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Case report

Moyamoya syndrome associated with sickle cell trait in a child

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Abstract

Moyamoya syndrome is a chronic, progressive occlussion of cerebrovascular arteries that leads to the development of characteristic collateral vessels. It is usually accompanied with sickle cell disease and other hemoglobinopathies. We report a 7-year-old boy, who admitted to our clinic with headache, diagnosed as moyamoya syndrome associated with sickle cell trait. To date, two such cases have been reported in the literature. As far as we know, this patient is the first child reported.

Keywords: Moyamoya syndrome; Sickle cell trait; Child; Headache

1. Introduction

Moyamoya syndrome is a chronic, progressive occlussion of cerebrovascular arteries that leads to development of characteristic collateral vessels [1]. The typical clinical symptoms are headaches, recurrent transient ischemic attacks, ischemic and hemorrhagic strokes, seizures and visual deficits in pediatric patients. The exact etiologic process is unclear, whereas genetic, environmental and viral–bacterial infection diseases represent a risk factor [1,2]. Moyamoya syndrome is a relatively uncommon neurovascular complication of SCD. However, to our knowledge two such cases have been reported with moyamoya syndrome associated with sickle cell trait in the literature [3,4].

In this paper, we report a case of moyamoya syndrome in a child with sickle cell trait. To the best of our knowledge, this patient is the first child reported with moyamoya syndrome associated with sickle cell trait.

2. Case report

A previously healthy 7-year-old boy is presented with complaints of headache for 3 weeks duration. He had been admitted to another hospital and cerebral magnetic resonance imaging (MRI) was normal. When he referred to our clinic, his headache became deteriorated. He complained that his headache was so severe and especially in the mornings and evenings nausea and vomiting were added to his clinic. Headache was used to recover with analgesics for a while but it recurs then. The patient's medical history and family history was unremarkable.

In physical examination, his pupils were equal, round and reactive to light. Extra ocular muscles were intact. Muscle strength in bilateral upper and lower extremities, and deep tendon reflexes were normal. Babinski sign was negative and no clonus was elucidated. There were

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no signs of cerebellar dysfunction. Meningeal irritation signs were negative. Skin examination was normal. His laboratory tests on admission produced findings of hemoglobin 13.6 mg/dl, hematocrit 38.6%, white blood cells 7880/mm^3, platelet 417,000/mm^3. MRI was re-evaluated by an experienced radiologist in our hospital. Imaging revealed findings such as severe stenosis in the supraclinoid segment of the left internal carotis artery and collateral vessels within the ambient cistern which were also confirmed by magnetic resonance angiography (MRA) performed in our radiology department (Fig. 1).

Etiology of the moyamoya syndrome was investigated; liver function tests, total protein, albumin, blood urea nitrogen, creatinine, ECO cardiography, test for collagene vascular disease (ANA, Anti-DNA, p-ANCA, c-ANCA, anticardiolipin antibodies and antiphospholipid antibodies), protein S and C, antithrombine III, coagulation parameters, serum iron, total iron binding capacity and ferritin level were normal. Hemoglobin electrophoresis was HbA1: 58.1%, HbS: 38%, and HbA2: 3.9%. According to beta gene mutation results, heterozygote HbS mutation was detected by using pyrosequencing methodology. In the family screening, also we detected heterozygote HbS mutation in his father.

The patient was diagnosed to have moyamoya syndrome, applied medical treatment with the calcium-channel blocker (nimodipine) and has been stable since then.

3. Discussion

Moyamoya syndrome is a clinical and radiological entity, which is characterized by chronic progressive stenosis of the supraclinoid internal carotid artery. Etiopathogenesis of moyamoya syndrome is currently unknown however environmental, genetic and infectious factors may have a role in the development of the disease [1,2]. Moyamoya syndrome is a well-known complication of SCD. Patients with SCD who develop moyamoya syndrome appear to be at risk for recurrence of strokes. This was illustrated in a retrospective study of 44 patients maintained on chronic transfusions [5]. It was detected that the risk of recurrent stroke was greater in patients with moyamoya than those without the disease. Inspite of the well known relationship between SCD and moyomoya syndrome, a relationship with sickle cell trait is not known. To our knowledge, two such cases have been reported with moyamoya syndrome associated with sickle cell trait in the literature [3,4]. Recently, Agrawal et al. reported a 44-year-old man presented with left-sided weakness and numbness. His MRA revealed bilateral moyamoya syndrome and diagnosis of sickle cell trait was confirmed with high performance liquid chromatography [3].

Sickle cell trait occurs in approximately 300 million people worldwide, it is considered to be a benign state. However, sickle cell trait occasionally can be associated with significant morbidity and mortality. It is associated with rare but often fatal renal medullary cancer, hematuria, renal papillary necrosis, hyposthenuria, splenic infarction, exertional rhabdomyolysis, and exercise-related sudden death. Additionally, it has been suggested that sickle cell trait is probably associated with venous thromboembolic events. In some scattered reports, researchers indicate that sickle cell trait, can be associated with cerebrovascular complications including stroke. The 21 children with sickle cell trait were searched for brain abnormalities and it was detected that two children had mild abnormalities at MRI, and four had arterial tortuosity. Ratio of HbS was significantly greater in children with tortuosity than that in controls [6]. It was detected that laboratory markers of coagulation activation such as TAT com-

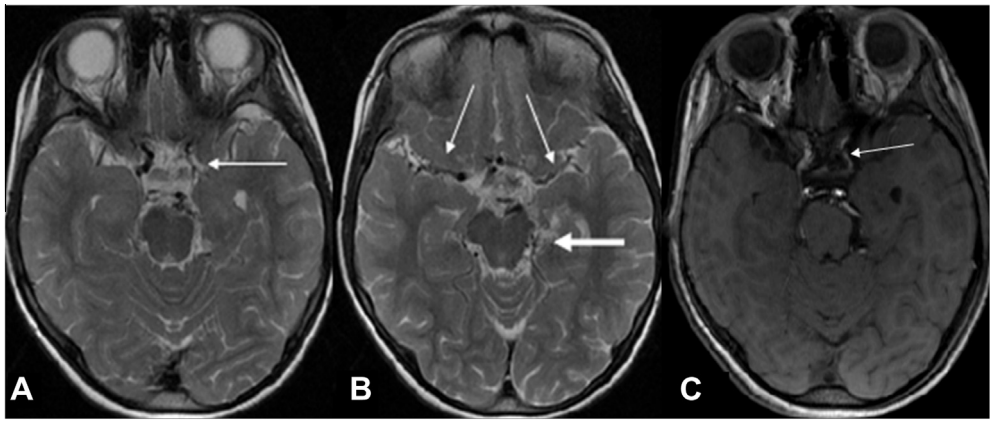

Fig. 1. Axial T2 weighted image at the suprasellar level (A) shows severe stenosis in the supraclinoid segment of the left internal carotis artery (arrow). Axial T2 weighted image at the mesencephelon level (B) demonstrates narrowing of both middle cerebral arteries (thin arrows) and collateral vessels within the ambient cistern (thick arrow). Magnetic resonance angiography (C) confirms narrowing in the supraclinoid segment of the left internal carotis artery (thin arrow).

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plexes, d-dimers, and prothrombin fragment F1.2 were elevated in persons with HbAS compared with those with HbAA, and were the highest among those with HbSS. Increased venous thromboembolic events in the sickle cell trait patients was explained that membranes of sickle cell erythrocytes show loss of normal phospholipid asymmetry, and the resulting abnormal phosphatidylserine exposure was thought to contribute to the hemostatic perturbations seen in persons with SCD [7]. The sickle cell trait with higher HbS may need follow-up with regular brain MRI. In our patient, moyamoya syndrome could be associated with increased venous thromboembolic events in sickle cell trait.

The neurological symptoms of moyamoya syndrome are numerous that headache, seizures, ischemic strokes, intracranial hemorrhages, cognitive deficits, recurrent transient ischemic attacks. Headache is the first and common symptom [1]. Also, pediatric moyamoya syndrome may present with recurrent transient ischemic attacks and/or completed ischemic strokes. In Guzman et al.'s study presenting symptoms in the majority of cases were 51% ischemic attack and 44% headache [8]. Scott et al. reported 67.8% stroke (43.4% transient ischemic attack) and 6.3% headache as presenting symptoms [9]. Our patient complained about three-week-long headache and had no other neurological symptoms. In 6 months follow-up there was no ischemic event.

As a result, moyamoya syndrome should be kept in mind for the patients with sickle cell trait and headache in countries SCA is common such as Turkey and brain MRI should be performed in early period in these patients.

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