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RESEARCH ARTICLE

HETEROZYGOUS PROTEIN-C DEFICIENCY PRESENTING AS STROKE DUE TO CEREBRAL VENOUS SINUS THROMBOSIS: A CASE REPORT

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ABSTRACT

Plasma protein-C is a natural anticoagulant in our body & has inhibitory effects on factors V and VIII. Hereditary protein C deficiency is transmitted as an autosomal dominant disorder. In Homozygous individuals it usually manifests as purpura fulminans in newborns whereas heterozygous protein C-deficient individuals are at increased risk for venous thrombosis. We are presenting a case of young male patient with heterozygous protein-C deficiency who experienced right sided hemiparesis due to cranial venous sinuses thrombosis without underlying major risk factors. Cerebrovascular accidents in young without underlying major risk factors should be evaluated for thrombophilia including protein C deficiency.

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INTRODUCTION

A deficiency of protein C disturbs the balance between procoagulant and anticoagulant proteins and engenders a prothrombotic state. Cardinal manifestation of protein-C deficiency is venous thromboembolism. However, there are several case reports of arterial stroke (Kohler, 1990 and Camerlingo, 1991) and myocardial infarction occurring in young adults with congenital protein-C deficiency. Cerebral (dural) venous sinus thrombosis is an uncommon condition, but its clinical presentation is varied and often dramatic & usually includes headache, lethargy, motor or sensory deficits, seizures, neck stiffness & sometimes seizures. It often affects young- to-middle-aged patients, and more commonly women specially in post partum period. Although recognized for more than 100 years (Bousser, 1999), it is being diagnosed in recent years frequently due to greater awareness among treating physicians and neurologists regarding the hereditary thrombophilia, and partly to improved imaging techniques. The superior sagittal and lateral sinuses are commonly (70%) individually involved by thrombosis. In 30%, both are affected, in addition to cortical and cerebellar veins (Ameri, 1992). More common conditions include hereditary thrombophilia, pregnancy & purperium, post operative state, use of oral contraceptives, intracranial & local infections. The literature in recent decades on intracranial venous thrombosis appears to be increasing toward cases in which prothrombotic states are causal, rather cases related to infections.

CASE REPORT

25 year old male presented with sudden onset of right half body weakness since 2 days, altered sensoreium & generalised tonic clonic abnormal body movements since 1 day. There was no preceding history of fever or headache. No history of similar episode previously. The patient had been healthy until this event, and there were no obvious precipitants of thrombosis (i.e., no trauma, intoxication, or dehydration). The patient had neither hypertension nor diabetes. On admission his vitals were: BP 126/84 mmHg, PR 82/min regular, Respiratory rate 18/min, temperature 98.6*F. General physical examination was nomal. Cardiovascular examination did not reveal any abnormality. Neurologically, patient was drowsy & not fully oriented. Cranial nerve examination was not possible because of his altered mental status. Power in both right upper & lower limb was <3/5 as he was unable to maintain posture of limb against gravity. Plantars were extensors on right side & flexors on left side. Deep tendon reflexes were exaggerated on right & normal on left side. Investigations showed normal haemogram, renal & liver function test, lipid profile & serum electrolytes. Chest X Ray, USG abdomen 2D echocardiography were normal. NCCT Head revealed petechial haemorrhagic bleed measuring 17×18×10 mm in left frontoparietal deep white matter. Bilateral carotid arteries on colour doppler showed normal intimal thickness with normal wave flow pattern.MRI Brain showed a lesion in left frontoparietal region which is hypointense on T1W, hyperintense on T2W & FLAIR showing blooming on FFE. Few areas showing restriction on DW- ? Haemorrhagic Infarct

with midline shift of 12 mm.MR Venography showed left transverse sinus & left sigmoid sinus thrombosis (Figure1,2).

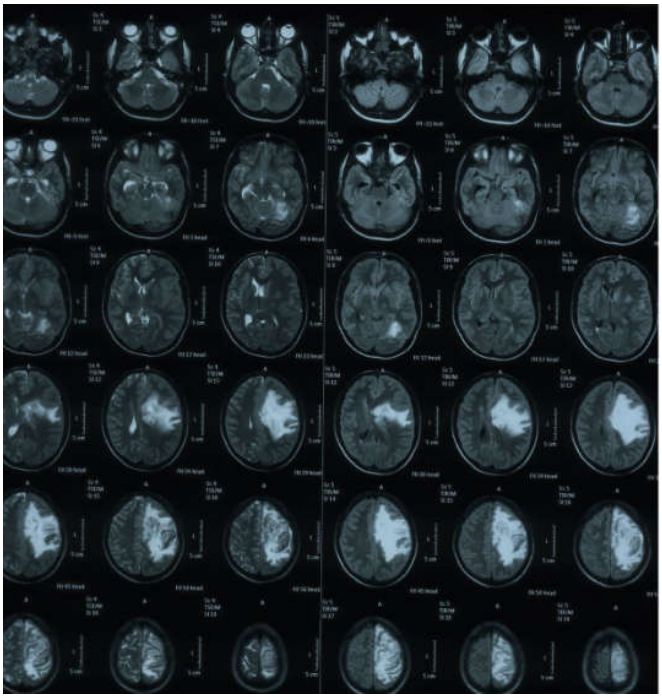

Figure 1.

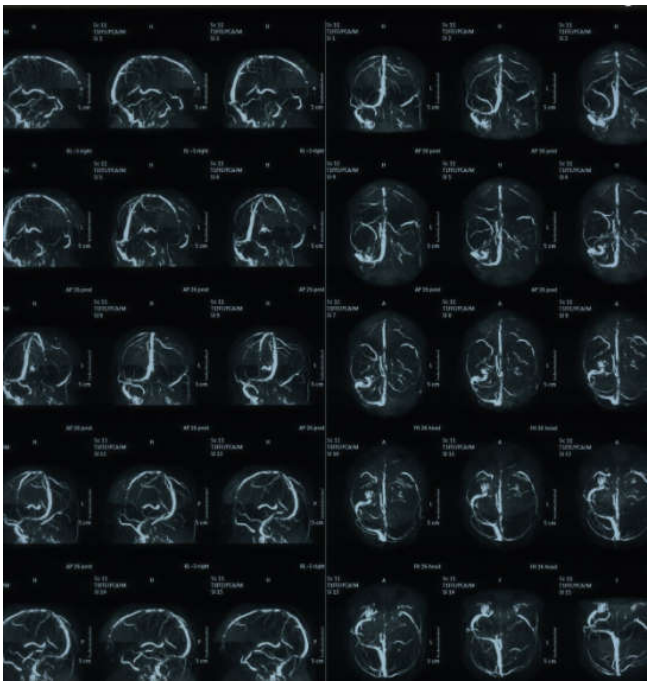

Figure 2.

MR Venography & MRI brain film of patient showing thrombosis of left transverse & sigmoid sinus with hemorrhagic infract

Patient was evaluated for hereditary thrombophilia after about 6 months later the event & after discontinuing the anticoagulation for 2 weaks (Gustavo Saposnik, 2011).

Test	Patient value	Reference range
Protein-C activity	2.4%	60-120%
Protein-S activity	62.4.0%	60-120%
Anti Thrombin III activity	121%	70-150%
Factor V leiden mutation	Not Detected	
Homocystiene	7.12 µmol/L	3.7 -13.9 µmol/L

Protein C Ag level was not assessed (not available in institute). His repeat Protein C activity after 1 month of previous study showed activity 5.4%. which revealed persistently low Protein C activity. The antiphosholipid antibodies profile was normal. The family history was positive for thromboembolic disease; that is, the patient's paternal grandmother had died of stroke at age 54 years & his father had history of deep vein thrombosis in left lower limb at age 46 years. Protein C activity was measured in plasma samples from his family members. The patient's mother and two of his siblings had normal protein C activity, whereas his one sister (29.3%) & his father (34.2%) showed protein C deficiency; the pattern suggestive of auosomal heterozygous transmision in family. Initially he was treated with low molecular weight heparin 60 mg subcutaneous BD for 5 days & later on switched on to acitrom 3 mg OD. Patient was also treated initially with anti epileptics & Injection mannitol to decrease the raised intracranial pressure. Patient improved on follow up & now able to walk & do other daily routine works normally.

DISCUSSION

Cerebrovascular events in young and middle-aged persons should be evaluated properly since numerous disorders may lead to a stroke. In some cases, the cause remains unclear (Bogousslavsky, 1987; Hart, 1983 and Grindal, 1978). In the general population Protein-C deficiency by plasma level alone is found in 1 in 200 to 1 in 500 persons (Tait, 1995 and Miletich, 1987). However, many affected individuals remain asymptomatic throughout life. The usual clinical manifestation of heterozygous protein C deficiency is venous thromboembolism (Martinelli, 1998 and Koster, 1995). Protein C deficiency has been known for some time to be a major risk factor for venous thrombosis. Its prevalence seems to be 6-8% in patients <40 years old with a history of venous thrombosis (Kohler, 1990). Thrombosis of the cerebral veins, however, seems to be rare in heterozygous patients (Pabinger, 1986). There have been a few reports on cerebral hemorrhagic infarction caused by sinus thrombosis in homozygous protein C-deficient infants (Tarras, 1988).

In our patient, thrombosis of left transverse sinus & sigmoid sinus led to hemorrhagic infarction in left frontoparietal region with the clinical symptoms of right hemiparesis. It could be argued that sinus thrombosis by itself could lower the protein C concentration by way of increased consumption and that our patient was falsely assumed to have an inherited protein C deficiency. However, this hypothesis would not explain his consistently low protein C activity after the event. Moreover, protein C concentrations do not differ significantly between patients suffering from acute stroke and healthy controls (D'Angelo, 1988).

Conclusion

A patient with right hemiparesis due to cranial venous sinus thrombosis is reported. There was strong family history of thromboembolic events. Young ischemic stroke in Indian population are usually secondary to other causes like cardioembolic (RHD, IE), OCP induced etc. Hereditary thrombophilias are not as common as in western countries. So in Indian scenario also awareness regarding inherited hypercogulable states is required to prevent long term complications of these events specially with strong family history & young unprovoked thrombotic events.

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