

CASE REPORT

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Atypical presentation of pulmonary embolism and deep vein thrombosis due to protein S deficiency in a young female with chest pain

Saurabh Puri*, Ashok Kumar Grover, Ankita Kaur Narula, Pankaj Nand Choudhry and Arjun Prem Gupta

Abstract

Venous thromboembolism has many risk factors including protein S deficiency, which poses a significant diagnostic challenge as it presents with atypical complaints. A treatable yet potentially fatal condition, acute pulmonary embolism, is currently third most common cause of cardiovascular death. Clinicians should include pulmonary embolism as differential diagnosis in young adults with atypical symptoms with 2 D ECHO findings of the dilated right atrium, right ventricle, and elevated pulmonary artery pressure, and diagnosis is confirmed by computed tomography pulmonary angiography (CTPA). Anticoagulants including NOACs should be initiated promptly to improve the outcome for patients.

Keywords: Protein S deficiency, Pulmonary embolism, Young female, Deep vein thrombosis

Introduction

Protein S is a vitamin K-dependent glycoprotein that functions as a cofactor for activated protein C in the degradation of coagulation factors Va and VIIIa. The prevalence of protein S deficiency in the general population is 0.03 to 0.13% and 1 to 13% in individuals with venous thromboembolism and can be inherited or acquired causing a significant risk of thrombosis. We present the case of a young female with atypical presentation of protein S deficiency with no risk factors and was diagnosed and promptly managed with anticoagulants

Case report

A 25-year-old young, unmarried lady come to the OPD with complaints of persistent stabbing chest pain for the last 7 days. She had no fever, shortness of breath, or any recent trauma. She had no comorbidity, was non-smoker,

no contraceptive use, or any prolonged recumbency/recent operation. Examination revealed a blood pressure (BP) of 110/70 mmHg, heart rate (HR) of 110/min, respiratory rate (RR) of 18/min, and oxygen saturation (SpO₂) of 97% at room air. Initial laboratory investigations revealed mild normocytic normochromic anemia (Hb 11.7 g/dl) with normal leukocyte and platelet count (TLC $9.71 \times 10^9/L$, platelet count $159 \times 10^9/L$). Liver function and renal profile were within normal limits. Cardiac enzymes were within the normal range (CPK 55 U/L, CK-MB 0.8 ng/ml, Trop I 0.02 ng/ml). An initial electrocardiogram (ECG) showed sinus tachycardia at a rate of 110 beats per minute. 2D ECHO revealed no regional wall motion abnormality and good left ventricle function; however, RA and RV were dilated and she had mild pulmonary arterial hypertension. The D dimer was raised (6919 ng/ml). Chest X-ray showed a well-defined rounded opacity in the right lower zone likely representing consolidation (Fig. 1). In view of these findings, computed tomography pulmonary angiography (CTPA) was done which revealed the presence of thrombus in the

*Correspondence: saurabhपुरी119@gmail.com
Department of Internal Medicine, Max Super Specialty Hospital, Vaishali, Ghaziabad, India

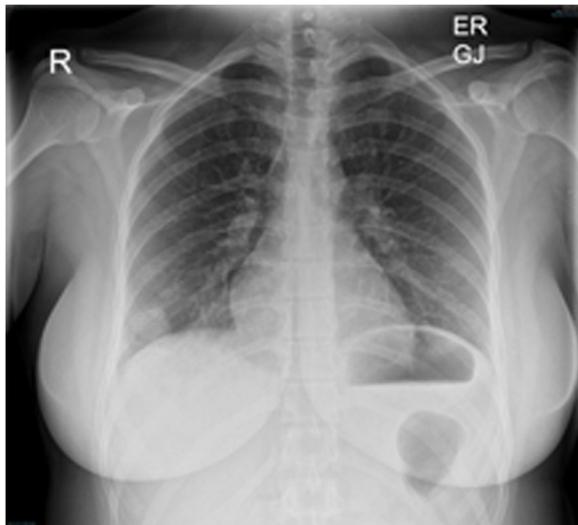


Fig. 1 Chest X-ray showed well defined rounded opacity in right lower zone likely representing consolidation

distal main pulmonary trunk, right and left pulmonary, and its ascending and descending branches suggestive of pulmonary thromboembolism (Figs. 2 and 3). Venous Doppler of the lower limb revealed deep vein thrombosis

involving left common, external iliac, common, superficial and deep femoral, and popliteal veins with extension into a short saphenous vein (Figs. 4, 5, 6, 7, 8 and 9). She was managed with subcutaneous enoxaparin and was started on oral vitamin K antagonist, warfarin with international normalized ratio (INR) monitoring.

Further investigation showed homocysteine 12.4 micromol/L, factor V Leiden mutation, prothrombin gene mutation, MTHFR gene mutation, antinuclear antibody, and vasculitis panel were all negative, anti-phospholipid antibody IgG 2.18 AU/ml, anti-phospholipid antibody IgM 0.67 AU/ml, antithrombin III 122%, and protein C 91%, but her protein S (free) level was low at 15.1%.

Her chest pain improved and was discharged on day 6 on an oral anticoagulant. She was continued on oral anticoagulant and was doing well on regular follow-ups from the last 6 months.

Discussion

Vitamin K-dependent glycoprotein, protein S, is a cofactor for activated protein C reducing thrombin generation by inactivating procoagulant factors Va and VIIIa, along with enhancing fibrinolysis and inhibiting prothrombin activation [1–6]. It is an inherited thrombophilia

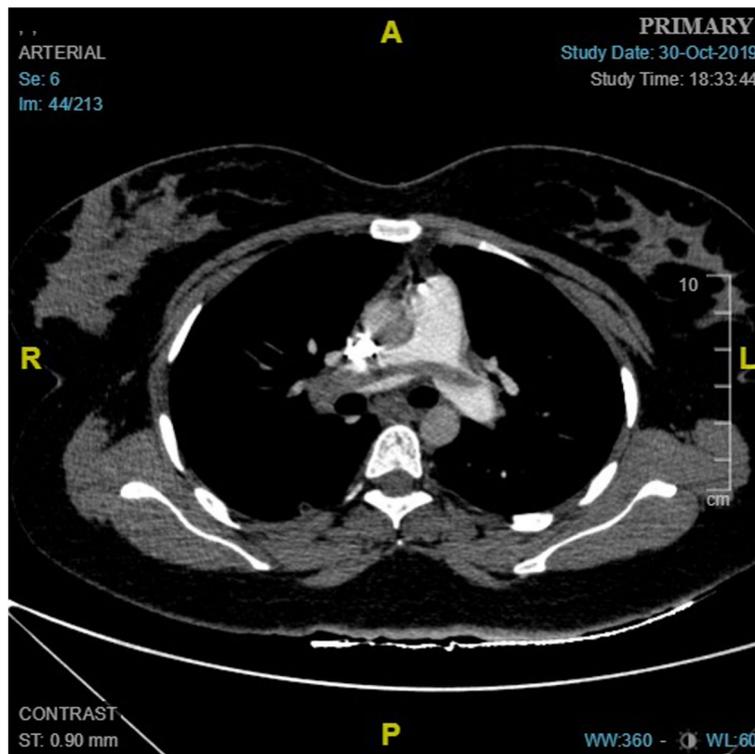


Fig. 2 Computed tomography pulmonary angiography (CTPA) was done which revealed the presence of thrombus in distal main pulmonary

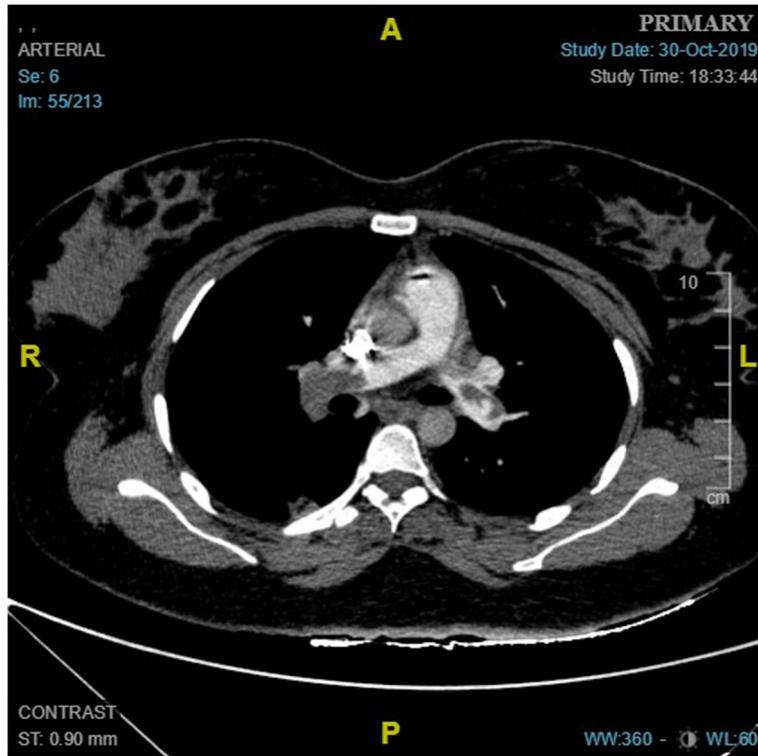


Fig. 3 Computed tomography pulmonary angiography (CTPA) was done which revealed the presence of thrombus in distal main pulmonary

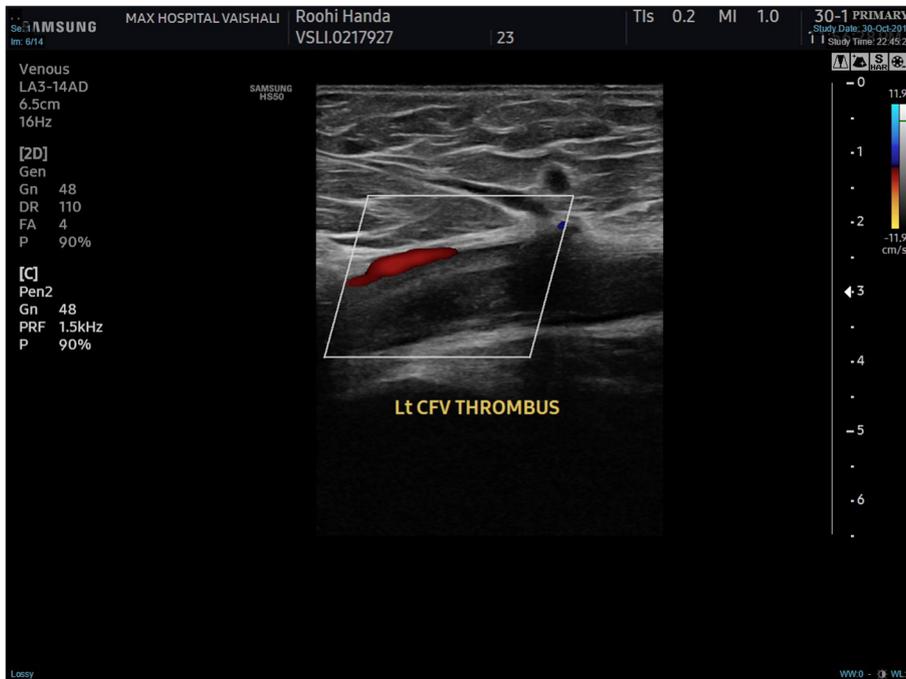


Fig. 4 Venous Doppler of the lower limb revealed deep vein thrombosis involving left common, external iliac, common, superficial and deep femoral, and popliteal veins with extension



Fig. 5 Venous Doppler of the lower limb revealed deep vein thrombosis involving left common, external iliac, common, superficial and deep femoral, and popliteal veins with extension

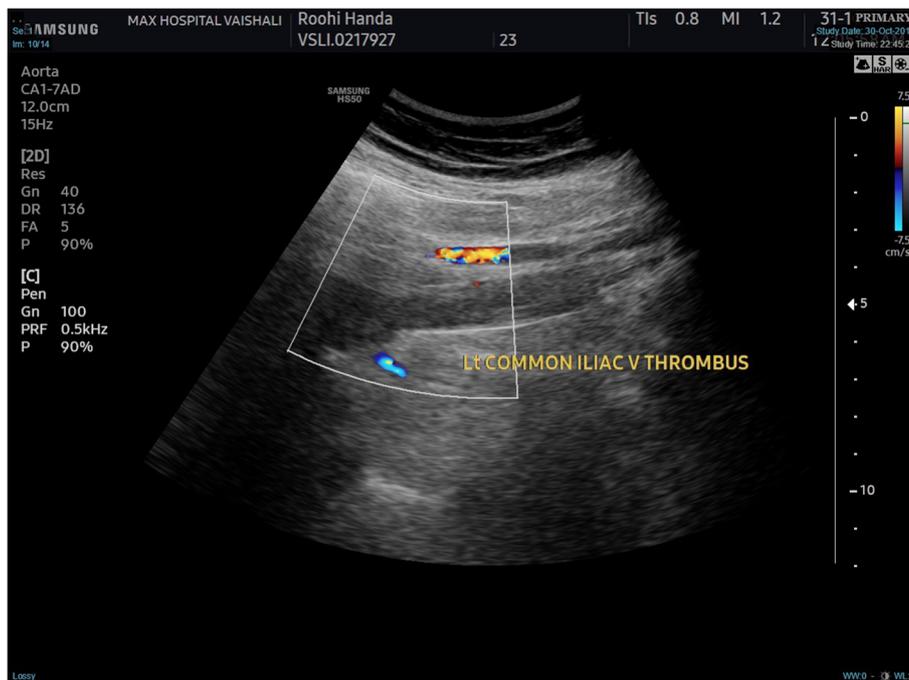


Fig. 6 Venous Doppler of lower limb revealed deep vein thrombosis involving left common and external iliac

transmitted in an autosomal dominant manner due to PROS1 gene mutation on the third chromosome causing an increased risk of thromboembolism [7–9]. Inherited protein S deficiency has been subdivided into three types

I—classic type causing reduced both level and function of protein S, II—reduced protein S function, and III—quantitative reduction in free protein S level along with its function [10]. Pregnancy, oral hormonal contraceptive

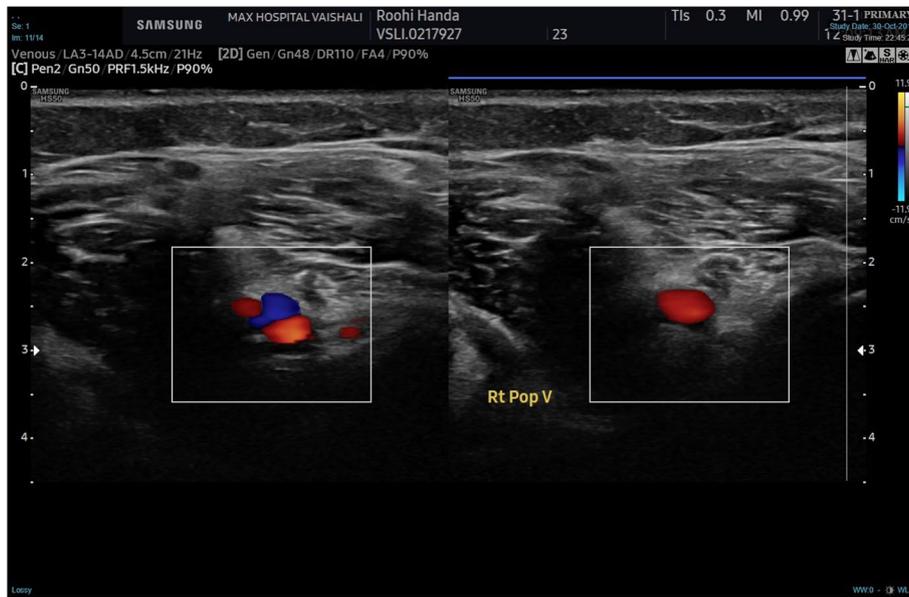


Fig. 7 Venous Doppler of the lower limb revealed deep vein thrombosis involving right popliteal veins with extension into short saphenous vein

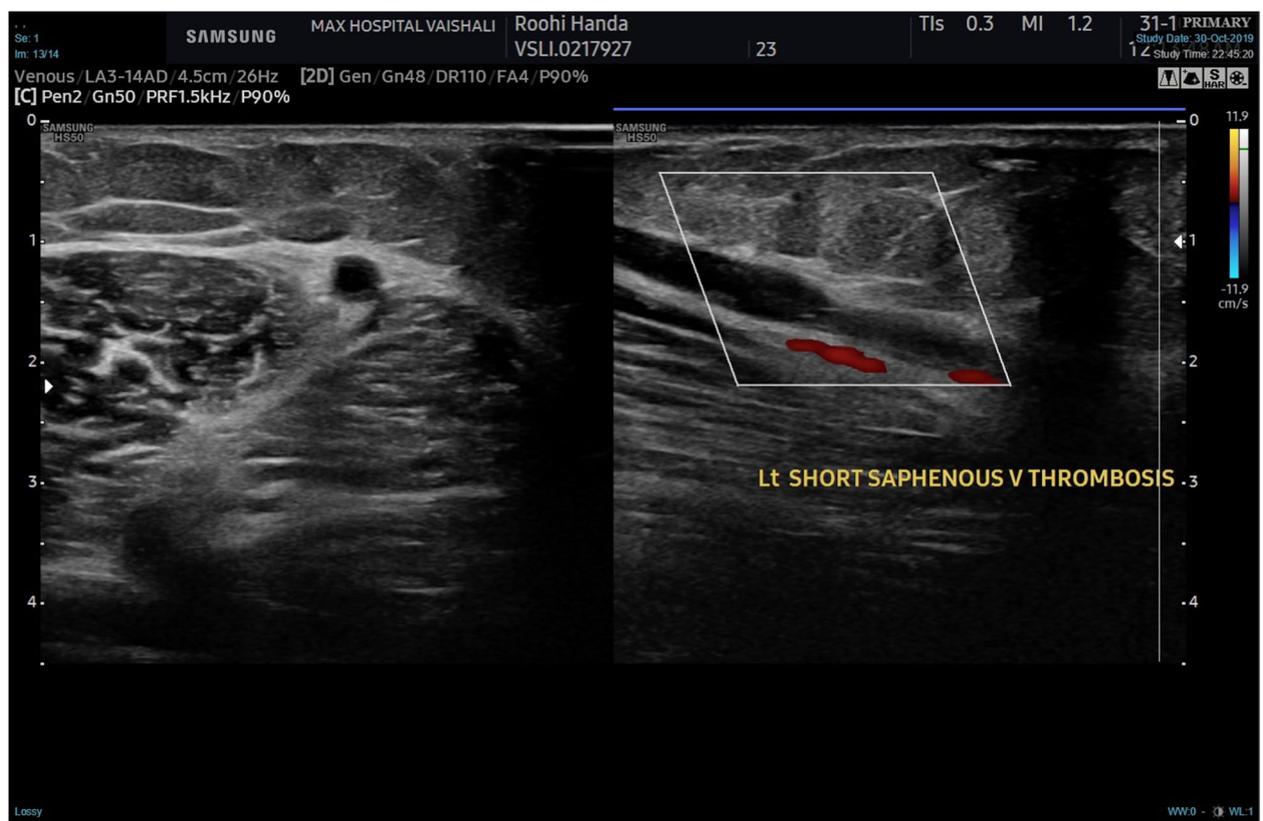


Fig. 8 Venous Doppler of the lower limb revealed deep vein thrombosis involving left common, external iliac, common, superficial and deep femoral, and popliteal veins with extension

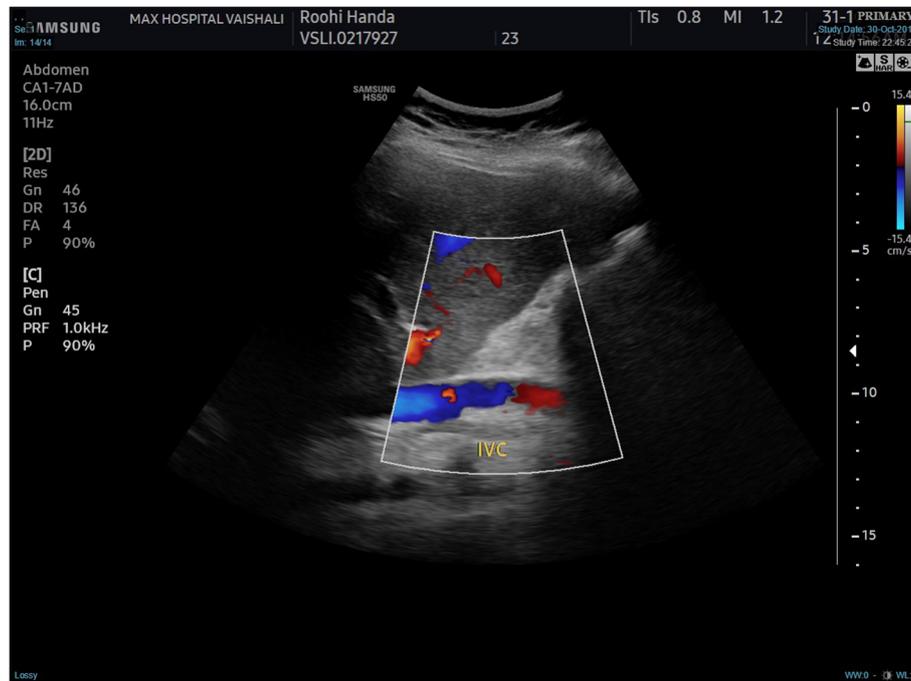


Fig. 9 Venous Doppler of the lower limb revealed deep vein thrombosis involving left common, external iliac, common, superficial and deep femoral, and popliteal veins with extension

use, disseminated intravascular coagulation, acute thrombosis, HIV infection, nephrotic syndrome, and liver disease along with PROS1 gene mutation causes reduced protein S level. Protein S deficiency incidence among patients with venous thromboembolism is 2–8%, whereas the 2013 MEGA study showed the frequency of 0.9% [11]. VTE (including DVT and pulmonary embolism), arterial thrombosis, neonatal purpura fulminans, and obstetrical complications are the myriad of presenting manifestations of protein S deficiency. 14.5 years was the median age for first thromboembolic event, and pulmonary embolism incidence was 17% [12]. Suspicion of protein S deficiency should be raised in patients with VTE in a strong family history of VTE or protein S deficiency, or first VTE event before 50 years, unusual site VTE such as portal mesenteric, cerebral vein, and recurrent VTE. Protein S deficiency diagnosis confirmation is very difficult among all hereditary thrombophilias with a preferred approach for screening and testing for true deficiency ID estimating the level of free protein S [13, 14]. The lower level of protein S is more predictive for an increased risk of VTE in asymptomatic patients or having first VTE in the absence of strong family history [15].

Inherited thrombophilias (factor V Leiden mutation, protein C deficiency, antithrombin deficiency, prothrombin G20210A mutation) along with acquired

risk factors like immobility, surgery, trauma, cancer, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria, disseminated intravascular coagulation, oral contraceptive use, and hormonal changes in pregnancy are the differential diagnosis of VTE which should be evaluated and ruled out. The management of acute VTE includes anticoagulation for at least 3 to 6 months. Anticoagulation continuation depends on whether thrombosis is provoked or unprovoked along with other factors including recurrent thrombosis, life-threatening thrombosis, and unusual site thrombosis. The higher dose of DOAC is used if chosen for a long-term prevention of recurrent VTE, as protein S deficiency is more thrombophilic among the hereditary thrombophilias.

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Authors' contributions

1. Dr. Saurabh Puri: manuscript writing. 2. Dr. Ashok Kumar Grover: clinician. 3. Dr. Ankita Kaur Narula: editing. 4. Dr. Pankaj Nand Choudhry: editing. 5. Dr. Arjun Prem Gupta: proofreading. The authors read and approved the final manuscript.

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Declarations

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Given.

Consent for publication

Given.

Competing interests

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