

# Protein S Deficiency - An Uncommon Cause with Common Presentation

Kora N<sup>1</sup>, Das R<sup>2</sup>, Som S<sup>3</sup>, Laha S<sup>4</sup>, Bannerji N<sup>5</sup>, Rana KS<sup>6</sup>

## Abstract

Stroke in child poses a major health problem. Thrombophilic factors have been implicated in 4-8% of young stroke worldwide. Protein S deficiency is a very rare cause of stroke. A few cases have been reported in literature. We are reporting a rare case of protein S deficiency causing stroke in a two year old child.

**Key words:** Stroke, Thrombophilic factors, Protein S deficiency

## Introduction

Stroke or cerebro-vascular accident poses a major health problem. Thrombophilic factors have been implicated in 4-8% of young stroke worldwide<sup>1</sup>. Protein S is a naturally occurring vitamin K dependant protein, which in conjunction with active protein C inhibits the clotting cascade. Protein S deficiency is known to be of clinical significance in patients with deep venous thrombosis or pulmonary emboli. The incidence of deep vein thrombosis is one episode for every 1000 persons. Protein S deficiency is found to be associated with cerebro-vascular occlusion, although exact role is controversial. Till now no case has been reported having protein S deficiency presenting as proptosis followed by hemiplegia. So we want it to bring into the notice of every clinician.

## The Case

Dipali Tudu, a two year old female child with body weight of 8 kgs was admitted in our institution with high grade fever for three days and unilateral proptosis of the right eye. She had history of development of furuncle over right side of nose two days before development of fever. There was no contact history of TB.

On examination, surface temperature was raised (103° F). Proptosis was noticed on right eye, pupil was normal in size, reacting normally to light, while left eye was normal on examination. Heart rate-110/min, Respiratory rate -28/min, Blood pressure of 90/60 mmHg. On auscultation the chest was clear. There were no associated abnormal neurological signs.

For Orbital cellulitis of right eye and high grade fever, the patient was put on intravenous antibiotics, antipyretics and other supportive management. On the second day of admission, patient

<sup>1</sup>Dr. Nabanita Kora, Senior Resident, MBBS, MD, <sup>2</sup>Dr. Rajib Das, RMO, MBBS, DCH, MD, <sup>3</sup>Dr. Sabyasachi Som, Associate Professor, MBBS, MD, <sup>4</sup>Dr. Sumanta Laha, Assistant professor, MBBS, MD, <sup>5</sup>Dr. Nayan Bannerji, MBBS, Post Graduate Student, <sup>6</sup>Dr. Kriti Sundar Rana, MBBS, Post Graduate Student. All from the Department of Paediatrics, Burdwan Medical College and Hospital, Burdwan, West Bengal, India.

## Address for correspondence:

Dr. Nabanita Kora

E-mail: nabanitacmc@gmail.com

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developed left sided complete hemiparesis with UMN type of facial nerve palsy (left).

Baseline investigations were done that revealed Hb-11.5 gm%, RBC-6.48million/cumm, WBC-17300/cumm (N79,L2,E0,M1,B0), Platelets-4.96 lakhs/cumm, ESR-75/120 mm fall in 1<sup>st</sup> hour, PCV-30.2%, MCV-58.6%, MCH-22.8pg, MCHC-35.5gm/dl, CRP-65mg/dl, Na-137meq/l, K-3.8meq/l.

Ophthalmological opinion confirmed orbital cellulitis. CT scan revealed increased hypodensity in right parieto-frontal region with obscured adjacent cortical sulci, maxillary antrum/ethmoid.

MRI and MR angiography showed vaso-occlusive disease by thrombus involving whole of right internal carotid artery. Screening of brain suggested cortical infarction at right frontal and basal ganglia region. Echocardiography (2D) revealed 10mm ostium secundum ASD with L-R shunt without any evidence of pulmonary hypertension.

IV antibiotics were continued and aspirin was started along with physiotherapy.

**Table 1:** Showing results for thrombophilias

Test	Results	Normal Values
Protein S function	30	50-140
Protein C	84	70-140
Antithrombin III	120	80-120
Factor V Leiden mutation	Not detected	-
MTHFR gene mutation	Not detected	-
Prothrombin gene mutation	Not detected	-
Anticardiolipin antibody	Normal	-
Lupus anticoagulant	Normal	-

Workup for thrombophilias revealed reduced protein S function 32(50-140), whereas protein C-84 (70-140) and Antithrombin III-120(80-120) level were within normal limit. Factor V Leiden mutation, MTHFR gene mutation and Prothrombin gene mutation were not detected. Anticardiolipin antibody and lupus anticoagulant were within normal limits.

During first two weeks of treatment, the patient gradually became afebrile and began to walk with support regaining lost power and was ultimately discharged after about three weeks when the patient was able to perform her normal daily activities and was asked to come for follow-up.

## Discussion

Stroke in young population has a high incidence of approximately 25-35%, according to some studies in India. Abraham et al<sup>2</sup> from Vellore reported an incidence of 25% in population less than 40 years of age. Munts et al<sup>3</sup> reported that idiopathic coagulation disorders were found in about a quarter of young stroke patients, though there was no clear cut data from India. Carod-A et al<sup>4</sup> 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 drew a conclusion that prothrombotic conditions were more frequent in 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<sup>5</sup> and Sie et al<sup>6</sup> 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<sup>7</sup> studied 105 patients with protein S deficiency, out of which 14 had arterial thrombotic accidents involving central nervous system or the myocardium, while most studies revealed a weaker association between the two<sup>8,9,10</sup>. Douay et al<sup>9</sup> 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<sup>8</sup> also supported the fact that acquired deficiency of free protein S is not a major factor for ischemic stroke. There were only few case reports showing association with arterial thrombosis as reported by Ok E J et al<sup>11</sup>. Pantam M et al<sup>12</sup> reported a 20 years old case of protein S deficiency, presented with homonymous hemianopia and decreased sensation in right side of the baby.

In this two year old patient without any risk factors, the factor S deficiency possibly played a role for the internal carotid artery thrombosis. 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 adults who has had a stroke.

## Conclusion

Therefore when dealing with a case of stroke in children, protein S deficiency could also be thought of before making proper diagnosis. As protein S deficiency predisposes to recurrent thrombophilic accidents, long term follow up is required after diagnosis. Early diagnosis and targeted approach can help such patients to prevent recurrent thrombotic episodes.

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