Recurrent thrombosis in a young female: unmasking protein S deficiency

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ABSTRACT

Background: Hereditary protein S deficiency is a rare but significant cause of unprovoked, recurrent venous thromboembolism (VTE) in young individuals. Early recognition is essential to prevent recurrence and complications.

Case Presentation: A 23-year-old female with previous episodes of deep vein thrombosis (DVT) in 2022 and 2023 presented with acute dyspnea. Imaging revealed pulmonary thromboembolism with bilateral DVT. Coagulation testing confirmed protein S deficiency. She received systemic thrombolysis with tenecteplase followed by heparin infusion and was later transitioned to long-term direct oral anticoagulants. Cardiac function improved following treatment.

Conclusion: This case highlights the importance of considering hereditary protein S deficiency in young patients with recurrent VTE, where early diagnosis and lifelong anticoagulation can prevent morbidity and improve outcomes.

Keywords: Protein S deficiency, inherited thrombophilia, venous thromboembolism, pulmonary embolism, anticoagulation, case report.

Type of Article: CASE REPORT **Specialty:** Internal Medicine

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Background

Venous thromboembolism (VTE) - comprising deep vein thrombosis (DVT) and pulmonary embolism (PE) - remains a major cause of morbidity and mortality worldwide [1,2]. While most cases are linked to acquired risk factors such as surgery, trauma, or malignancy, inherited thrombophilias like protein S deficiency may go unrecognized, particularly in young patients without traditional risk factors [3,4].

Protein S deficiency, an autosomal dominant disorder caused by PROS1 gene mutations, disrupts the anticoagulant role of activated protein C, predisposing individuals to recurrent thrombosis [3,5]. This report underscores the diagnostic and management challenges in a young female with recurrent VTE due to hereditary protein S deficiency.

Case Presentation

A 23-year-old female with prior DVT episodes in 2022 and 2023 presented with acute-onset dyspnea that worsened over 1 day. There was no family history of thrombotic disorders, oral contraceptive use, or other risk factors.

On admission, she was hemodynamically stable but showed signs of right heart strain. CT pulmonary angiography revealed thrombi in the descending pulmonary artery and left lower lobe pulmonary vein. Venous Doppler demonstrated bilateral lower limb DVT. Echocardiography showed a left ventricular ejection fraction of 40%, improving to 50% after thrombolysis.

Laboratory findings showed elevated D-dimer and reduced functional protein S levels. Tests for antiphospholipid antibodies, protein C, and antithrombin III were normal.

She was managed in the ICU with intravenous heparin infusion and systemic thrombolysis using tenecteplase due to the extensive clot burden and right ventricular dysfunction. Following clinical improvement, she was discharged on DOAC therapy for lifelong anticoagulation.

Family screening for protein S deficiency was not performed as the family was not willing, despite extensive counselling, and genetic testing (PROS1 mutation) was not attempted; the diagnosis was based on functional assays.

Discussion

Protein S acts as a cofactor for activated protein C, regulating coagulation by inactivating factors Va and VIIIa [3,5]. Its deficiency - hereditary or acquired - leads to hypercoagulability and recurrent VTE. Acquired causes

include liver disease, pregnancy, oral contraceptives, and vitamin K deficiency[3,5].

In this case, the patient's recurrent thrombosis in the absence of secondary risk factors strongly suggested hereditary protein S deficiency.

Differential diagnosis in young adults with recurrent thrombosis includes: Factor V Leiden mutation, prothrombin gene mutation, protein C or antithrombin III deficiency, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria, and myeloproliferative disorders [6,7].

Thrombolysis with tenecteplase was used successfully in this patient due to extensive clot burden and right heart dysfunction. Transition to direct oral anticoagulants provided an effective and safer long-term option compared to warfarin, which can lower protein S levels further.

The novel aspect of this case lies in the recurrent thrombosis at a young age, the diagnosis following PE and bilateral DVT, and the successful use of thrombolysis followed by DOAC therapy [6,8,9].

Patients with hereditary protein S deficiency are prone to recurrence and require lifelong anticoagulation. Multidisciplinary follow-up with hematology and cardiology is vital for monitoring complications and adherence.

Conclusion

This case underscores the importance of evaluating inherited thrombophilias in young patients with recurrent, unexplained VTE. Early identification and tailored management with lifelong anticoagulation, supported by multidisciplinary care, are essential for preventing recurrence and improving outcomes.

What's new

This report highlights a rare presentation of hereditary protein S deficiency causing recurrent VTE at a young age, demonstrating successful management with thrombolysis and DOAC therapy, and emphasizing the need for early detection and lifelong preventive care.

Conflicts of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

Funding

None.

Consent to participate

Written consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Summary of the case

1	Patient (gender, age)	23 years, female
2	Final diagnosis	Protein S deficiency
3	Symptoms	Shortness of breath
4	Medications	Symptomatic treatment given
5	Clinical procedure	Thrombolysis followed by oral anticoagulants
6	Specialty	Internal Medicine