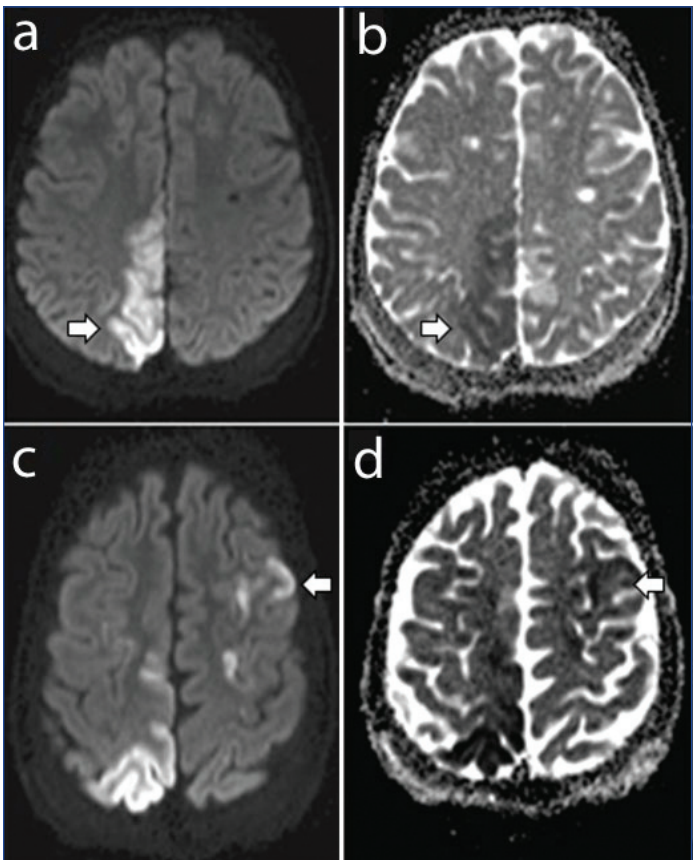


[Table/Fig-2]: MR Angiography 3-dimensional (3D) time of flight (TOF) Maximum Intensity Projection (MIP) images: a) Narrowing of the M1 segment of left MCA; b) Showing narrowing of supraclinoid portion of bilateral MCA; c) Showing prominent lenticulostriate vessels on either side (Moyamoya pattern).

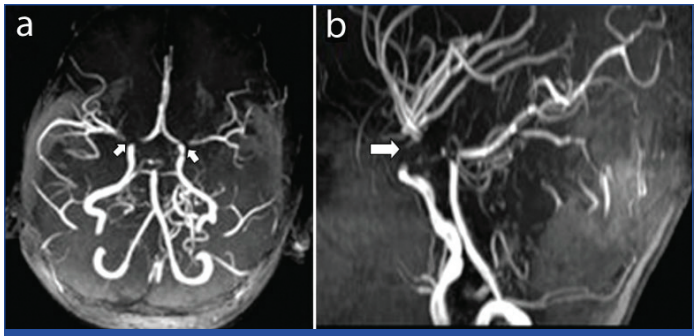


[Table/Fig-3]: Magnitude images of SWI sequence show dilated collateral vessels (lenticulostriate arteries)as multiple punctate and linear prominent vessels in the basal ganglia region (a, b, c, and d).

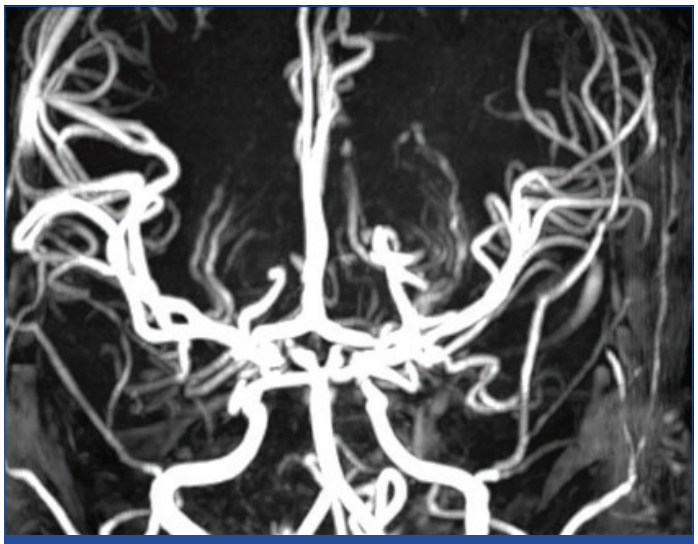
high frontal region [Table/Fig-4]. MRA depicted bilateral supraclinoid ICA narrowing with narrowing of M1 segments of both MCA and A1 segment of right Anterior Cerebral Artery (ACA) [Table/Fig-5] with an increase in the previously noted bilateral collaterals [Table/Fig-6]. The patient was treated with antiplatelet, statins and advised physiotherapy with favourable clinical recovery.



[Table/Fig-4]: MRI Brain: DWI and ADC sequence showing acute infarct in right parafalcine parietal region (ACA territory, Images a,b) and left high frontal region showing diffusion restriction on DWI with low ADC values (Images c,d) in the follow-up MRI after 3 months.



[Table/Fig-5]: MR Angiography 3D TOF MIP images: (a,b) showing narrowing of supraclinoid portion of bilateral ICA, the proximal portion of the M1 segment of bilateral MCA, and proximal portion of the A1 segment of right ACA in the follow-up MRI after 3 months.



[Table/Fig-6]: MR Angiography 3D TOF MIP images show an increase in the previously noted collaterals (lenticulostriate arteries) in the follow-up MRI after 3 months.

DISCUSSION

Occlusion or stenosis of internal carotid arteries causes extensive arterial collaterals resembling puff of smoke. The term moyamoya in Japanese means puff of smoke [1,2]. This is distinct from MMS, which arises when comparable stenosis or occlusion occurs due to inherited or acquired disorders [3].

Moyamoya disease affects the circle of Willis and supraclinoid internal carotid arteries and is a progressive, non inflammatory idiopathic, non atherosclerotic vaso-occlusive disease. MMS, pattern or phenomenon is due to conditions that result in arterial occlusion of the circle of Willis with collateral formation and imaging features similar to moyamoya disease [4]. Thalassaemia is a rare cause of MMS [5]. Children under the age of 10 are more likely to develop it. They usually present with Transient Ischaemic Attack (TIA) and complaints of hemiplegia, monoparesis, and sensory impairment. MRI, MRA, and conventional angiography help in the diagnosis. Within a year or two, unilateral insults frequently lead to bilateral insults [3].

Sickle cell disease is an established risk factor for MMS [6]. There are only a few reports of its association with thalassaemia [5]. Authors reported a case of male aged 16 years with β-Thalassaemia major and MRI findings indicative of MMS. On literature research, only three cases of MMS in a splenectomised patient diagnosed with β-thalassaemia intermedia have been published. This is the first case of MMS reported in splenectomised patient diagnosed with β-thalassaemia major [5].

A chronic hypercoagulable state exists in thalassaemia major condition [7,8]. An excess of α-chain molecules causes damage to the erythrocyte cell membranes due to oxidative stress augmenting anionic phospholipids surface expression (phosphatidylserine) which initiates platelet activation and resultant procoagulant effect

of thalassemic erythrocytes. Anaemia in thalassaemia causes tissue hypoxia with resultant hypertrophic vascular endothelium which leads to microvascular stenosis. Arterial occlusion and multiple cerebral infarcts in thalassaemia occur due to a chronic hypercoagulable state. The hypercoagulable state occurs due to red blood cell membrane abnormalities, altered platelet function, endothelial activation leading to alteration in coagulation protein levels, and activation of coagulation cascades [8]. Vasa vasorum flow can be hindered by deformed erythrocytes in thalassaemia. This leads to internal carotid arteries wall ischaemia, the proliferation of the intimal layer of vessels, and occlusion leading to progressive vasculopathy [2].

Patients with β-Thalassaemia major receiving regular transfusions have a lower incidence of thrombotic events than the patients not on regular transfusions [8]. Splenectomy raises the risk of embolic and stroke episodes due to hyperlipidaemia and thrombocytosis [2]. Postsplenectomy thrombocytosis and weaning from transfusions exacerbated hypercoagulability associated with abnormal erythrocytes in the present case, potentially lead to the formation of moyamoya arteries.

Marden FA et al., described a case of ischemic stroke with moyamoya disease in a female patient aged nine years diagnosed with β-Thalassaemia. The patient presented with haemolytic anaemia at four months of age and later at 19 months of age with cerebral infarction. MRI brain showed right cerebral infarct. However, MRA did not reveal findings of moyamoya disease. No catheter angiography was done at that time. The patient received transfusion therapy for haemolytic anaemia. MRA done seven years later showed numerous deep collaterals suggestive of moyamoya disease indicating progression of disease and interval development of collaterals [9]. Our case revealed changes of moyamoya disease on MRA at the time of diagnosis.

Parker TM et al., described a diagnosed case of β-Thalassaemia presented at 13 years with breathlessness on exertion and fatigue with reduced weight and height at 10-25th percentile. Growth Hormone (GH) stimulation revealed GH deficiency. MRI brain was performed for hypothalamic-pituitary dysfunction. It revealed left internal carotid artery narrowing, possible mild narrowing of the left anterior and MCA and small vessels were noted in basal ganglia suggestive of MMS [3].

Sanefuji M et al., reported a case of a female patient aged 14 years with β-Thalassaemia intermedia who had transient ischemic attacks with right hemiparesis at 12 years of age after splenectomy. MRI brain revealed stenosis of bilateral ICA and perforating branches dilatation with resultant Moyamoya vessels, however, with no demonstrable infarcts [2].

A female child patient aged 14 months presenting with hemiparesis was reported by Inati A et al., [10]. Patient developed symptoms at the age of three months, when she developed left tonic posturing and left sided neck deviation. She experienced transient tonic posturing with high-pitched cry after staying asymptomatic until she was 13-month-old. She suffered acute right hemiparesis two weeks later. Multiple acute infarcts involving the cortex were detected on MRI in the left posterior occipital, parietal and frontal lobes. MRA revealed stenosis at the origin of posterior cerebral arteries, narrowing of the right MCA in the M1 segment, attenuated peripheral branches of the left MCA and multiple collaterals around the circle of Willis, indicative of moyamoya disease. Patient was diagnosed with β-Thalassaemia major [10].

In the present case, in addition to the MRA changes and cerebral infarct, subsequently developed acute infarct in right ACA and left MCA territories in the follow-up MRI after three months.

CONCLUSION(S)

Thalassaemia major plays a role in the aetiology of MMS. MMS is a complication that occurs in thalassaemia. Its early detection is essential to avoid disability due to stroke or intracranial haemorrhage with resultant neurodeficit. Better prognosis may be aided by a greater index of suspicion and screening for early detection of MMS. Early intervention with direct or indirect revascularisation could improve the patient's prognosis and prevent the vasculopathy from progressing silently.

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