CASE REPORT

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An Unusual Case of Cerebral Vein Thrombosis in an Adolescent Male

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Abstract

Cerebral venous thrombosis (CVT) is a distinct cerebrovascular disorder that mostly affects young adults. The clinical symptoms vary and may include severe headache (90%), focal lateralising signs (50%), seizures (40%) as well as behavioural symptoms, loss of consciousness. Usually CVT are due to secondary causes (70%) and in 30% cases, it is associated with genetic prothrombotic conditions, such as deficiency of antithrombin III, protein C, or protein S, mutation of factor 'V' or prothrombin genes, resistance to activated protein C and hyperhomocystinaemia. We report a case of a 17-year-old male adolescent with cerebral vein thrombosis due to a rare genetic cause.

Key words: Cerebral vein thrombosis, prothrombotic.

Case report

A 17-year-old male presented with complaints of headache and vomiting followed by one episode of partial seizures involving left upper limb and lower limb. There was no preceding aura, loss of consciousness, or focal neurological deficit. He is not a known case of diabetes, heart disease, chronic kidney disease, hypertension, chronic lung disease, seizure disorder, and no significant family history or history of any chronic drug intake. All vitals parameters including blood pressure and physical examination were absolutely normal. CNS examination, gait, tone, power were normal. No cranial nerve abnormality was noted.

Blood investigations including complete haemogram, serum electrolytes, liver and renal functions were normal. Chronic infection disease (e.g., tuberculosis, HIV, HBV and HCV) work-up was not significant. Coagulation profile of this patient is given below.

Coagulation profile of the patient

Test	Test result	Normal range
PT-INR	Normal	
Anti thrombin-III	114	80 - 120
Protein S level	≤ 12.5	60 - 150%
Protein C level	82.89%	70 - 140%
Factor V Leiden	No mutation	Normal pattern
Lupus anti coagulation	Not detected	
Homocysteine	8.59 µmol/l	5.46 - 16.20
Cardiolipin AB-IgG	1.26 GPL/ml	≤ 12 negative
IgM	0.52 MPL/ml	12 - 18 equivocale
IgA	1.99A PL/ml	≥ 18 positive

Imaging studies showed haemorrhagic infarct involving the right parietal region (Fig. 1) secondary to superficial cortical vein thrombosis ((Fig. 2).

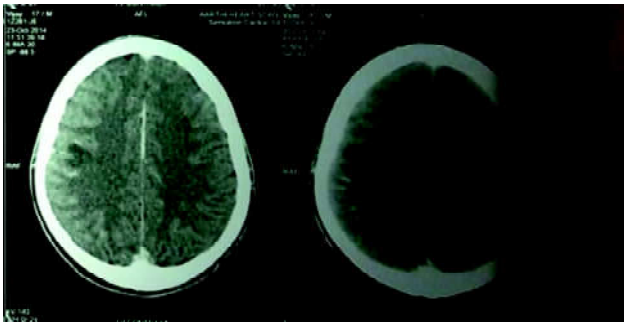

Fig. 1: *Focal hypodensity (oedema) in the right parietal region in post-central gyrus causing mass effect in the form of sulcal effacement with leptomeningeal enhancement.*

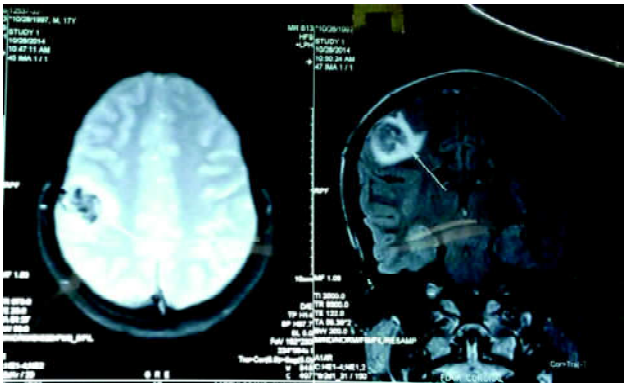

Fig. 2: *T2/flair hyper intensity noted in right parietal region which shows blooming gradient suggestive of haemorrhage.*

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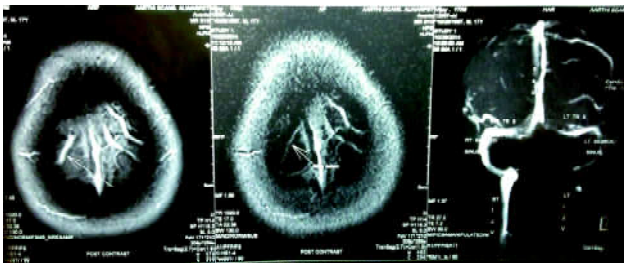

Fig. 3: *Contrast-enhanced MR venogram shows filling defect in the superficial cortical vein (vein of Tolard).*

The patient was initially stabilised with antiepileptic drug, mannitol, and other supportive management. Later on, after the imaging studies, patient was put on low molecular weight heparin and then warfarin. Patient was discharged on oral anticoagulant with proper counselling regarding disease nature, periodic monitoring and treatment details and advised for regular follow-up and screening of the family members for coagulopathy. But due to economic constrains, screening of the other family members had not been done. The patient did not have further symptoms until recent follow-up.

Disscusion

Cerebral venous thrombosis (CVT) is an uncommon, serious disorder due to thrombosis of cortical veins and draining venous sinus. Clinical manifestations can include headache, papilloedema, visual loss, focal or generalised seizures, focal neurologic deficits, confusion, altered consciousness, and coma[1]. Cerebral venous thrombosis is more common in women than men (female to male ratio 3:1). The estimated annual incidence is 3 to 4 cases per million, with 75 per cent of cases occuring in women[2]. This imbalance may be due to the increased risk of CVT associated with pregnancy and puerperium and with oral contraceptives. The incidence of cerebral venous thrombosis in children is at least 0.67 per 1,00,000 children per year[3].

Cause of cortical vein thrombosis including genetic (e.g., protein C, protein S deficiency, anti thrombin, and factor V Leiden mutation deficiency) and acquired disorders (e.g., dehydration, infection, malignancy, drugs, heart disease, head injury, anti-phospholipid syndrome, nephrotic syndrome, and acute gastroenteritis). Prothrombotic conditions are either genetic or acquired[4].

Pathogenesis: The pathogenesis of CVT remains incompletely understood because of the high variability in the anatomy of the venous system . Thrombosis of cerebral veins or dural sinus leads to cerebral parenchymal lesions or dysfunction and occlusion of dural sinus, resulting in decreased cerebrospinal fluid (CSF) absorption, and elevated intracranial pressure. Obstruction of the venous structures results in increased venous pressure, decreased capillary perfusion pressure, and increased cerebral blood volume. Dilatation of cerebral veins and recruitment of collateral pathways play an important role in CVT.

Protein S deficiency is a rare cause of CVT. Protein S - a vitamin K-dependent glycoprotein, is a co-factor of the protein C system. It is synthesised by both hepatocytes and megakaryocytes and circulates in two forms: 40 to 50 per cent as the free form and the remainder bound to the complement component; only the free form has activated protein C co-factor activity. Protein S deficiency may be genetic or acquired[5].

Genetics of protein S deficiency: Two homologous genes for PS map to chromosome 3. PROS1 (active gene) and PROS2. It is inherited predominantly as an autosomal dominant trait and heterozygous individuals in these families frequently had recurrent thromboembolism. Severe thrombotic complications, including neonatal purpura fulminans, occur in the rare newborn with very low protein S levels, which is occasionally due to homozygous deficiency.

Three phenotypes of PS deficiency have been defined on the basis of total PS concentrations, free PS concentrations, and activated protein C co-factor activity.

Type I: The classic type of protein S deficiency is associated with approximately 50 per cent of the normal total S antigen level, and more marked reductions in free protein S antigen and protein S functional activity (i.e., a quantitative defect).

Type II: Type II protein S deficiency is characterised by normal total and free protein S levels, but diminished protein S functional activity (i.e., a qualitative defect).

Type III: Type III deficiency is characterised by total protein S antigen measurements in the normal range and selectively reduced levels of free protein S and protein S functional activity to less than approximately 40 per cent of normal.

In a patient, phenotypes are described as quantitative (types I or III) or qualitative (type II).

Acquired protein S deficiency: Acquired protein S deficiency occurs during pregnancy and is associated with use of oral contraceptives. Protein S levels may be low in some disorders like disseminated intravascular coagulation and acute thromboembolic disease, HIV infection, nephrotic syndrome[6].

Clinical manifestation

The clinical presentation of patients with heterozygous protein S deficiency are deep venous thrombosis, superficial thrombophlebitis, arterial thrombosis or pulmonary embolism. The mean age is 25 years with the range being 15 to 60 year.

Diagnosis

Levels of total or free PS antigen < 60 to 65 International units/dl are considered to be in the deficient range. Erroneous diagnoses can be made due to the influence of acute thrombosis, co-morbid illness, during pregnancy, and in association with the use of oral contraceptives.

Treatment

The main goals is achieved anticoagulation, using either low molecular weight heparin (LMWH) or heparin followed by oral anticoagulant. Whenever available, endovascular thrombolysis is another option, but its use is typically restricted to patients with a poor prognosis who have not responded to anticoagulation. Antiplatelet drugs may be used as alternatives when anticoagulants are contraindicated.

In a case of life-threatening first thrombotic event or unusual CVT (cerebral and mesenteric vein) most experts recommend lifelong warfarin.

Conclusion

Protien S deficiency is a rare cause of cortical vein thrombosis. Hereditary protein S deficiency is an autosomal dominant trait. Isolated cortical vein thrombosis involving vein of Trolard without involving the deep venous system is an unusual presention of CVT. This case is to highlight one of the unusual presentations of CVT with a rare genetic cause.

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