



## Protein C Protein S deficiency AARTHE S

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**Abstract :** Hypercoagulability is a condition in which there is an increased tendency to form blood clots. It may be hereditary or acquired. Combined deficiency of Protein C and Protein S is one of the causes of hypercoagulability and usually manifests as venous thrombosis. Arterial thrombosis is very rare. Herewith, we are presenting a case of arterial thrombosis presenting as gangrene right forefoot due to combined Protein C and Protein S deficiency.

**Keyword :** LV clot, arterial thrombosis, gangrene, Protein C and Protein S deficiency



Child after forefoot amputation



Child with right forefoot gangrene

### INTRODUCTION :

There exists a balance between prothrombotic and fluidic states in our body due to the presence of natural anticoagulants like antithrombin 3, Protein C, Protein S. Deficiency of Protein C and Protein S lead to a state of hypercoagulability and cause arterio-venous thrombosis. Amongst the various hereditary causes of hypercoagulability, Protein C deficiency is seen in 1 in 500, while Protein S deficiency is seen in 1 in 33000.

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### CASE HISTORY :

A 2yr old female child, first born of 3rd degree consanguinous parents admitted with complaints of fever, cough and breathlessness for 3 days followed by pain and blackish discolouration of right foot. There was no history of trauma or weakness of limbs. There was no other significant history suggestive of dehydration or vasculitis. Antenatal, natal, postnatal history was uneventful. Child was developmentally normal and immunized upto age. There was no family history of similar illness.

On examination, child had high grade fever and tachypnea, with bilateral crepitations and features of septic cardiogenic shock. Examination of the right lower limb revealed gangrene upto midfoot with absent pulses in right femoral and peripheral arteries. Sensation was also impaired in right lower limb.

On evaluation, the child had elevated serum CPK levels; Chest X ray revealed features of bronchopneumonia and cardiomegaly. USG doppler of right lower limb showed partial occlusion in distal common iliac, external iliac arteries and evidence of reduced flow velocity in femoral artery, monophasic flow in popliteal artery, dampened flow in anterior tibial, posterior tibial and dorsalis pedis arteries. ECHO revealed a LV clot of 12X8 mm and an ejection fraction of 24%.

A provisional diagnosis of Acute myocarditis/ Broncho pneumonia/ Septic cardiogenic shock with LV Clot and thromboembolic occlusion of right lower limb arteries was made.

Child was started on inotropes, anticoagulants, intravenous antibiotics. Child's cardiac status improved after few days of therapy. Repeat ECHO showed an improved EF of 64%. Initially, an above knee amputation was planned, after improvement in the ejection fraction. Repeat Doppler showed, recanalisation with biphasic flow in femoral and popliteal arteries. Hence, it was planned to amputate the limb after clinical non-progression of the gangrene, according to the vascular surgeon's opinion.

The child was kept under watchful expectancy and simultaneously evaluated further for liver function tests, PT, aPTT, INR, which were normal. Prothrombotic work up which was done revealed normal serum anticardiolipin antibody, antiphospholipid antibody, homocysteine levels.

But Serum Protein C and Protein S levels were reduced markedly; hence, a diagnosis of Protein C and Protein S deficiency was made.

After 4 weeks of careful monitoring and iv anticoagulants, repeat Doppler showed good flow in femoral and popliteal arteries. Clear line of demarcation appeared in right forefoot . Hence, amputation of the right forefoot was proceeded with. Child improved well with adequate post operative care and symptomatic management. ECHO done prior to discharge showed normal cardiac function with no LV clot and Doppler study of right lower limb showed normal flow velocities in femoral and popliteal arteries.

Child was continued on oral acenocoumarin and advised to continue physiotherapy. Forefoot prosthesis was applied, prior to discharge. Child is on regular follow up now.

#### **DISCUSSION :**

Protein C and Protein S are vitamin K dependent anticoagulants. Heterozygous protein C deficiency is inherited in an autosomal dominant pattern in chromosome 2. Nearly 200 mutations were described, of which Proc gene mutations are most found<sup>1</sup> . Incidence is 1 in 500, but most of them are subclinical. Only 2 to 5% are symptomatic. Homozygous pattern is very rare with an incidence is 1 in 2,00,000. Usually presents as purpura fulminans in newborn. Acquired causes are hepatic diseases or vitamin K deficiency.

Protein C deficiency is of two types. Type 1 is quantitative whereas Type 2 is qualitative. Protein C inactivates clotting factors Va and VIIIa, thereby prevents clotting. Protein S gene is found in chromosome 3. Major function of Protein S is to facilitate activated Protein C. Protein S deficiency may be hereditary or acquired.<sup>3</sup> types of Protein S deficiencies are reported. Quantitative defect involves deficiency of both total and free Protein S. Type 1 is characterized by a deficiency of both total and free Protein S, whereas in Type 2 there is only free Protein S deficiency. Type 3 is characterized by a qualitative defect alone.

Clinically, this condition presents mostly as venous thromboembolism. Other manifestations are neonatal purpura fulminans, childhood stroke, pulmonary embolism, portal vein thrombosis, and rarely, arterial thrombosis and very rarely as peripheral arterial disease following myocarditis and thrombus in heart<sup>2,3,4,5</sup>. Evaluation of these patients involves qualitative and quantitative assessment of various anticoagulants like Protein C, Protein S, antithrombin 3, factor V Leiden and prothrombin 20210 mutations, homocysteine, APLA levels. Management of these patients involves conventional or low molecular weight heparin with Protein C concentrate or fresh frozen plasma, followed by long term oral anticoagulants which may sometimes lead to complete disappearance of myocardial thrombus<sup>6</sup>. Patients are advised to avoid dehydration, as a preventive measure. Prophylactic use of Heparin is recommended in case of major orthopedic surgeries.

#### **PROGNOSIS :**

Depends on the site, extent of thrombosis and nature of damage to the target organ being involved.

#### **FOLLOW UP :**

Regular follow up of patients with PT, aPTT, INR values is mandatory and dose of oral anticoagulants is adjusted accordingly.

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