Case Report

Ischemic stroke of undetermined etiology in a 14 year old girl

Shoeb Khan[1], Abdul Rafe Abdul Qadeer[2*]

[1]Ex-Resident, [2]Assistant Professor, Department of Surgery, Government Medical College, Aurangabad, Maharashtra, INDIA.
Email: trumanin1@gmail.com

Abstract

Ischemic stroke is the most common cerebrovascular disease, most often due to atherothrombotic diseases and uncommonly by disorders of hypercoagulation. Disorders of coagulation and associated thrombotic disorders account for approximately 1% of all ischemic strokes and 4-8% of strokes among younger people. Similarly combined deficiency of protein C and S along with increased levels of homocystine and factor 5 mutation can lead to hypercoagulable state and rarely present as cerebrovascular accident. Stroke is not common in the young patients but when it occurs due to rare causes of hypercoaguable states warrants for different approach for investigation and management. Here we describe a case report of stroke in a 14 year old girl. It is emphasised that Protein C deficiency though rarely associated with thrombotic events but when dealing with a case of cerebral infarction (arterial thrombosis) in young patient, screening for Protein C and S should be made, especially when patients are below 45 years, have a personal history of recurrent thrombosis without precipitating factors, thrombosis in unusual sites, thrombosis during pregnancy, a positive family history of thrombosis.

Keywords: Stroke, ProteinC, Protein S

[*]**Address for Correspondence:**
Dr. Abdul Rafe Abdul Qadeer, Assistant Professor, Department of Surgery, Government Medical College, Aurangabad, Maharashtra, INDIA.
Email: trumanin1@gmail.com
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INTRODUCTION

WHO defines stroke as an event caused by the interruption of the blood supply to the brain, usually because a blood vessel bursts or is blocked by a clot. This cuts off the supply of oxygen and nutrients, causing damage to the brain tissue[1]. Globally, stroke is the third commonest cause of mortality [2] and the fourth leading cause of disease burden[3]. Ischemic stroke is the most common cerebrovascular disease, most often due to atherothrombotic diseases and uncommonly by disorders of hypercoagulation. Disorders of coagulation and associated thrombotic disorders account for approximately 1% of all ischemic strokes and 4-8% of strokes among younger people. Similarly combined deficiency of protein C and S along with increased levels of homocystine and factor 5 mutation can lead to hypercoagulable state and rarely present as cerebrovascular accident. Stroke is not common in the young patients but when it occurs due to rare causes of hypercoaguable states warrants for different approach for investigation and management. Stroke in young individual poses a major problem as these young family members are the major income earner of the family. Abraham *et al*[4] from Vellore, South India reported that 25% cases of the stroke were less than 40 years of age. Other Indian studies have highlighted a high incidence 24-35% of stroke in young population[5]. Atherothrombotic diseases are most common cause for ischemic stroke, however disorder of coagulation although uncommon but can lead to hypercoagulability resulting in ischemic stroke.

CASE REPORT

A 14 year old girl presented with sudden onset of left side weakness since morning. On general examination patient was drowsy and irritable, Pulse=88/min, BP=110/70, Afebrile, Pupils equal and reactive to light, No pallor, cyanosis, icterus.

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Neurologic examination revealed

Left hemi paresis, Bilateral plantar reflexes, Power of the muscles on left side was 3/5 in both upper and lower extremities. Patient had history of fall in the morning followed by the above symptoms. There were no known precipitating factors such as obesity, diabetes, hypertension, valvular heart disease, bleeding tendencies. Family history was negative for vascular events or other predisposing factors for stroke. Patient's parents had died in an accident. Other systemic examination was within normal limit. Routine investigation revealed haemoglobin value of 13gm/dl, leucocyte count 12000/dL, platelet count 1.52 lakh/mm3 with haematocrit of 39%, ESR 28 mm, prothrombin time 13 seconds (control 12 second), INR 1.1 and activated partial prothrombin time 22 seconds (control 20 seconds). Urine analysis, chest X-ray and fund us examination were unremarkable. Renal and liver function tests were within normal range. Transthoracic and transesophageal echocardiography did not reveal any abnormality. Laboratory findings including antinuclear factor, antiphospholipid antibodies and VDRL titre were normal. Factor V Leiden mutation was not detected. Protein C level was 55 units/ml (normal 67-195 units/ml), protein S level was 30 units/ml (normal 55-123 units/ml) and antithrombin III level was 93 units/ml (normal 70-122 units/ml) with normal serum homocystiene level and lipid profile and ANA levels.

Figure 1

Figure 2

Figure 3

Figure 4

Differential diagnosis of ischemic stroke in young age includes antiphospholipid antibodies, hyperhomocysteinemia and high plasma levels of fibrinogen, hypofibrinolysis and resistance to activated protein C. We started patient on anti-platelet therapy with Aspirin, clopidogrel and physiotherapy was also started. Patient was discharged from hospital after 2 weeks in good condition with follow up within 2 months.

DISCUSSION

Stroke means different pathological processes, all of them having as an end point the focal cerebral ischemia. 85% of the strokes are ischemic and 15% hemorrhagic. The importance of thrombophilic disorders in arterial stroke has been debatable. Even among the patients with ischemic stroke, a number of pathologically different processes are responsible as cardioembolism, large artery disease with arteriolosclerosis and thromboembolism, and small artery disease. Protein C is a vitamin K- dependent plasma protein that acts first as an anticoagulant by proteolytically degrading the activated factor V and inactivating factor VIII and secondly facilitates thrombolysis by its fibrinolytic activity. Protein S serves as a cofactor for protein C in its anticoagulant properties[6]. The relevance of deficiencies of these naturally occurring anticoagulants for venous thrombosis or pulmonary embolism is widely accepted. The prevalence of protein C, S and antithrombin III in ischemic stroke varies up to 23% in different studies[7]. Protein C deficiency has occasionally been associated with arterial ischemic stroke[8]. In a meta-analysis published in 2003, reports of cases and studies regarding the deficiencies of proteins C,

S, antithrombin, and factor V Leiden in ischemic strokes were mentioned. Protein C deficiency was found in only one of the 329 patients aged between 15 and 45 years. The conclusion of the meta-analysis was that it appears that protein C deficiency is weakly associated with the arterial stroke[9]. Protein S deficiency has been associated with cerebral arterial ischemia more often than protein C deficiency. Studies from Indian scenario and other countries shows conflicting reports limit the reliability of this association. Girolami *et al*.[10] and Sie *et al*.[11] were among the first who reported the association of familial deficiency of protein S as a cause of ischemic stroke in young. Mayer *et al*.[12] also supported the fact that acquired deficiency of free protein S is not a major risk factor for ischemic stroke. Douay *et al*.[13] 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. Wiesel *et al*.[14] 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 these two[12]. A Swedish study of 107 patients aged between 18 and 44 years found only one with protein S deficiency, this meta-analysis describes case-reports and studies published until 2003 regarding this subject: they reported a frequency of this deficiency of 13.8% (5/36), 19% (8/35), 23% (19/98) in patients aged less than 45 years and 6% (4/66) in patients aged less than 60 years[9]. In this last study, all protein S deficiency patients had elevated anticardiolipin antibodies. This study suggests an association between antiphospholipid syndrome and protein S deficiency in ischemic stroke patients. Antithrombin deficiency has only rarely been associated with stroke. Different studies show frequencies of 5% (3/66), 8% (5/60), but there were studies that reported just one case, thus, the evidence linking antithrombin deficiency with arterial stroke is weak[9]. The factor V Leiden mutation, the cause of activated protein C resistance (in 90% of cases) is the most common inherited coagulopathy associated with stroke. A study performed in Turkey and published in 2005, on 29 children with ischemic stroke and 20 with intracerebralhemorrhage, all of whom were compared with 20 controls. The authors found no evidence of an association between factor V Leiden mutation and ischemic stroke or intracerebralhemorrhage. The conclusion was that factor V Leiden mutation did not seem to be associated with a risk of cerebrovascular disease[15]. The risk of a stroke is high for person with factor V Leiden combined with other vascular risk factors, such as smoking and contraceptive use. A study investigated the prevalence of these mutations in 468 patients with an acute stroke or transient ischemic attack (TIA) before the age of 60 and in a healthy control population individually matched for age and gender. A significant interaction between the factor V Leiden, smoking, and risk of stroke in women was found: female smokers without the factor V Leiden had a somewhat increased risk of stroke of 2.6 (95% CI, 1.5 to 4.6; P=0.001) compared with nonsmoking non-carriers of the factor V Leiden. No such interaction was observed in men[16].

CONCLUSION

It is thus emphasised that Protein C deficiency though rarely associated with thrombotic events but when dealing with a case of cerebral infarction (arterial thrombosis) in young patient, screening for Protein C and S should be made, especially when patients are below 45 years, have a personal history of recurrent thrombosis without precipitating factors, thrombosis in unusual sites, thrombosis during pregnancy, a positive family history of thrombosis.

REFERENCES

1. WHO. Stroke, Cerebrovascular accident. August 2010, http://www.who.int/topics/cerebrovascular_accident/en/. Accessed on 14 Nov 2012.
2. Warlow C, Sudlow C, Dennis M, Wardlaw J, Sandercock P. Stroke. Lancet. 2003; 362:1211–1224.
3. Strong K, Mathers C, Bonita R. Preventing stroke: saving lives around the world. Lancet Neurology. 2007; 6:182–187.
4. Abraham J, Rao PS, Inbaraj SG, Shetty G, Jose CJ. An epidemiological study of hemiplegia due to stroke in South India. Stroke 1970; 1:477-481.
5. Bansal BC, Prakash C, Jain AL, Brajimanandan KRV. Cerebrovascular disease in young individuals below the age of 40 years. Neurol India. 1973; 21:1-18.
6. Clouse LH, Comp PC. The regulation of hemostasis: The protein C system. N Engl J Med. 1986; 314:1298-1304.
7. Bushnell CD, Goldstein LB. Diagnostic testing for coagulopathies in patients with ischemic stroke. Stroke. 2000; 31:3067–3078.
8. Hirsh J, Colman RW, Marder VJ, Clowes A, George JN. Overview of thrombosis and its treatment. In: Colman RW, Hirsh J, Marder VJ, Clowes A, George JN (editors): Hemostasis and Thrombosis. Basic Principles and Clinical Practice. 4th edition. Philadelphia: Lippincott Williams and Wilkins; 2001, pp. 1071–1084.
9. Moster M. Coagulopathies and arterial stroke. Journal of Neuro–Ophthalmology. 2003; 23(1):63–71.
10. Girolami A, Simioni P, Lazzaro AR, Cordiano I. Severe arterial thrombosis in a patient with protein S cerebral deficiency (moderately reduced total and markedly reduced free proteinS): A family study. ThrombHaemost. 1989; 61:144-147.
11. Sie P, Boneu B, Bierme R, Wiesel ML, Grunebaum L, Cazenave JP. Arterial thrombosis and protein S deficiency. ThrombHaemost 1989; 62:1040.

12. Mayer SA, Sacco RL, Hurlet-Jensen A, Shi T, Mohr JP. Free protein S deficiency in acute ischemic stroke. A case-control study. Stroke. 1993; 24:224-227.
13. Dovay X, Lucas C, Caron C Goudemand J, Leys D. Antithrombin, protein C and protein S in 127 consecutive young adults with ischemic stroke. ActaNeurol Scand. 1998; 98:124-127.
14. Wiesel ML, Borg JY, Grunebaum L, Vasse M, Levesque H, Bierme R, Sie P. Influence of protein S deficiency on the arterial thrombosis risk. Presse Med. 1991; 20:1023-1027.
15. Buyru N, Altinisik J, Somay G. Factor V Leiden Mutation in Cerebrovascular Disease. Clinical and Applied Thrombosis/Hemostasis. 2005; 11:339–342.
16. Lalouschek W, Schillinger M. Matched Case–Control Study on Factor V Leiden and the Prothrombin G20210A Mutation in Patients with Ischemic Stroke/Transient Ischemic Attack Up to the Age of 60 Years. Stroke. 2005; 36:1405–1410.

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