Case Report

Carotid Dissection Causing Stroke in a 13-Year-Old Boy with Mild Hyperhomocysteinemia: Case Report

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The author describes a 13-year-old Thai boy who developed stroke caused by carotid dissection and found mild elevation of plasma homocysteine (tHcy). The patient improved after anticoagulation therapy and his plasma tHcy decreased after vitamin supplement. With long-term follow-up, he is having normal neurological condition. This case proposes that the pathogenesis of carotid dissection may associate with mild hyperhomocysteinemia.

Keywords: *Hyperhomocysteinemia, Pediatric, Carotid dissection*

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Cervicocephalic arterial dissection has long been considered a rare cause of ischemic stroke in children[1]. The natural history of cerebral arterial dissections in childhood remains poorly understood. Recently, mild hyperhomocysteinemia was identified as independent risk factor for vascular disease[2].

Case Report

A previously healthy 13-year-old Thai boy had the history of sudden fall and dizziness during exercise, two weeks prior. His speech was later slurred with weakness on the right side of his face. Only mild weakness on the right side of his face and right arm were detected without other abnormalities on physical examination. The provisional diagnosis was cerebrovascular accident. Magnetic resonance image (MRI) showed infarction on the left side of basal ganglia, anterior and genu of internal capsule (Fig. 1). Magnetic resonance angiography (MRA) demonstrated double luminal sign at the left proximal internal carotid artery (ICA) with severe narrowing of both intra- and extracranial parts of left ICA with severe stenosis of the left distal ICA and middle cerebral artery (Fig. 2). Doppler ultrasonography (U/S) later confirmed the diagnosis of left carotid dissection with the additional finding of mixed atheromatous plaques with 50-75% stenosis in the right carotid artery. He was extensively investigated for other risk factors for juvenile stroke. EKG, echocardiogram, lipid

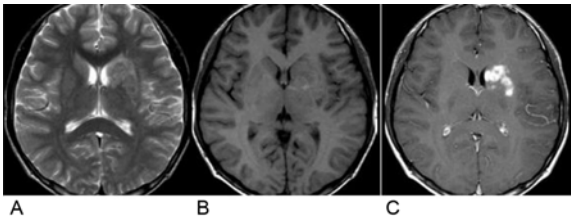

Fig. 1 A: axial T2W, B: axial T1W, C: axial T1W+Gd showing subacute subcortical infarction of the left basal ganglion region

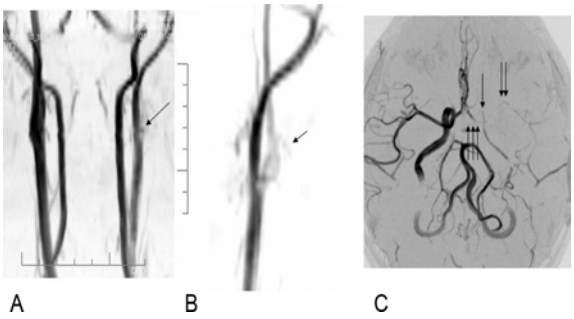

Fig. 2 A & B: 2D TOF MRA of the neck and C: 3D TOF MRA of the brain. Arrow in A&B shows double lumen of the proximal left ICA at the carotid bulb, In C, severe occlusion of the clinoid of left ICA (single arrow), the left MCA (middle cerebral artery) (double arrows) and the left ACA (anterior cerebral artery) (triple arrows) are depicted

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profile, CBC, coagulogram, antithrombin III, protein C, protein S, antinuclear antibody, methytetrahydrofolate reductase gene polymorphism (MTHFR), fibrillin gene screening for exon 25, 34, 35, 44, vitamin B12, and folic acid level yielded normal results except his plasma tHcy level was slightly elevated (13.22 micromol/L (μmol/L)). Heparin was administered for two weeks with serial Doppler U/S monitoring until recanalization of stenotic carotid artery and then switched to warfarin for three months. After stopping warfarin, aspirin, folic acid and B1-6-12 were administered. Plasma homocystine level repeated three months after supplement of folic acid and B1-6-12 was 11.09 μmol/L. After seven years follow-up, the patient is still having normal physical and neurological examination.

Discussion

Craniocervical arterial dissection is increasingly recognized as an important cause of childhood arterial ischemic stroke. It is increasing from 7.5% to 20% due to the current, less invasive imaging techniques. The elevated blood levels of tHcy have been linked to increased risk of premature coronary artery disease, stroke and thromboembolism, even among people who have normal cholesterol levels. Factors influencing homocysteine metabolism include genetic defects, impaired metabolism and nutritional deficiency of folate, and vitamin B6, B12. Pezzini A, et al found the association between increased total plasma tHcy concentration above the cutoff level of 12 μmol/L, cervical artery dissection (CAD), and genetic mutation *i.e.*, homozygosity for the thermolabile form of MTHFR[2] and 677C-T mutation[3]. Spence, et al have pointed out that the presence of a carotid plaque per se justifies the measurement of tHcy, independent of the MTHFR genotype[4]. As shown in the present patient, the carotid atheromatous plaques with stenosis had been demonstrated by Doppler ultrasound on both sides, although he had arterial dissection only on the left side showing the underlying abnormalities in his carotid arteries. Accordingly, his plasma tHcy found mild elevation without other risk factors of juvenile stroke, neither the mutation of MTHFR gene. With these findings, they indirectly strengthen the hypothesis of a link between increased levels of tHcy and CAD. The exact pathomechanism of arterial dissection is not fully understood. Independence of the type of dissection mechanism, the endothelial damage appears to be an important step. However, the relationship between CAD and hyperhomocysteinemia seems to be complex, since CAD is not considered an atherosclerotic disease[5]. Several *in vitro* and *in vivo* studies demonstrated that hyperhomocysteinemia can induce endothelial damage[2]. Endothelial dysfunction can be a key for the early events of atherogenesis and could be responsible for a weakness of the arterial wall in patients with CAD. *In vitro* studies demonstrate that high levels of plasma Hcy result in a decrease in the elastin content of the arterial wall due to blocking aldehydic groups in elastin, which is necessary for the cross-linking of collagen. Thus, Hcy may have an influence on the elastic properties of the arterial wall. These findings are supported by the higher incidence of dissection in aortic and carotid arteries that have more elastic laminas than femoral and brachial arteries. Although the conventional cerebral angiography was shown to be safe for children with cerebrovascular disease, MRA especially contrast-enhanced MRA and fat-saturated MRI[6] combined with Doppler U/S can be highly sensitive in diagnosis particular for the carotid arteries. In the present patient, both MRA and Doppler U/S were used for establishing the diagnosis of carotid dissection, furthermore, Doppler U/S could provide the additional information of atheromatous plaque in both carotid arteries and be used for monitoring during the treatment until the resolution of carotid dissection. Antiplatelet drugs and anticoagulants have been recommended in adults to prevent transient attacks or completed stroke in arterial dissection but remains unclear in children[7]. However, according to the guideline in adults, heparin followed by warfarin and later aspirin were administered in this child with complete recanalization of carotid artery without any complication. Lowering the serum concentration of tHcy has been proven to reduce the risk of adverse cardiovascular events among people with homocystinuria but have not yet determined whether reduces the incidence of strokes among people with mildly elevated tHcy levels[8,9] but many experts believe that. There has been strongly support data from a four-year study of Genest et al in which 101 men with vascular disease were given supplementary doses of folic acid, B6 and B12. They found a decrease in the amount of carotid plaque in their arteries, with the greatest effect in those whose homocyteine levels had been highest before the treatment began[10]. Accordingly, the present patient received folic, B1-6-12 supplement to prevent recurrent ischemic stroke. With long-term follow-up, he has still not had a recurrent stroke. From the present study, it can be concluded that plasma tHcy should be evaluated in carotid dissecting children with carotid plague.

Treatment should include antiplatelet drug, anticoagulants and tHcy lowering agents with long-term monitoring for the clinical and other contributing factors to the cerebrovascular risks.

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Potential conflicts of interest

None.

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ภาวะหลอดเลือดแคโรติดฉีกขาดทำให้เกิดภาวะหลอดเลือดสมองอุดตันเฉียบพลันในเด็กชายอายุ 13 ปี ซึ่งพบปริมาณสารโฮโมซีสเตอีนในเลือดสูงกว่าปกติเล็กน้อย: รายงานผู้ป่วย

อาภาศรี ลุสวัสดิ์

ผู้นิพนธ์รายงานผู้ป่วยเด็กชายไทยหนึ่งรายอายุ 13 ปี ที่มีอาการหลอดเลือดสมองอุดตันเฉียบพลันจากภาวะหลอดเลือดแคโรติดฉีกขาด และพบปริมาณสารโฮโมซีสเตอีนในเลือดสูงกว่าปกติเล็กน้อย โดยไม่พบสาเหตุอื่นของการเกิดภาวะเส้นเลือดสมองอุดตันในเด็ก หลังจากรักษาโดยการให้ยาต้านการแข็งตัวของเลือดผู้ป่วยอาการดีขึ้นและระดับสารโฮโมซีสเตอีนในเลือดลดลงหลังจากได้รับยาวิตามินร่วมด้วย จากการติดตามการรักษาในระยะยาวเป็นเวลา 7 ปี ผู้ป่วยไม่มีความผิดปกติของระบบประสาทใด ๆ อีกเลย เป็นที่น่าสังเกตุว่าภาวะหลอดเลือดแคโรติดฉีกขาดอาจจะมีความสัมพันธ์กับภาวะโฮโมซีสเตอีนในเลือดสูงกว่าปกติเล็กน้อยในผู้ป่วยรายนี้