Case Reports

A rare cause of acute ischaemic stroke due to combined deficiency of protein C and protein S in an infant

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Introduction

Isolated protein C and protein S deficiencies are documented causes of acute ischaemic stroke (AIS) in children[1]. However, combined protein C and S deficiency has not been reported in the literature.

Case report

An 11 month-old boy was admitted with left sided hemiparesis and left sided facial weakness without loss of consciousness. He had a history of tonic clonic focal seizures of the left half of the body on day 2 of weakness, lasting for 15 minutes without secondary generalization. Neurological examination showed left sided hemiparesis, left extensor Babinski reflex and upper motor neuron type of facial nerve palsy. General physical examination, including anthropometry and eye examination, was normal. After 5 days, his weakness completely resolved. Family history was negative for thrombosis, heart disease or early death. Brain computerized tomography (CT) on day 2 showed an acute infarct in right middle cerebral artery (MCA) territory involving right fronto-parietal region. Magnetic resonance imaging (MRI) of brain done the next day showed fronto-parietal infarct (Figure 1) and magnetic resonance angiography revealed thrombosis of right sided MCA (Figure 2).

Electrocardiogram was normal. Chest X-ray, echocardiogram and haematological examination including haemoglobin electrophoresis, lipid profile, activated partial thromboplastin time, prothrombin time and bleeding time were unremarkable. Plasma amino acid, antinuclear antibody (ANA), antineutrophil cytoplasmic antibodies (P-ANCA and C-ANCA), metabolic profile (including homocysteine, ammonia and lactate) and arterial blood gas analysis were normal. Protein C, Protein S, anti-thrombin III, Factor V Leiden were measured at that time. Protein S level was 39U/ml (1-5 year range 54–118U/ml) and protein C level was 28.7U/ml (1-5 year range 40-92U/ml). The anti-thrombin III level was 116U/ml (range 82- 139U/ml) and fibrinogen level was 191 (range 170-405). Factor V Leiden level was within the normal range. Protein C and S levels of his parents were normal. Patient was treated with low molecular weight (LMW) heparin and oral warfarin with target international normalised ratio (INR) of 2.5-3.5. Fresh frozen plasma was given 12 hourly until D-dimer was normal. After six weeks follow up MRI brain was normal but protein C and protein S levels were still subnormal. Even after 9 months of follow up protein C and protein S levels are still low.

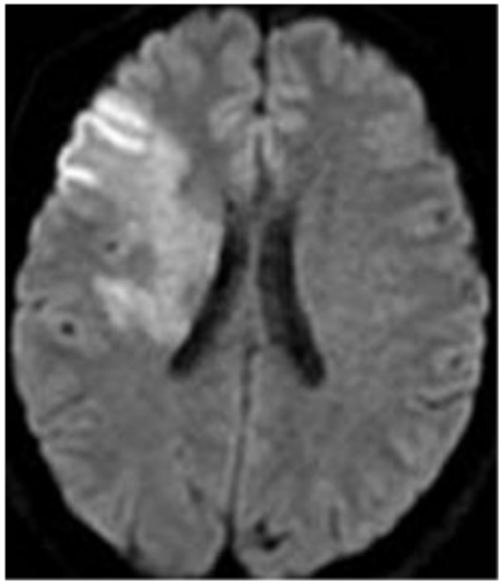

Figure 1: ***MRI of brain showing infarct in right fronto-parietal lobe***

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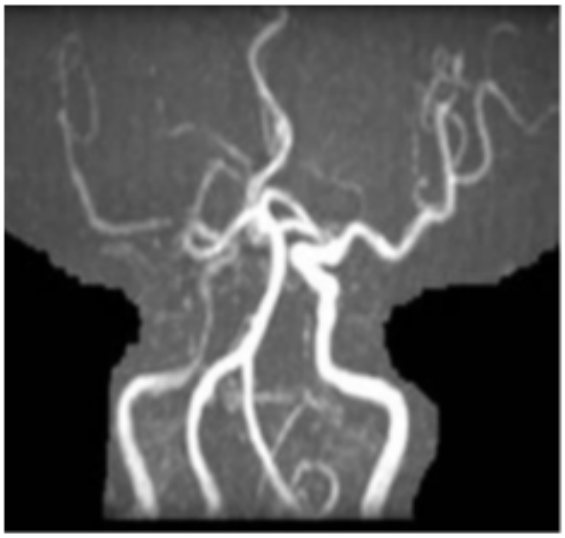

Figure 2: ***MRA showing blockade of right middle cerebral artery***

Discussion

In one study by Engesser L et al. the mean age at the first thrombotic event among 71 patients with heterozygous protein S deficiency was 38 years with a range of 15 to 68 years[2]. However, homozygous protein S deficiency usually presents in the neonate[3]. In this case report, the patient presented at 11 months of age. Girolami et al. and Sie P et al. first described familial deficiency of protein S as a cause of ischaemic stroke in young people[4,5]. Proteins C and S are 2 vitamin K-dependent plasma proteins working in concert as a natural anticoagulant system. Activated protein C is the proteolytic component of the complex and protein S serves as an activated protein C binding protein that is essential for assembly of the anticoagulant complex on cell surfaces. The anticoagulant activity is expressed through the selective inactivation of Factors Va and VIIIa[6]. Clinically, patients with protein C and S deficiency are at increased risk for venous thromboembolic disease and occasionally arterial thrombosis can occur[7-9]. The identification of a prothrombotic factor in children with AIS assists determination of cause and recurrent risk and this might have implications for prevention of systemic thrombosis in that patient and family members[10]. In this case the patient presented at an earlier age compared to previously reported cases. Moreover, combined deficiency of both protein C and protein S presenting as AIS has not been reported as yet.

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