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CASE REPORTS

PROTEIN C DEFICIENCY PRESENTING AS CEREBRAL VENOUS SINUS THROMBOSIS. A CASE REPORT

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INTRODUCTION

Congenital protein C deficiency carries a high risk of venous[1] and rarely arterial[2] thrombosis and usually manifests as recurrent deep vein thrombosis or pulmonary embolism in young people. We describe a case of protein C deficiency who suffered from thrombosis of multiple blood vessels in the body.

CASE REPORT

A 47 year old male presented with history of sudden onset of severe pain right side of the chest and abdomen. There was no history of cough or sputum production. Clinical examination was unremarkable. He had tachypnoea and tachycardia. His ECG showed non-specific T wave changes and cardiac enzymes were raised. On the basis of initial assessment myocarditis was suspected. His 2D echo revealed normal size cardiac chambers and good left ventricular function. Ultrasonography of abdomen showed a hyperechoic area in the caudate lobe of the liver. A contrast enhanced CT scan of abdomen was performed which revealed thrombosis in the hepatic vein, portal vein and inferior vena cava, enlarged caudate lobe of the liver, pulmonary infarct of the lateral basal segment of the right lower lobe and mild splenomegaly. Thrombophilia screening of the patient was performed that showed a low normalized ratio of ProC global (0.71, reference rane > 0.80) using ProC Global kit, Dade Behring, Germany. There was decreased protein C activity of 43% (reference rane 65-140%) and it was confirmed with a repeat test. Based on this patient was diagnosed with IVC thrombosis resulting from protein C deficiency.

Patient remained asymptomatic for a period of 8 years while on warfarin. He again presented with sudden onset of headache, numbness and weakness of left half of the body and slurring of speech. He also gave history of not using warfarin for the last 06 months. Neurological examination showed a power of 4/5 in both left upper and lower limbs, reflexes and sensations were intact and plantars were bilaterally downgoing. An urgent CT scan brain with out contrast was performed that showed thrombosis of the posteroinferior part of the superior saggital sinus, torcular heterphili and straight sinus (Fig-1). MRI and MRV brain showed filling defects in postero-inferior part of superior saggital sinus, right transverse, right

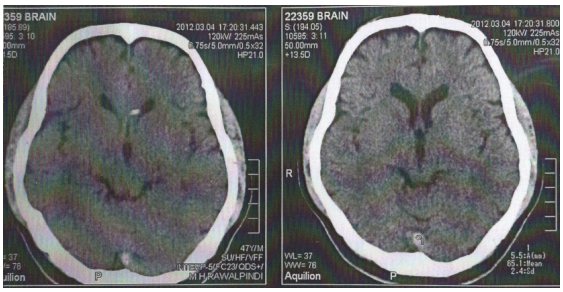

Figure-1: A hyperechoic area involving the posteroinferior part of the superior saggital sinus.

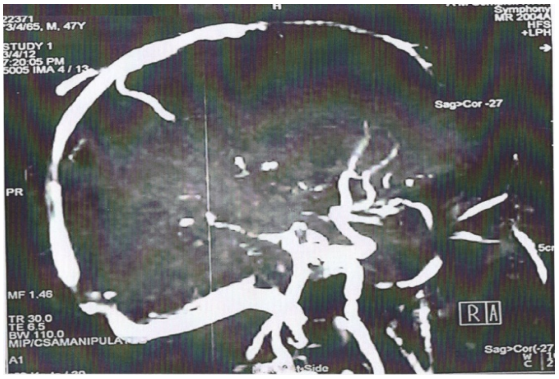

Figure-2: Filling defects are noted in the posteroinferior part of superior sinus, right sigmoid sinus, straight sinus and torcular heterophili.

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sigmoid sinus, straight sinus and torcular heterophili. Flow signal of inferior saggital sinus and deep cerebral vein was also not visualized (Fig-2). A diagnosis of dural sinus and cerebral vein thrombosis resulting from protein C deficiency was made. The patient was managed conservatively with inj ceftriaxone and enoxaparin 1 mg/kg s/c 12 hourly. He improved over next few days with improvement in power. Lately patient has developed papilledema and persistent headache which is gradually resolving. He is on oral warfarin and aspirin with a target international normalized ratio (INR) between 2 to 3. His two brothers are suffering from same condition and are on anticoagulants.

DISCUSSION

The prevalence of protein C deficiency in caucasion population is 0.2 %[3]. Protein C and S are the major regulatory proteins of the hemostasis. These are vitamin K dependent proenzymes synthesized in liver. Thrombin-thrombomodulin complex on the surface of endothelial cells is the site for interaction of proteins C and S. Protein C becomes activated after binding to these complexes. Protein S acts as a cofactor in this process. Activated protein C inhibits factor VIIIa and factor Va thus exhibiting its anticoagulant property and also enhances fibrinolysis through the inhibition of plasminogen activator inhibitor. There are two main types of mutations that lead to protein C deficiency; Type 1 is quantitative defect of protein C (low production or short protein half life) and type 2 is a qualitative defect in which interaction with other molecules is abnormal. The majority of people with protein C deficiency lack only one of the functioning genes, and are therefore heterozygous. Before 1999, only sixteen cases of homozygous protein C deficiency had been described (two abnormal copies of the gene, leading to absence of functioning protein C in the bloodstream).

Patients with Protein C deficiency are at increased risk of venous thromboembolism, rarely arterial thrombosis, childhood purpura fulminans and childhood stroke. Acquired causes of protein C deficiency are seen in liver disease, disseminated intravascular coagulation (DIC), therapy with L-asparginase and coumarin and acute severe bacterial infections[4]. Before labeling a patient with inherited protein C deficiency, it is mandatory to rule out acquired causes of the deficiency such as liver disease, vitamin K deficiency, renal insufficiency, disseminated intravascular coagulation and postoperative states. Thus it is essential to repeat an assay after 4-6 weeks to confirm the deficiency.

The management of these patients is with heparin anticoagulation, either un-fractionated or low molecular weight heparin along with protein C concentrate or fresh frozen plasma followed by oral anticoagulation. Life threatening progressive disease warrants use of protein C concentrates available for i/v usage. Cryoprecipitates also contain protein C but cannot be used in this condition because of their pro-coagulant potential. During the initial coumarin treatment period high dose heparin administration must be sustained, because protein C concentration falls dramatically with warfarin intake due to short half life of protein C (6 hours)[5]. Lifelong anticoagulation with warfarin is recommended in young patients of protein C deficiency who present with cerebral sinovenous thrombosis. Liver transplantation may be considered curative for homozygous protein C deficiency[6].

Conflict of Interest

This study has no conflict of interest to declare by any author.

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