Bangladesh Journal of Neuroscience 2012; Vol. 28 (1) : 59-62

CASE REPORTS

Protein S Deficiency: Ischemic Stroke in Young adult – A Case Report

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Abstract:

Stroke is the third most common cause of mortality in Westernised countries and

Accounts for 12% of all deaths in the UK. The economic cost of stroke is enormous. Twelve per cent of first strokes occur in patients under 45 years of age, of which approximately 50% are ischaemic in nature. Stroke in young adult poses a major health problem. The causes of ischaemic stroke in young adults are many and diverse.Such patients usually require more extensive investigations in order to find an underlying cause than more elderly patients. Principal causes are cardioembolism, premature atherosclerosis, haematological and immunological disorders and migraine. Thrombophilic factors have been implicated in 4-8% of the young adult strokes worldwide. Protein S deficiency is a rare cause of ischemic stroke in young population. Only a few sporadic cases have been described in the literature. We are reporting a case of protein S deficiency-related ischemic stroke in a 40-year-old man. Early diagnosis and targeted approach can help such patients to prevent recurrent thrombotic episodes.

Keywords: *Protein S deficiency, Ischemic stroke, young adult stroke*

Introduction:

Protein S is a vitamin K-dependent plasma protein that potentiates the inactivation of factors Va and Vllla by protein C[1]. Hereditary deficiency of free protein S (FPS), the active form, results in a prothrombotic state and has been associated with both recurrent venous thrombosis[2-4] and arterial thrombosis.[5,6] The overall estimated incidence of deep vein thrombosisis is one episode for every 1,000 persons. Protein S deficiency has been also found to be associated with cerebrovascular occlusion, although the exact role is controversial. More recently, FPS deficiency has gained recognition as a possible risk factor for ischemic stroke. Case reports[7-10] have suggested that familial FPS deficiency may play a causative role in young patients with cryptogenic stroke. Acquired FPS deficiency has been reported as a possible cause of cerebral infarction in patients with nephrotic syndrome[11] and inflammatorybowel disease.

Case Report

A 40-year-old smoker, normotensive, nondiabetic, right handed person, presented to our hospital 1 month back with history of sudden onset weakness of right half of the body & deviation of angle of mouth towards left side for last 12 hrs .He also had speech difficulties in the form of difficulty in naming objects with emotional lablity at that time. His condition was initially detetriorating for first few hours then became static. He had no history of trauma, headache, vomiting blurring of vision, or any history of fever prior to onset of this illness. No similar episode occurred before. Family history was negative for vascular events or other predisposing factors for stroke.

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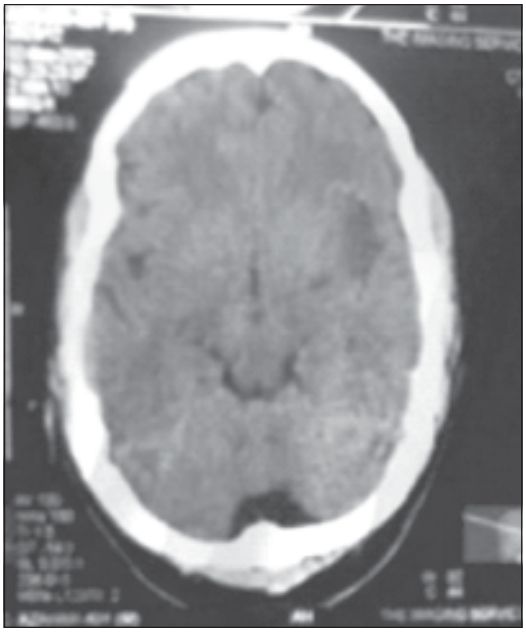

Fig.1: *Illdefined hypodense areas are seen in left fronto-parietal regions suggestive of acute cerebr.*

Discussion

Stroke in young adult population has a high incidence of approximately 24–35%, according to some studies in India. Abraham *et al*[12]. from Vellore reported an incidence of 25% in population less than 40 years of age. Munts *et al*[13] reported that idiopathic coagulation disorders were found in about a quarter of young stroke patients, although the clear-cut data has been lacking from India. Carod-A *et al*[14] studied about ischemic stroke subtypes and prevalence of thrombophilia in Brazilian stroke patients. They examined 130 consecutive young and 200 elderly patients. Prevalence of thrombophilia was, respectively: protein S deficiency (11.5% versus 5.5%), protein C deficiency (0.76% versus 1%). They concluded that prothrombotic conditions were more frequent in stroke of undetermined causes.

The importance of thrombophilic disorders in arterial stroke has been debatable. Ischemic stroke has been reported as a rare manifestation of protein S deficiency. Girolami *et al*.[15] and Sie *et al*.[16] were among the first who reported the association of familial deficiency of protein S as a cause of ischemic stroke in young. Wiesel *et al*.[17] studied 105 patients with protein S deficiency, out of which 14 had arterial thrombotic accidents involving the central nervous system or the myocardium, while most studies revealed a weaker association between the two.[18] Douay *et al*.[19] reported that hereditary deficiencies of coagulation inhibitors are rare in ischemic stroke patients under 45 years and their systematic detection seems to be of poor interest. Mayer *et al*.[20] also supported the fact that acquired deficiency of free protein S is not a major risk factor for ischemic stroke.

In this 40-year-old patient without any risk factors, the acquired factor S deficiency possibly played a role in the ischemic stroke. Factor S deficiency should be considered in venous stroke, recurrent pulmonary embolism, unusual site of venous occlusion, family history of vascular events, and stroke in young population. Aetiology of such vascular events in young must be thoroughly investigated so as to guide prevention and treatment of this devastating disease. Measurement of total and free protein S levels should be a part of the evaluation for any young adult who has had a stroke.

Clinical examination revealed a young confused man. Pulse rate was 84/min,Blood pressure 130/80 mm Hg and respiratory rate was18/min.His GCS was 13, with nominal aphasia. Cranial nerve examination revealed right sided upper motor type facial nerve palsy.Motor findings consistent with right-sided hemiplegia having muscle power 0/5 on the right side, but 5/5 on the left side,deep tendon reflexes were brisk in the right side but normal in the left side, plantars were extensor in the right side with flexor in the left side.Cerebellar & sensory function could not be performed.

CT head [Figure 1] revealed ill-defined hypodense areas are seen in left fronto-parietal regions suggestive of acute cerebral infarct (left).Routine hematological investigations, haemoglobin level was 16.2 g/dl,total leucocyte count was 13000/cumm with normal differentials.Platelet count was 200 000/cumm. Serum electrolytes & serum creatinine report was normal.ECG & Chest x-ray did not reveal any abnormality. The patient was negative for HIV, syphilis and hepatitis B serology. Other factors were tested included FBS, lipid profile, coagulation

profile, echocardiography including both transthoracic & transesophageal, and duplex scanning of neck vessels were unremarkable. Vasculitis profile was negative.

Workup for thrombophilias revealed reduced protein S function (18% of normal) alongwith protein C; , antithrombin III, anticardiolipin antibodies, and lupus anticoagulant, homocysteine were within normal limits. A diagnosis of protein S deficiency was kept and the patient was managed with low molecular weight heparin followed by oral anticoagulants. Neurological functions improved, muscle power became 4/5,completely recovered from nominal aphasia and patient was discharged two weeks after initiation of treatment.He was advised to take oral anticoagulants & for regular follow up at stroke clinic with INR after 1 week & planned for repeat protein S after after 3 months.

Conclusion:

Stroke is one of the foremost causes of morbidity,mortality & a socioeconomic challenge, more so in Bangladesh where health system including the rehabilitation is not the reach of oridinary people. It is crystal clear that, this devastating condition affecting the young adult group, not only affects the patient but also their family , as well as the economy of whole nation. Protein S deficiency is rare cause of ischemic stroke. Patient with protein S dficiency has got tendency to reccurent thrombotic events. So, early diagnosis & targeted approach can save life & prevent further events.

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