CASE REPORT

Childhood moyamoya disease accompanying leigh syndrome

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Abstract

Moyamoya disease is a cerebrovasculopathy of unknown etiology during the course of which the main and terminal veins of the internal carotid artery undergo progressive vein occlusion. Leigh syndrome is a mitochondrial encephalomyopathy that occurs due to "cytochrome c oxidase deficiency" characterized by psychomotor retardation, difficulty in eating, seizures, hypotonia, respiratory disorders and high lactate levels. Many diseases and syndromes have been defined that are associated with Moyamoya disease. To the best of our knowledge, the association of moyamoya disease with Leigh syndrome has not been defined as yet. In this study, the clinical and imaging results of a 3-year old male child displaying the association of Moyamoya disease and Leigh syndrome are presented.

Keywords: Leigh disease, Moyamoya syndrome, Childhood, MRI.

Introduction

Moyamoya disease is a cerebrovasculopathy of unknown etiology; during the course of which the main and terminal veins of the internal carotid artery undergo progressive vein occlusion.[1] The brain forms compensatory collateral arterial structures in an attempt to achieve a build-up of blood. This collateral circulation seen by Suzuki and Takaku in 1969 during catheter angiography was named Moyamoya disease since it resembled cigarette smoke.[2,3] Moyamoya disease is a significant cause of paralysis during childhood and the average peak age is 5. Fast diagnosis and treatment is important for long term prognosis.[4] In cases where the pathological findings of cerebral angiography are observed together with events such as meningitis, neurofibromatosis, neoplasms, Down's syndrome, Noonan syndrome, Seckel syndrome and polycystic kidney disease, the sickness is named Moyamoya syndrome.[5] To the best of our knowledge, there are no previously published studies in literature on the subject of Moyamoya disease with Leigh syndrome association.

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Case Report

A 3-year old male patient was brought into the Emergency Department of Harran University, Sanliurfa, Turkey, as a followup visit, in 2009, with complaints of sudden loss of strength and convulsions. During the neurological examination, the patient was unconscious and had no response to verbal stimuli. Hemiparesis in the right half of the body with a 2/5 loss of strength, Babinski positivity and an increase in deep tendon reflexes were detected. Pupil light reflex was performed bilaterally and the pupillary isochoric and fundus examination results were normal. With these findings it was thought that the patient had undergone a cerebral stroke and brain magnetic resonance imaging (MRI) was carried out. Signal intensity was observed at the bilateral globus pallidus, hypothalamus, bilateral cerebral peduncles, nucleus ruber, pons posterior, cerebellar dentate nuclei, bilateral periventricular deep white matter, and subthalamic nuclei

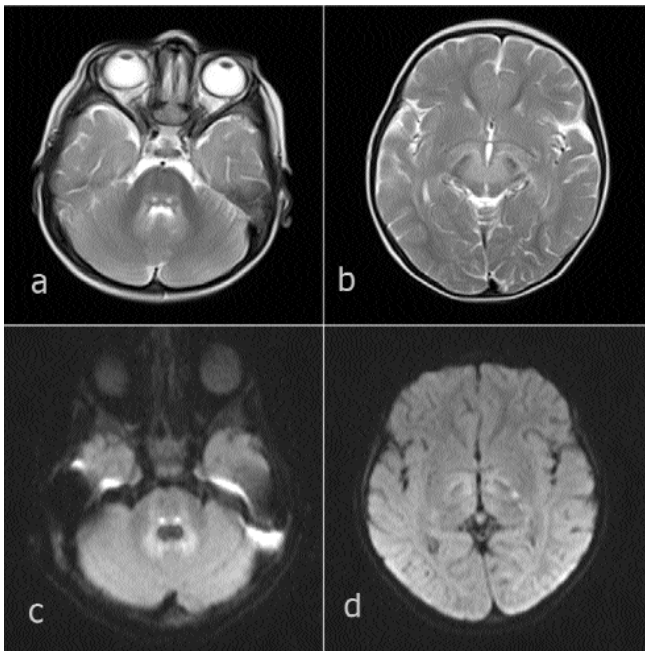

Figure-1: The axial T2-weighted MR image (a) shows signal increases in bilateral dentate nuclei, pons posterior and the axial T2-weighted MR image (b) shows symmetric signal increases in bilateral cerebral peduncles along with diffusion restrictions in axial DAGs (c, d) passing through these levels.

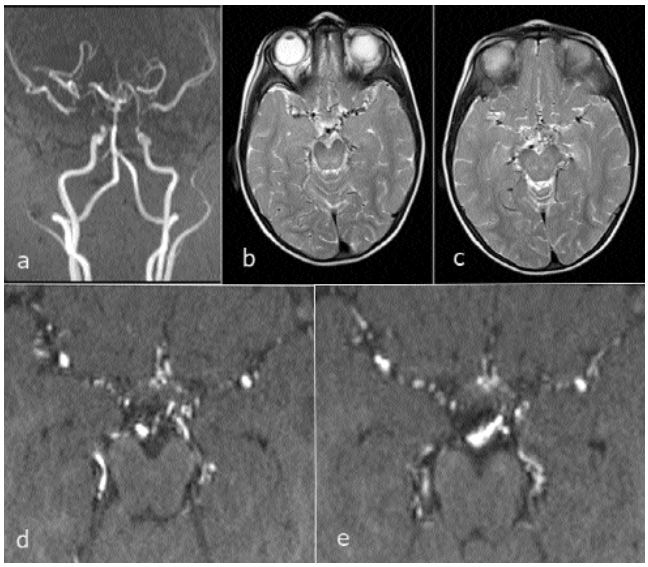

Figure-2: Frontal projection 3D TOF MRA image (a) shows total occlusion of the right supraclinoid internal carotid artery (ICA), excessive shrinkage in the left ICA and basilar artery and filling of the bilateral middle cerebral artery (MCA), anterior cerebral artery (ACA) and posterior cerebral arteries (PCA) via collaterals. The axial T2-weighted MR images (b, c) and source images of 3D TOF MRA (d, e) show collaterals around circle of willis, in the ambient cisterns and sylvian valleys.

and secondary ischaemia on T2-weighted images (Figures: 1a and 1b). Diffusion constriction was observed in diffusion weighted series at bilateral dentate nuclei, pons posterior and cerebral peduncles (Figures: 1c and 1d). MR angiography, determined occlusion at the right supraclinoid internal carotid artery (ICA), about 80 % shrinkage in the left ICA and basilar artery, and filling of the bilateral middle cerebral artery (MCA), anterior cerebral artery (ACA) and posterior cerebral arteries (PCA) via collaterals (Figure-2a). The axial T2-weighted MR images (Figures: 2b, c) and source images of 3D TOF MRA (Figures: 2d, e) show collaterals around circle of Willis, in the ambient cisterns and sylvian valleys. The patient was admitted to the Pediatric Neurology Department for further examination based on the suspicion of Moyamoya disease associated with Leigh syndrome. Total cholesterol, triglyceride, lipid electrophoresis, creatin phosphokinase levels were measured during laboratory tests carried out for stroke etiology and the results were determined to be normal. Haemorrhagic diathesis tests, complementary C3 and complementary C4 levels, anti nuclear antibody (ANA) and anti ds-DNA levels were normal. There was no S band in the haemoglobin electrophoresis of the patient and the sickling test was negative. Telecardiography, electrocardiography, echocardiography and cervical Doppler US imagings were normal. The antithrombin- lll, protein C, protein S levels measured for the etiology of vascular disease in the patient were normal and no factor V-Leiden mutation was determined. Blood lactate levels were determined to be high (40 mg/dl). The patient was diagnosed with Leigh syndrome after the lactate levels were determined to be high in repeated tests and since typical MR imaging findings were not observed. Treatment of 3mg/kg/day Coenzyme Q and 50 mg/kg/day L-Carnitine was started. Muscle biopsy was planned and blood samples were sent for genetic investigation. Follow-up is still continuing in the Paediatric Neurology Polyclinic.

Discussion

Leigh syndrome or 'subacute necrotizing encephalomyelopathy' occurs mostly due to 'cytochrome c oxidase'' deficiency. It is a mitochondrial encephalomyelopathy characterized by psychomotor retardation, feeding difficulty, seizure, hypotonia, respiratory disorders and high lactic acid levels in the early suckling period.[6] Generally, this disease is progressive and results in death within a few years.[7] In laboratory examinations the blood tests may display abnormal oxidative metabolism or organ dysfunction. Blood lactate and pyruvate levels are frequently high. A lactate/pyruvate level exceeding 20 means a respiratory chain defect. In addition, a great majority of children with mitochondrial diseases may have normal lactate levels in their blood. CSF lactate level measurement is more valuable for these patients.[8]

There were no outstanding features in the medical history of the patient; neither was there any finding regarding neurological or genetic diseases. The important clinical findings at the admission stage were sudden loss of consciousness, convulsion and loss of strength in the right half of the body. A significant level of blood lactate from which acute cerebral paralysis was considered is central to mitochondrial diseases in which the central nervous system is affected the most and 45 % of children in this situation come with neurological findings.

In magnetic resonance imaging reflecting the neuropathological features of focal necrotic lesions radiologically, basal ganglion (globus pallidus, caudate nucleus, thalamus, putamen) is observed and symmetric hyperintense lesions are observed in brain stem nuclei (periaquaductal grey matter, substantia nigra, medullar reticular formation, olivary nucleus) in T2-weighted imaging. In further stages, white matter lesions may be present in both cerebral hemispheres.[7,9,10] In the case presented here, symmetric hyperintensities were present in the bilateral globus pallidus, hypothalamus, bilateral cerebral peduncles, nucleus ruber, pons posterior, cerebellar dentate nuclei, bilateral periventricular deep

white matter and subthalamic nuclei.

Leigh syndrome diagnosis depends firstly on suspicion of the sickness clinically. An accurate diagnosis can be made after muscle biopsy and enzyme examinations for patients suspected of Leigh syndrome due to brain MRI typical findings, together with high lactic and pyruvic acid levels.[7] Although treatment options are limited L-carnitine treatment is suggested as coenzyme Q and secondarily carnitine deficiencies occur.[8]

In the case presented here, the diagnosis was made from typical brain MRI findings, high lactic acid levels in the blood and the accompanying clinical findings. Muscle biopsy was planned for the polygraphic analyses to evaluate the electron transport chain functionally along with spectrophotometric analyses. The patient was observed to benefit from the coenzyme Q and L-carnitine treatment along with the physical treatment programme and in the follow-up it was determined that the loss of strength in the right half of the body had returned to normal.

Conclusion

Moyamoya disease should be considered for children brought in with complaints of paralysis. In addition, it should be kept in mind that Moyamoya disease can be accompanied by many other diseases and syndromes. Therefore, clinical and neuroradiological imaging findings are valuable. The case presented here is of significance, as to the best of our knowledge; it is the first case in literature of Moyamoya disease accompanied by Leigh syndrome.

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