Congenital Absence of Internal Carotid Artery and Complex Cerebral Vascular Abnormalities with Thalassemia Intermedia: A Novel Association?

Sir,

A 10 years old boy presented to emergency services with complaints of headache for the past 1 day. Headache was continuous, severe, and throbbing in character, diffuse in location, and was associated with dizziness, restricted activity, and sleep disturbance. He also had three episodes of right focal seizures that were spontaneously aborted and lasted for less than 5 min followed by three episodes of vomiting. There was a history of blood transfusion (twice) in the previous week. After receiving the transfusion, all these symptoms completely resolved and the child remained asymptomatic for 2 days, following which the child developed neurological symptoms. His central nervous system examination, blood pressure, and fundus examination were within normal limits. However, the abdomen examination showed mild splenomegaly.

Investigations revealed hemoglobin: 7.7 g/dL, microcytic hypochromic red blood cells (RBCs) (MCV: 71, MCH: 20), anisopoikilocytosis and nucleated RBCs in peripheral smear suggesting hemolytic process. A Hb electrophoresis by high-performance liquid chromatography showed decreased HbA and increased HbA2 and HbF levels (HbA: 48%, HbA2: 4.9%, and HbF: 46%). Non-contrast CT scan of the brain showed subarachnoid hemorrhage (SAH) in the left frontal lobe. Magnetic resonance imaging (MRI) of the brain with the time of flight (TOF) revealed SAH along the left Sylvian fissure and in the left frontal lobe [Figure 1a]. Left cervical and intracranial internal carotid artery (ICA) including petrous and cavernous segment were not visualized [Figure 1c, d]. CT neck and cerebral angiography showed absent left ICA from the origin with non-visualization of the petrous and cavernous segment [Figure 2a and c]. The left terminal ICA was reformed through PCom [Figure 1d]. Left anterior cerebral artery (ACA) was reconstituted through anterior communicating artery (ACom). There was a trifurcation of ACA [Figure 2c]. The bone window revealed an absent left bony carotid canal [Figure 3a]. The rest of the aortic arch branches appear normal with no evidence of stenosis or any mural thickening. Widened diploic marrow spaces along with the hair on end appearance were also seen in parietal bone consistent with chronic hemolytic anemia [Figure 3b].

The child was managed conservatively with antiepileptic drug levetiracetam and other symptomatic management. The child recovered completely within 72 h and on follow-up at 3 months he did not have any cognitive or motor abnormalities.

The absence of a congenital ICA is an extremely rare developmental anomaly and is seen in around 0.01% of the population. Depending on the development, it includes agenesis, aplasia, and hypoplasia of ICA.[1-5] The radiological diagnosis of the congenital absence of ICA includes two major criteria first one is non-visualization/absence of ICA on angiography and second is an absence or hypoplastic bony which differentiates it from acquired conditions like occlusion or vasculitis.[6,7]

Most of the patients are asymptomatic due to various collateral flow pathway, however, the most common pathway is the circle of Willis. Other common collateral pathways include intercavernous anastomosis or persistent embryonic vessels or the branches of the external carotid artery. Symptomatic patients commonly present with headache, seizures, transient ischemic attacks, and hemiplegia. The imaging findings depicted in these patients are infarct or SAH as seen in our case. Various associated anomalies such as cerebral hemiatrophy, Klippel-Trenaunay syndrome, cardiac anomaly, arachnoid cyst have been reported.[6] The index child presented with anemia and showed radiographic features of chronic hemolytic anemia in the form of a widening of diploic space and hair on end appearance.

English literature showed only two cases of spontaneous SAH in thalassemia patients.[8,9] The first case was a 27-year-old female with beta-thalassemia major, who developed

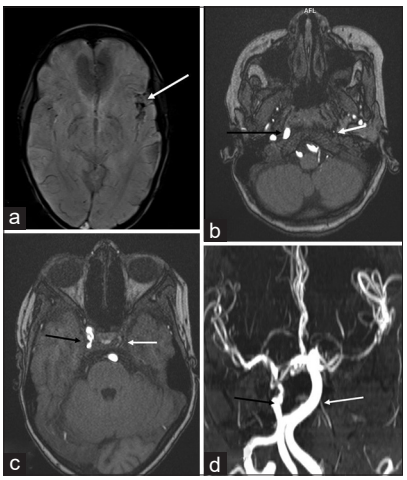

Figure 1: (a) Axial susceptibility-weighted (SW) image shows subarachnoid hemorrhage along the left Sylvian fissure (arrow). (b) Time of flight (TOF) angiographic axial image shows the absent flow in the left petrous segment of the left internal carotid artery (ICA) (white arrow). Normal flow is seen in the right ICA (black arrow) (c) TOF angiographic axial at the upper level displays an absence of flow in the cavernous segment of left ICA (white arrow). Normal flow is seen on the right side. (d) Reformatted TOF angiographic image shows the normal flow in the right ICA (black arrow) and absent flow in the left ICA. Bilateral vertebral artery and basilar artery (white arrow) are seen

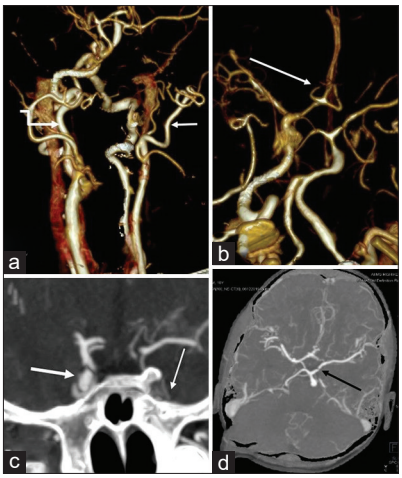

Figure 2: (a and b) Volume rendered image shows the absence of left cervical ICA, however, the origin of left ECA is normal. (Straight white arrow). Note the normal right-sided ICA (curved arrow). Trifurcation of ACA is seen (b, arrow), (c and d) The maximum intensity projection (MIP) axial image at the level of cavernous sinus depicts the absence of left cavernous ICA (thin white arrow). Note the normal opacification of right cavernous ICA (thick white arrow). Reconstitution of left ICA is seen through PCom (d, black arrow)

postpartum crisis due to SAH over cerebral convexities. On angiography, she did not have any symptomatic aneurysm, but like our case, she had an absence of supraclinoid segment of the left internal carotid artery and abnormally developed left cortical and lenticulostriate perforator artery. In this patient, histopathological vascular examination showed atrophy of internal elastic lamina and tunica media of cerebral blood vessels, probably due to obstruction of vasa vasorum, weakening the vessel wall, and predisposing to SAH.[8] They postulated that chronic hypercoagulable state in beta-thalassemia and increased expression of procoagulant phospholipids on the surface of pathological erythrocyte membranes further aggravates this obstruction of vasa vasorum.[8] Moreover, there was compensatory vasodilatation in left frontal territories with relative hypoperfusion. We propose similar multifactorial flow-related phenomena, relative hypoperfusion, and intracranial vascular anomalies that contributed to the development of SAH in our case.

The unusual development of cerebral cortical arterial branches probably testifies the presence of abnormal collateral circulation in response to hemodynamic disorder generated by aplasia of the internal carotid artery.[8] An epidemiological study reports an increased incidence of multiple cerebral vascular abnormalities in subjects with beta-thalassemia of intermediate (27% of arterial stenosis, 17% aneurysms, 60% of small silent subcortical infarctions).[10] The intracerebral hemorrhages in beta-thalassemia are rarely described after repeated transfusions and our case also received transfusion twice 2 days before SAH.[10]

The second patient was a 49-year-old female with beta-thalassemia minor, who presented with a severe headache and on evaluation was found to have SAH in the basilar cistern and over cerebral convexities.[9] Angiography repeated, twice in her on 3rd and 24th day after SAH were normal. However, unlike our case, she had a history of spontaneous bleed in the anterior chamber of the eye 3 years back and bleeding time was found to be prolonged, along with normal platelet count. So, the PFA100 test was conducted, which revealed platelet storage pool disease with alterations during the degranulation and aggregation functions. She responded excellently to a trial of desmopressin. Platelet function assay by PFA100 was within normal limits in the indexed child.

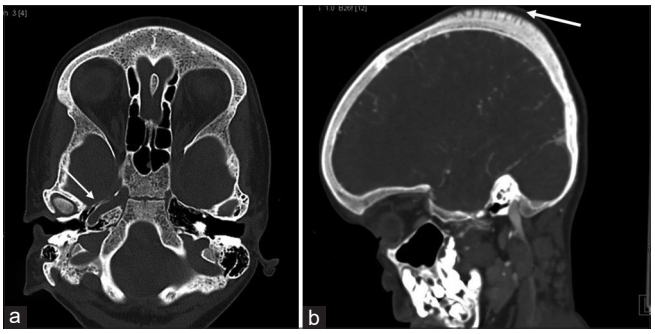

Figure 3: (a) Axial bone window image shows absent bony left carotid canal on the left side. Note the normal bony carotid canal on the right side (arrow). (b) Sagittal image shows hair on end appearance (arrow) of parietal bone signifying chronic hemolytic disease

To conclude, a spontaneous cerebral hemorrhage, in the absence of impaired coagulation or aneurysms, is rarely possible in thalassemia patients. In our patient, cortical SAH appears to be related to the development of an abnormal cortical collateral network secondary to hemoglobinopathy and internal carotid artery aplasia.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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