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Case Report

Moyamoya Syndrome in a known case of Beta Thalassemia Major: A Rare Case Report

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Abstract

Moyamoya disease is a progressive cerebrovascular disease with specific finding on cerebrovascular angiography consisting of prominent collateral vessel formation due to either unilateral or bilateral stenosis or complete occlusion of arteries in or around the circle of Willis, typically the supraclinoid internal carotid arteries Moyamoya syndrome is frequently associated with haematological conditions. We describe a case of 16-year-old male diagnosed case of Beta thalassemia who presented with right side hemiparesis and aphasia indicating a cerebrovascular accident along with previous history of stroke an year ago, signifying recurrent stroke.

Key words: Moyamoya syndrome, Beta thalassemia, Recurrent stroke, MRI.

Introduction:

Moya-Moya Syndrome is a cerebrovascular condition signifying the vascularity in the intracranial vessels, characterised by progressive stenosis of intracranial internal carotid arteries & their proximal branches, with development of prominent small vessel collaterals giving a smoky appearance on angiography, like a puff of smoke in air translating to “Moya-Moya” in Japanese which is puffy or hazy appearance[1].Affected patients present with stroke. Moya-Moya disease (MMD) was initially described in year 1957 in Japan. Majority of the cases were reported in Japan and neighbouring Asian countries. Moyamoya syndrome (MMS) is associated with Sickle cell disease, Neurofibromatosis type1, Cranial therapeutic irradiation Down’s syndrome [1], different types of anaemias, Hemoglobinopathies, & BetaThalessemias.[2].

Case Report:

A 16-year-old male presented to our hospital with right upper and lower limb weakness since 10 days and sudden onset aphasia with recurrent seizures since 7days.There was no H/o fever& loss of consciousness, photophobia,& delayed milestones. Past history given by patient’s mother that he is a diagnosed case of Beta-thalassemia major at the age of 5 years, with CD15 and IVS 1-5 pathogenic variants detected were c.47G>A and c.92+5G>C in the HBB Gene at age of 5 months, He received first blood transfusion at age of 5 months, splenectomy was done at age of 12 years. Patient had a history of right-side facial weakness and right upper limb weakness in 2016, with MR imaging confirming a Left Middle cerebral artery territory

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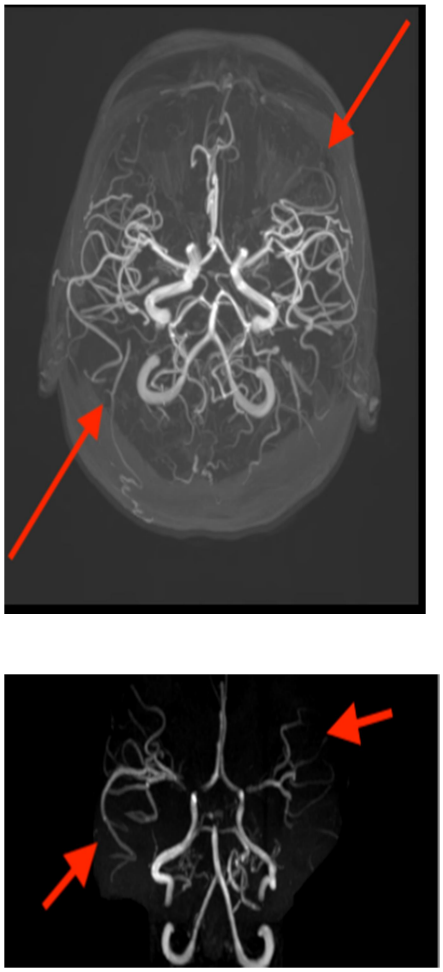
infarct. At the time of presentation, patient had been started on Tablet Hydroxyurea 100mg OD, and Tablet Thalidomide 5000mg weekly thrice, for 5 years. His latest laboratory reports suggest Hb level of 6.4gm/dl and a platelet count of 40,000/microL. Peripheral blood smear shows moderate anisocytosis with, poikilocytosis, with target cells and thrombocytopenia), Serum Ferritin was 900. Following the latest episode of hemiplegia, an MR imaging angiography was done that showed narrowing with reduced flow signals in clinoid and supraclinoid portion of bilateral ICAs. Mild narrowing and irregularity of wall in M1 segment of left MCA, loss of flow signal in M1 segment of right MCA. Prominent lenticulostriate arteries/ collaterals in bilateral basal ganglia - Suggesting Moyamoya pattern. Reduced flow signals in the top of the basilar artery and P1 segments of bilateral PCA's. Other ACA, MCA, PCA branches appear prominent - likely due to anaemia. Radiological diagnosis coupled with clinical presentation were compatible with a diagnosis of Moya-Moya syndrome.

Other causes of stroke in young such as vasculitis, autoimmune conditions, infections, thrombophilia's, protein C&S deficiency and connective tissue disorders were ruled out on history, physical examination, and relevant blood investigations. Blood transfusions were given accordingly, and antiplatelet therapy was continued.



Photograph 1) MR Angiography showing extensive collateral formation due to revascularisation giving it a smoke like pattern – "Moya-Moya" in Japanese.

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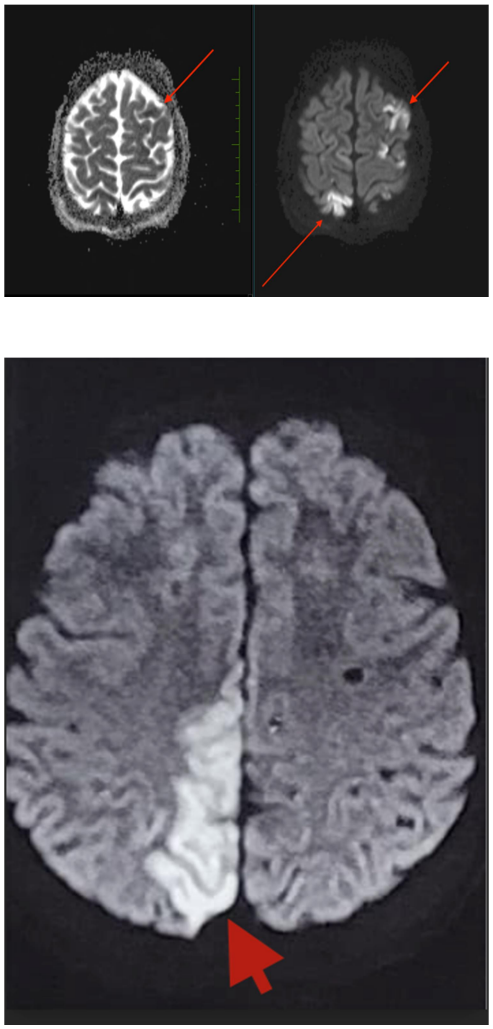

Photograph 2) Diffusion Weighted MRI Imaging shows Right MCA, ACA territory acute non-haemorrhagic infarcts, and corresponding ADC images.

Discussion:

The aetiology of Moya-Moya disease (MMD) is unknown, but genetic associations have been identified. Moya-Moya syndrome (MMS) has been associated with multiple haematological conditions, most Common is, Sickle cell anaemia[2] Rarely it is associated with Beta thalassemia[3],Fanconi's anaemia [4]&, Hereditary spherocytosis[5].Patient with MMS are at high risk of developing thromboembolic stroke & TIA'S. Hypercoagulability followed by thromboembolic episodes is considered as a common complication of thalassemia. Risk factors include, previous history of thrombotic events, splenectomy, severe anaemia & high serum ferritin levels[6].

Thalassemia,& anaemia may cause tissue hypoxia and hypertrophic vascular endothelium, leading to microvascular stenosis. [7]. Multiple cerebral infarcts and large arterial occlusions in Beta thalassemia-associated MMS has also been related to its chronic hypercoagulable state. Hypercoagulable state in thalassemia is multifactorial attributed to endothelial activation, altered platelet function, red blood cell membrane abnormalities[8,9].

A genetic susceptibility may be implicated in MMD, while underlying associated conditions trigger the development of MMS. Vascular changes in Moya-Moya are associated with evidence of increased angiogenesis-related factors, including endothelial colony-forming cells, various cytokines, vascular endothelial growth factor (VEGF), and basic fibroblast growth factor (bFGF).[10] High levels of fibroblast growth factor, which may stimulate arterial growth, have been found in the vascular intima, media, and smooth muscle as well as cerebrospinal fluid among patients with Moya-Moya. Transforming growth factor beta-1 (TGFB1), which mediates neovascularization, may also contribute to the pathogenesis[11].

In Moya-Moya syndrome, symptoms of cerebral ischemia are associated with regions of the brain supplied by the internal carotid arteries & middle cerebral arteries & these regions are the frontal, parietal & temporal lobes.

Common Symptoms &Signs are Hemiparesis, Aphasia, Dysarthria Cognitive impairment & Seizures[1]

Conclusion:

Moya-Moya syndrome secondary to beta thalassemia is very rare .& also a cause of recurrent stroke in young.

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Ischemic stroke and transient ischemic attacks affecting the anterior circulation are the most common clinical presentations. Transfusion dependency in beta thalassemia major might not be able to prevent the progression of MMS.

The diagnosis of Moya-Moya syndrome is confirmed by characteristic MRI/MR Angiography findings . Revascularization can be effective in preventing stroke in patients with Moya-Moya disease.

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