

Extensive Apparently Unprovoked Bilateral Proximal Deep Vein Thrombosis in a Young Woman with Antiphospholipid Antibody Positivity: A Case Report

Dr. Om Shivgunde¹, Dr. Jitendra Ingole², Dr. Swapnaja Biradar³, Dr. Anushk Deshmukh⁴

¹Department of General Medicine, Smt. Kashibai Navale Medical College and General Hospital, Narhe, Pune, Maharashtra, India
Corresponding Author Email: [omshivgunde\[at\]gmail.com](mailto:omshivgunde[at]gmail.com)

^{2, 3, 4}Department of General Medicine, Smt. Kashibai Navale Medical College and General Hospital, Narhe, Pune, Maharashtra, India

Abstract: Background: Deep vein thrombosis (DVT) in a young individual without an identifiable provoking factor warrants evaluation for acquired and inherited thrombotic risk factors. Antiphospholipid antibody (aPL) positivity may suggest antiphospholipid syndrome (APS), but diagnosis requires appropriate clinical and laboratory correlation and demonstration of persistent antibody positivity. Case Presentation: A 36-year-old woman presented with a few days of bilateral pedal edema, more prominent on the left side, associated with mild tenderness, erythema and warmth. There was no history of recent surgery, trauma, prolonged immobilization, pregnancy, oral contraceptive use or previous thrombotic event. Bilateral lower-limb venous Doppler demonstrated extensive thrombosis involving the proximal deep venous system, with complete thrombosis of the left femoral, common femoral and external iliac veins and associated great saphenous vein thrombosis. The right lower limb showed partial femoral vein thrombosis with thrombosis of the proximal great saphenous vein extending to the saphenofemoral junction. D-dimer was elevated at 5.2 µg/mL. Renal and hepatic functions were preserved. Thrombophilia evaluation revealed positive antinuclear antibody (ANA) by immunofluorescence at a titre of 1:320 with a spindle apparatus pattern, negative anti-double-stranded DNA antibodies and normal complement levels. Anticardiolipin IgM was 38 MPL and anti-β2-glycoprotein I IgM was 42 U/mL, with negative IgG antibodies. Homocysteine was normal and MTHFR A1298C was heterozygous. She was treated initially with therapeutic enoxaparin followed by apixaban. Conclusion: This case highlights the importance of evaluating extensive proximal DVT in young patients even in the absence of conventional provoking factors. Initial aPL positivity raises suspicion for APS but does not establish the diagnosis without persistent positivity on repeat testing after the recommended interval. Positive ANA in the absence of clinical or serological evidence of systemic lupus erythematosus should similarly be interpreted cautiously.

Keywords: Deep Vein Thrombosis; Venous Thromboembolism; Antiphospholipid Antibodies; Antiphospholipid Syndrome; Thrombophilia; Anticoagulation; Case Report

1. Introduction

Deep vein thrombosis (DVT) is an important manifestation of venous thromboembolism (VTE) and may occur in association with transient provoking factors, persistent risk factors or thrombophilic disorders. Extensive proximal DVT in a young patient without an identifiable provoking factor raises consideration of acquired thrombophilia, inherited thrombophilia and anatomical venous outflow abnormalities [1].

Antiphospholipid antibodies (aPL) are an important acquired thrombotic risk factor. However, the presence of anticardiolipin or anti-β2-glycoprotein I antibodies on a single occasion is insufficient to establish definite antiphospholipid syndrome (APS) [2]. Persistent laboratory positivity, together with an appropriate clinical event, is required for classification [3]. Similarly, a positive antinuclear antibody (ANA) does not by itself establish systemic lupus erythematosus (SLE).

We report a young woman with extensive bilateral proximal DVT, including left iliofemoral involvement, in whom no major conventional provoking factor was identified and initial evaluation demonstrated IgM antiphospholipid antibody positivity and ANA positivity.

2. Case Presentation

A 36-year-old woman, homemaker and resident of Pune, presented with a history of bilateral pedal edema for a few days, more prominent in the left lower limb. The swelling was associated with mild discomfort on walking, tenderness, erythema and local warmth. There was no history of fever, dyspnea, chest pain, oliguria or gastrointestinal symptoms. There was no history of recent surgery, trauma, prolonged immobilization, hospitalization, pregnancy, oral contraceptive use or alternative medication use. She had no known history of diabetes mellitus, hypertension, thyroid disease, chronic pulmonary disease, tuberculosis or other major systemic illness. There was no documented previous thrombotic episode. Her last menstrual period was on 21 September 2026, with normal menstrual flow, and a urine pregnancy test was negative.

She consumed a mixed diet and denied tobacco and alcohol use.

On examination, she was hemodynamically stable. Bilateral pedal edema was present, more marked on the left, with mild tenderness, erythema and increased local temperature. The remainder of the cardiovascular, respiratory, abdominal and neurological examination was unremarkable.

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3. Laboratory Investigations

Table 1: Hematological, biochemical and coagulation investigations

Investigation	Patient Value	Interpretation
Hemoglobin	10 g/dL	Mild anemia
Total leukocyte count	6,030/mm ³	Within reference range
Platelet count	206,000/mm ³	Within reference range
MCV	100 fL	Borderline macrocytic
Hematocrit	35%	Mildly reduced
Urea	17 mg/dL	Normal
Creatinine	0.9 mg/dL	Normal
eGFR	131 mL/min/1.73 m ²	Preserved renal function
Sodium	138 mmol/L	Normal
Potassium	4.1 mmol/L	Normal
Chloride	104 mmol/L	Normal
Total bilirubin	0.5 mg/dL	Normal
Direct bilirubin	0.3 mg/dL	Normal
AST	36 U/L	Within reference range
ALT	43 U/L	Within/near reference range
ALP	114 U/L	Within reference range
Total protein	7.1 g/dL	Normal
Albumin	4.1 g/dL	Normal
Random blood glucose	121 mg/dL	—
HbA1c	5.2%	Normal
PT	14 seconds	Normal
INR	1.1	Normal
D-dimer	5.2 µg/mL	Elevated (ref <0.5 µg/mL)

Table 2: Urine, metabolic and infectious disease evaluation

Investigation	Patient Value	Interpretation
Urine routine exam	No significant abnormality	—
Urine microscopy	No significant abnormality	—
Urine protein–creatinine ratio	0.49	Elevated (ref 0.10–0.19)
Total cholesterol	133 mg/dL	—
Triglycerides	61 mg/dL	—
HDL cholesterol	35 mg/dL	—
LDL cholesterol	85 mg/dL	—
VLDL cholesterol	12 mg/dL	—
Thyroid function tests	Within reference range	No thyroid dysfunction
HIV / HBsAg / Anti-HCV	Negative	—
Urine pregnancy test	Negative	—

Because of the patient's young age and the absence of an identifiable major provoking factor, an evaluation for acquired and inherited thrombophilia was performed. The results are summarized in Table 3.

Table 3: Autoimmune and thrombophilia evaluation

Investigation	Patient Value	Interpretation
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Investigation	Patient Value	Interpretation
ANA by IFA	Positive (++)	Positive
ANA titre	1:320	Significant titre
ANA pattern	Spindle apparatus	Reported pattern
Anti-dsDNA	Negative	—
C3 / C4	Within reference range	No hypocomplementemia
Anticardiolipin IgM	38 MPL	Positive (assay-specific)
Anticardiolipin IgG	Negative	—
Anti-β2-glycoprotein I IgM	42 U/mL	Positive (assay-specific)
Anti-β2-glycoprotein I IgG	Negative	—
Lupus anticoagulant	Not documented	Further evaluation required
Homocysteine	13 µmol/L	Within reference range
MTHFR A1298C	Heterozygous	No thrombotic significance

4. Venous Doppler Ultrasonography

Bilateral lower-limb venous Doppler revealed extensive venous thrombosis:

- Right side: Partial thrombosis of the femoral vein along with thrombosis of the proximal two-thirds of the great saphenous vein extending to the saphenofemoral junction.
- Left side: Acute complete thrombosis involving the femoral, common femoral and external iliac veins, along with thrombosis of the great saphenous vein and a communicating vein.

Thus, the overall Doppler findings were consistent with extensive bilateral proximal DVT, with left-sided iliofemoral involvement.

Electrocardiography, chest radiography and two-dimensional echocardiography were unremarkable.

5. Treatment and Clinical Course

In view of the extensive bilateral proximal DVT, the patient was started on therapeutic anticoagulation with enoxaparin 60 mg subcutaneously twice daily for 7 days. She was subsequently transitioned to apixaban 10 mg orally twice daily for 7 days, followed by 5 mg twice daily, as per the treatment protocol.

Limb elevation and clinical monitoring were advised. There was no clinical evidence of pulmonary embolism during hospitalization. She remained hemodynamically stable and was discharged on oral anticoagulation.

The initial anticardiolipin IgM and anti-β2-glycoprotein I IgM positivity raised suspicion for APS. However, because these antibodies were demonstrated on a single occasion and lupus anticoagulant was not documented, definite APS could not be established at that stage. Repeat antiphospholipid antibody testing after an interval of at least 12 weeks was planned.

Although ANA was positive at a titre of 1:320, the patient had no clinical manifestations suggestive of SLE, anti-dsDNA was negative and complement levels were normal. Therefore, a diagnosis of SLE or secondary APS was not made.

6. Discussion

6.1 Extensive proximal DVT without an identifiable provoking factor

The patient had extensive bilateral proximal DVT involving the left iliofemoral venous system despite the absence of an obvious transient provoking factor such as recent surgery, trauma, prolonged immobilization, pregnancy or oral contraceptive exposure. The event can therefore be described as apparently unprovoked based on the available history [1].

The extensive clot burden and young age appropriately prompted evaluation for acquired thrombophilia. The elevated D-dimer supported the presence of active thrombotic disease, while renal function, hepatic function and platelet count were preserved.

6.2 Significance of antiphospholipid antibody positivity

The presence of anticardiolipin IgM and anti- β 2-glycoprotein I IgM antibodies is clinically relevant in a patient presenting with extensive venous thrombosis. However, a single positive antibody assessment cannot establish APS.

The revised Sapporo criteria and subsequent classification frameworks require persistent positivity of the relevant antiphospholipid antibody on repeat testing at least 12 weeks apart [2]. The 2023 ACR/EULAR criteria are classification criteria developed primarily for research purposes and should not be interpreted as a substitute for clinical diagnosis [3].

In this patient, lupus anticoagulant was not documented, while both anticardiolipin and anti- β 2-glycoprotein I antibodies were of the IgM isotype. The exact significance of the reported titres should therefore be interpreted according to the assay-specific reference range and 99th percentile used by the laboratory. Repeat testing after at least 12 weeks is essential before assigning a definitive diagnosis of APS [4].

6.3 ANA positivity and possible autoimmune disease

ANA was positive at a titre of 1:320 with a spindle apparatus pattern. However, ANA positivity alone is insufficient to diagnose SLE. The patient had no documented clinical features of SLE, anti-dsDNA was negative and complement levels were preserved.

The mild proteinuria, with a UPCR of 0.49, warrants follow-up but is not by itself sufficient to establish lupus nephritis, particularly in the absence of other clinical or immunological features of SLE. Therefore, the most appropriate current description is ANA positivity with antiphospholipid antibody positivity, rather than SLE-associated APS or secondary APS.

6.4 Significance of MTHFR A1298C heterozygosity

The patient was heterozygous for the MTHFR A1298C variant. Her homocysteine level was normal. Isolated MTHFR polymorphisms, particularly in the absence of hyperhomocysteinemia, are not considered clinically significant thrombophilic abnormalities and should not be regarded as an explanation for the extensive thrombosis.

6.5 Anatomical considerations

The extensive left-sided iliofemoral involvement also raises the possibility of an underlying anatomical venous outflow abnormality, such as iliac vein compression (May-Thurner syndrome). Although this was not demonstrated in the present evaluation, consideration of CT or MR venography may be appropriate if symptoms persist, thrombosis recurs or clinical suspicion remains high.

6.6 Anticoagulation and implications of possible APS

The patient was initially treated with therapeutic low-molecular-weight heparin and subsequently transitioned to apixaban [5]. The long-term anticoagulant strategy should be reassessed once repeat antiphospholipid antibody testing is available. If persistent APS is subsequently demonstrated, particularly in a high-risk antibody profile or in the presence of arterial thrombosis, vitamin K antagonist therapy is generally favored over direct oral anticoagulants [6]. Thus, confirmation or exclusion of persistent APS has important implications for long-term anticoagulant selection.

7. Clinical Lessons

- 1) Extensive proximal DVT in a young patient without an identifiable provoking factor warrants evaluation for acquired thrombophilia.
- 2) A single positive antiphospholipid antibody panel does not establish APS; persistence must be demonstrated on repeat testing after at least 12 weeks.
- 3) ANA positivity alone does not establish SLE, particularly in the absence of compatible clinical manifestations and supportive serology.
- 4) Mild proteinuria should be followed longitudinally but should not be labelled as lupus nephritis without appropriate clinical and laboratory evidence.
- 5) Isolated MTHFR A1298C heterozygosity with normal homocysteine should not be considered a clinically significant cause of thrombosis.
- 6) Extensive unilateral iliofemoral thrombosis should prompt consideration of anatomical venous outflow obstruction when clinically appropriate.
- 7) Confirmation of APS may influence the choice and duration of long-term anticoagulation.

8. Conclusion

This case demonstrates extensive bilateral proximal DVT with left-sided iliofemoral involvement in a young woman without an identifiable major provoking factor. Initial evaluation demonstrated antiphospholipid antibody positivity and ANA positivity, but the available findings were insufficient to establish definite APS or SLE. Repeat antiphospholipid antibody testing after the appropriate interval is therefore essential. The case emphasizes the

importance of careful interpretation of thrombophilia and autoimmune investigations and avoidance of premature diagnostic labelling based on isolated laboratory abnormalities.

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