A rare case of deep vein thrombosis in upper extremity: a case report

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ABSTRACT

The incidence of deep vein thrombosis (DVT) in upper limb is less common as compared to lower extremities. There were no institutional screening protocols for patients at risk of DVT in upper limb. Hence this case report was presented to describe the features of upper limb DVT.

Keywords: Upper limb deep vein thrombosis, Activated factor VIII, Protein C, Vitamin K

INTRODUCTION

In 1977, Di Scipio et al in Seattle first purified a new human plasma glycoprotein called protein S, in reference to its isolation and characterization in Seattle.

Protein S is an anticoagulant-dependent vitamin K protein. The main function is to promote the activity of activated protein C on its substrate, activated factor V (F Va) and activated factor VIII (F VIIIa). Protein S deficiency is usually clinically manifested as venous thromboembolism (VTE), although few researchers have also reported a relationship between protein S deficiency and arterial thrombosis.1–5

We describe a case of isolated protein S deficiency experienced by venous thrombotic events. Protein S deficiency is a rare cause that is not often considered.

CASE REPORT

A 47-year-old male patient presented with right upper limb painless swelling, on examination there was no signs of inflammation. On admission the patient was afebrile with pulse of 86 per minute and blood pressure within normal limits. Cardiovascular, central nervous system, respiratory system and per abdominal examination revealed no significant abnormalities.

Right upper limb Doppler showed thrombosis of right brachial, axillary and part of basilic vein. The patient was investigated for routine and specific parameters. All investigations including markers for inflammations were normal.

Among specific investigations, the patient was tested for protein S (functional) levels which were observed to be 27% (reference range being 60–140%). Both genetic and acquired deficiencies of protein S are associated with an increased risk of thrombosis. The prevalence of protein S deficiency in thrombophilic population is 7–12%. The recorded estimated risk is 10–15-fold in patients with this deficiency.

The patient was assessed for D-dimer levels, which was observed to be raised (1870 ng/ml).

Other investigations included lupus anticoagulant, antithrombin III activity and methylenetetrahydrofolate reductase activity and mean platelet volume.
The patient was started on warfarin with target prothrombin time-international normalized ratio (PT-INR) in the range of 2-3. During follow up, after one month of treatment the symptoms were improved. Follow up D-dimer levels were reported to be less than 100 (within normal limits). Follow up color Doppler of upper limb after 3 months revealed complete resolution of the thrombus.

**Table 1: Investigation reports.**

| Parameter                        | Value            |
|----------------------------------|------------------|
| Protein S level (%)              | 27               |
| D-dimer level (ng/ml)            | 1870             |
| IgG (IU/ml)                      | 0.6              |
| IgM (IU/ml)                      | 0.9              |
| Beta 2 glycoprotein IgG and IgM (IU/ml) | 1.7 and 10.86   |
| Anti-cardiolipin antibodies IgG and IgM (IU/ml) | 3.82 and 4.43 |
| Factor Leiden V mutation         | Not detected     |
| MTHFR mutation                   | Not detected     |
| Lupus anticoagulant (%)          | 1.2              |
| PT (sec)                         | 43.7             |
| INR                              | 4.5              |
| Anti-thrombin activity (%)       | 88.30            |

**DISCUSSION**

High case fatality, poor outcomes, high rate of emergency and subsequent vascular intervention to prevent death and limb loss among peripheral venous conditions poses high burden on clinical management.\(^6\)

Vascular disorders are among the foremost causes of mortality and disability globally. Acute limb ischemia is a sudden fall in limb perfusion which usually produces new or worsening signs and symptoms which often results in the limb loss.\(^7\) Acute limb ischemia is considered as a vascular emergency.\(^8\)

Congenital protein S deficiency is an autosomal dominant (AD) condition and its heterozygous status found among 2% of non-selected patients with venous thromboembolism. Protein S deficiency is found rare among healthy subjects without any abnormalities. The incidence is approximately about 1 in 700 based on a study among blood donors tested for protein C deficiency.\(^9\) The incidence of protein S deficiency rises to 3-6 per cent among a specified group of patients with chronic thrombosis or family history of thrombosis.\(^9\)

Subjects with protein S deficiency have a distinctive thrombotic illness, Purpura fulminans. Purpura fulminans can be distinguished from small vessel thrombosis with cutaneous and subcutaneous necrosis and occurs it in early ages of life, typically and usually during the neonatal periods or in the very first year of life.\(^10\)

Protein S (cofactor) combines with protein C (serine protease) which then binds to factor Va and factor VIIIa. Protein S/protein C complex then splits factor Va and VIIIa, and prevents the activation of factor X and thrombin, hence it prevents the thrombosis during normal physiological conditions. This mechanism fails during its deficiency, which results in thrombotic events.\(^11\) The differentiation between free and total protein S levels is important and it explains the mechanism of thrombotic events among patients. Approximately 30-40% of the total protein-S is safe in healthy individuals. Only free protein-S can function as a cofactor in the protein C system.

Some studies still debated over the possible correlation between protein S deficiency and arterial thrombosis. For pregnant women, protein S deficiency is also linked with fetal death.\(^12\)

Protein C deficiency is estimated to be three times higher in Japanese communities. The mutation of the factor V Leiden is normal in white populations. This mutation is uncommon and can hardly be detected in Japanese or Asian cultures. There is no difference in the rate of male-to-female occurrence. Race-related differences occur in thrombophilic disorders as one might conclude from genetic-based population traits. The exact incidence of protein S deficiency in the Indian population is unknown. There not many studies conducted in this context Protein S deficiency interaction and thromboembolic diseases have been identified in several families by Comp, Brokemans, Batard and Lieu.\(^13\)

Our patient was a 47-year-old male presented with right upper limb swelling, turned out to be a case of right upper limb deep vein thrombosis (DVT). A rational approach to deciding whether fibrinolytic therapy is indicated should be based on an assessment of the benefit that each particular patient will derive from fibrinolytic therapy weighed against that patient’s risk for major bleeding and intracranial haemorrhage. The success of thrombolytic therapy decreases with the increase in duration from the onset, and only less than 50% success rate is reported after four weeks from the onset. We archived a good clinical response to the thrombolytic in spite of a long duration of almost eight weeks from the time of onset.

The patient is on regular follow-up with lifelong anticoagulation on warfarin with monthly monitoring of target INR 2-3. The patient has no evidence of any haemorrhagic manifestations. The patient has been advised coagulation studies of his siblings and kins.

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