CASE REPORT

Protein C and Protein S Deficiency Presenting as Deep Venous Thrombosis

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We report a 7 year old girl with deep vein thrombosis due to combined protein C and protein S deficiency, who presented with swollen left thigh and restriction of movement of left hip joint.

Key words: *Deep venous thrombosis, Protein C, Protein S.*

A 7 yr old girl presented with severe pain in the left lower limb of 6 days duration, following a trivial fall. On examination, the child was febrile and had a swollen left thigh with engorged veins over its anterior and lateral aspects. There was restriction of movement of left hip joint and a positive Homan's sign in left calf muscles. There was no other significant finding on systemic examination. Peripheral arterial pulses were normal. The following differential diagnoses were considered: myositis, localized cellulitis, left hip arthritis, and deep vein thrombosis of left external and internal iliac veins.

Investigations revealed hemoglobin of 10.1g/dL, total leucocyte count 6800/cumm (N68L27E2M3), ESR102mm, prothrombin time 14 secs (control 12 secs), prothombin ratio 1.16, INR 1.31 and activated partial prothrombin time 28 secs (control 20secs). Radiographs of both hips were normal. Chest *X*-ray showed fluffy opacities in the right hilum. Urine analysis, mantoux test and ophthalmoscopic examination were unremarkable.

Ultrasonography of left thigh and hip joint revealed acute deep venous thrombosis extending from left sapheno femoral vein to the bifurcation of common iliac veins with evidence of subcutaneous edema. Duplex scan of left leg veins revealed an echogenic thrombus extending from inferior vena cava to the common illiac, internal illiac, and common femoral to superficial saphenous vein. CT scan confirmed deep venous thrombosis with sympathetic effusion on left hip joint.

Antinuclear Factor, antiphospholipid antibodies and VDRL titres were negative. Factor V Leiden mutation was not detected. Protein C level was 40 units/mL (N-67-195 units/mL), protein S level was 17 units/mL (N 55-123units/mL), and antithrombinIII level was 82 units/mL(70-122units/mL). Serum homocystiene level was within normal limit. Lipid profile was as follows-cholesterol-153mg/dL, HDL-24mg/dL, LDL-102mg/dL, VLDL-27mg/dL, triglyceride-149mg/dL. Protein C and protein S estimation of the other two siblings were within normal limit.

We managed this patient with injection low molecular weight heparin with empirical parenteral antibiotics, fresh frozen plasma, and other supportive management. She was discharged with advise of oral anticoagulant warfarin to maintain INR around 2 along with physiatric management.

DISCUSSION

Risk factors of DVT include past history of deep vein thrombosis, pulmonary edema, operative intervention, immobilization, trauma, neurological deficit, malignancies, sepsis, central venous catheter and hyper coagulable state etc.(1). The prothrombotic states encountered in children are protein C and S deficiency, activated protein C resistance, antithrombin III deficiency, elevated homocystiene level and abnormal lipid profile. The antiphospholipid syndrome, thrombocythemia(1,2), and severe bacterial infection cause acquired hypercoagulable states(3-5).

The exact incidence of protein C and protein S deficiency in our population is not known. Activated protein C- resistance was found to be the commonest pathogenic factor in juvenile deep vein thrombosis in India(2). In another case series from India on children with venous thrombosis, four patients had combined protein C and protein S deficiency(6).

Protein C and protein S system are the major regulatory system of hemostasis. Protein C and protein S are vitamin K dependent proenzymes synthesized in the liver. Thrombin- thrombomodulin complex on the surface of endothelial cells is the site for the interaction with protein C and S. Protein C becomes activated (activated protein C) 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.

Clinically, patients with protein C and S deficiency are at increased risk for venous thromboembolic disease, occasional arterial thrombosis, neonatal purpura fulminans and childhood stroke and even portal vein thrombosis(7-9). Acquired causes of protein C and S deficiencies are seen in acquired illness like liver disease, DIC, therapy with L-asparaginase and coumarin, and acute severe bacterial infections etc(10).

The management of these patients with deep vein thrombosis is with heparin anticoagulation, either conventional or low molecular weight along with protein C concentrate or fresh frozen plasma therapy.They are advised to avoid dehydration at any cost as a preventive measure(5).

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