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Deep Vein Thrombosis and Pleural Effusion as Initial Manifestations of Systemic Lupus Erythematosus with Secondary Antiphospholipid Syndrome in a Male: A Case Report

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Case Report

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Abstract

Introduction:

Systemic lupus erythematosus (SLE) with secondary antiphospholipid syndrome (APS) is an uncommon cause of unprovoked thrombosis and serosal inflammation, especially in males. Early recognition of autoimmune etiologies in thrombotic presentations is essential to prevent recurrence and long-term morbidity.

Case Presentation:

A 34-year-old male presented with 1 month history of high-grade fever, followed by relatively acute onset left-sided pleuritic chest pain and rapidly progressive, painful swelling of the left lower limb. Imaging revealed a left-sided pleural effusion and extensive deep vein thrombosis (DVT), with laboratory evaluations showing positive antinuclear antibodies (ANA), lupus anticoagulant, and anti-β2-glycoprotein I antibodies. Together with the patient's clinical manifestations, these findings established the diagnosis of SLE with secondary APS. The patient was treated with low-molecular-weight heparin for acute DVT, intravenous antibiotics, proton pump inhibitors, inhaled bronchodilators, corticosteroids, and supportive care. Over a week, the patient experienced complete resolution of fever, significant reduction in leg swelling, and improvement in pleuritic chest pain. He was discharged on long-term anticoagulation with a plan for rheumatology follow-up for immunomodulatory therapy.

Conclusion

This case illustrates a diagnostically challenging presentation of SLE with secondary APS in males, mimicking infectious or thromboembolic conditions. Early autoimmune work-up in young patients with unexplained thrombosis or serositis can facilitate timely treatment and prevent recurrence.

INTRODUCTION

Antiphospholipid syndrome (APS) is an autoimmune prothrombotic disorder characterized by the presence of antiphospholipid antibodies and clinical manifestations of recurrent venous or arterial thromboembolic events (1, 2). When occurring in the context of systemic lupus erythematosus (SLE), it is called secondary APS (3, 4).

Although SLE predominantly affects women of childbearing age, men may also experience severe thrombotic events (5–7). Respiratory involvement, such as pleural effusion, can coexist with thrombosis and mimic infectious processes, leading to delayed diagnosis and perhaps treatment (8, 9). This case report describes a young male patient presenting with deep vein thrombosis (DVT) and pleural effusion

as the first manifestation of SLE with APS, underscoring the importance of maintaining a broad differential in thromboembolic presentations.

CASE PRESENTATION

A married 34-year-old male, a fisherman by occupation, with a 14-pack-year smoking history and no known comorbidities, presented with complaints of one month of high-grade fever, left-sided chest pain for 12 days, and progressive swelling of the left lower limb for 5 days. The fever was documented as high grade (102°F), was sudden in onset, intermittent, and associated with chills, body aches, and a productive cough. The chest pain was sharp, non-radiating, and aggravated by coughing but relieved by postural change. The leg swelling appeared suddenly, progressed to involve the entire limb, and was painful on walking. There was no history of trauma, prolonged immobilization, recent surgery, or any chronic illness. Sexual history was positive for multiple partners, and there was no family history of autoimmune or thromboembolic disorders.

On examination, the patient was alert, well oriented, and vitally stable with a blood pressure of 120/70 mmHg, a pulse of 80 beats per minute, and a respiratory rate of 18 breaths per minute, and he maintained an oxygen saturation of 98% at room temperature. Mild pallor and right inguinal sub-centimetric lymph nodes were noted. Local examination of the left lower limb revealed pitting pedal edema extending up to the shins, associated with tenderness, warmth, and erythema. The left calf measured 38 cm in circumference, compared with 30 cm on the right. Pedal pulses were difficult to palpate because of edema, but there was no sensory or motor deficit. Respiratory exam demonstrated stony dull percussion, reduced air entry, and bronchial breathing with decreased vocal resonance at the left lung base. The rest of the systemic examination was unremarkable.

Significant laboratory results included a total leukocyte count of 17,000 cells/μL, ESR of 100 mm/hr, CRP of 205 mg/L, ferritin of 1992 ng/mL, serum iron level of 17 mcg/dL, and LDH of 263 U/L.

An ultrasound Doppler of the left lower limb revealed echogenic foci representing thrombus seen in the common femoral vein, extending to the superficial femoral and popliteal veins. Echocardiography showed a pulmonary artery pressure of 25 mmHg, while the rest of the scan was unremarkable. An X-ray of the chest revealed a homogeneous opacity in the left lower lung zone with blunting of the left costophrenic angle and obscuration of the left hemidiaphragm, consistent with a left-sided pleural effusion. (Fig. 1). A CT scan of the chest, abdomen, and pelvis revealed a left-sided pleural effusion, round atelectasis in the lateral basal segment of the left lower lobe, and no evidence of pulmonary embolism.

Immunologic testing revealed a positive ANA, positive lupus anticoagulant and markedly elevated anti-β2 glycoprotein I IgM levels, which, in combination with patient's clinical manifestations supported the diagnosis of SLE with secondary APS. (Table 1, 2)

Table 1

Summary of the 2019 EULAR/ACR systemic lupus erythematosus (SLE) classification criteria and the patient's respective clinical and immunologic findings.

Domain	2019 EULAR/ACR Criteria (Points)	Patient Finding	Score
Entry criterion	ANA ≥ 1:80 required	ANA positive (1:320)	Yes
Constitutional	Fever (2)	Fever for 30 days	2
Hematologic	Leukopenia (3), Thrombocytopenia (4), Autoimmune hemolysis (4)	None	0
Neuropsychiatric	Delirium (2), psychosis (3), seizure (5)	None	0
Mucocutaneous	Oral ulcers (2), Nonscarring alopecia (2), Acute cutaneous lupus (6), Subacute cutaneous OR discoid lupus (4)	None	0
Serosal	Pleural/pericardial effusion (5), acute pericarditis (6)	Left-sided pleural effusion	5
Musculoskeletal	Joint involvement (6)	None	0
Renal	Proteinuria > 0.5 g/day (4), Class II–V lupus nephritis (8–10)	None	0
Immunologic: Antiphospholipid	Anticardiolipin, anti-β2GPI, lupus anticoagulant (2)	Anti-β2GPI & lupus anticoagulant positive	2
Immunologic: Complement	Low C3 or low C4 (3), both low (4)	None	0
Immunologic: SLE-specific antibodies	Anti-dsDNA (6), Anti-Sm (6)	None	0
TOTAL	≥ 10 = SLE	Definite SLE	**9**

Table 2
2006 Revised Sapporo (Sydney) Criteria with corresponding patient findings.

Category	Criteria	Patient finding
Clinical	*Vascular thrombosis*	
	≥ 1 clinical episode of arterial, venous, or small-vessel thrombosis confirmed by imaging (e.g., Doppler, CT, MRI) or histopathology	Acute left-leg DVT confirmed clinically and by Doppler findings
	Pregnancy morbidity	
	≥ 1 unexplained deaths of a morphologically normal fetus at ≥ 10 weeks gestation	Not applicable
	≥ 1 premature birth < 34 weeks due to eclampsia, severe pre-eclampsia, or placental insufficiency.	
	≥ 3 consecutive unexplained spontaneous miscarriages < 10 weeks gestation	
Laboratory	Lupus anticoagulant present on ≥ 2 occasions ≥ 12 weeks apart	Positive
	Anticardiolipin IgG/IgM > 40 GPL/MPL or > 99th percentile present on ≥ 2 occasions ≥ 12 weeks apart	Negative
	Anti-β2 Glycoprotein I IgG/IgM > 99th percentile present on ≥ 2 occasions ≥ 12 weeks apart	Positive
APS is present if ≥ 1 clinical criteria and ≥ 1 laboratory criteria are met.		

The patient was treated with intravenous piperacillin/tazobactam 4.5 g three times daily, low-molecular-weight heparin (enoxaparin 40 mg subcutaneously twice daily), intravenous omeprazole 40 mg once daily, nebulized bronchodilators (ipratropium bromide and salbutamol every 6 hours), and inhaled corticosteroid (beclomethasone every 8 hours), along with oral folic acid 5 mg daily. Over one week, the fever subsided, the chest pain resolved, and the leg swelling markedly improved. The patient was discharged in stable condition on anticoagulation therapy and advised to follow up with rheumatology for initiation of long-term immunomodulatory treatment.

DISCUSSION

APS is a hypercoagulable state characterized by the presence of vascular thrombosis and/or obstetrical events in addition to the presence of autoantibodies, including lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein 1 antibodies (12, 13). Most patients with APS are diagnosed between the ages of 15 and 50 years (14, 15). When APS occurs with underlying systemic lupus erythematosus (SLE), it is termed secondary APS. The coexistence of these two debilitating disorders substantially increases the risk of thromboembolic events and potential end-organ damage (16).

A 34-year-old male, presented with unprovoked deep vein thrombosis (DVT) and left-sided pleural effusion, which led to the diagnosis of SLE with secondary APS. Although SLE mostly affects women, men are often diagnosed at an older age and may even exhibit more severe disease manifestations, including renal and thromboembolic complications (17). The mechanisms of thrombosis in APS involve activation of endothelial cells, deposition of complement proteins, platelet aggregation, and suppression of natural anticoagulant pathways (18). These processes collectively create a hypercoagulable environment that predisposes to venous and arterial thrombosis. When superimposed on SLE-related immune dysregulation, the risk of thromboembolic complications increases several fold.

Pleural effusion is the most common thoracic manifestation in SLE, reported in up to 50% of cases, often resulting from immune-complex–mediated pleuritis. However, in some cases, the effusion may be due to pulmonary embolism secondary to APS (19). In our patient, pleural effusion was exudative in nature, most likely due to inflammatory pleuritis, although a thromboembolic mechanism could not be entirely excluded. Secondary APS should be suspected when DVT or pulmonary embolism occurs alongside systemic symptoms such as fever, serositis, or cytopenias. Early identification is critical because thrombotic events in APS carry a high recurrence rate without adequate anticoagulation (20).

The mainstay of treatment for APS-associated thrombosis is long-term anticoagulation, traditionally with warfarin, although low-molecular-weight heparin (LMWH) is recommended during acute management. In cases secondary to SLE, immunomodulatory therapy is indicated to control systemic inflammation and prevent further antibody-mediated vascular injury (21). Our patient was treated with LMWH, antibiotics, and supportive therapy, with a good clinical response. Long-term management should include a smooth transition to oral anticoagulation and rheumatology follow-up for disease-modifying agents such as hydroxychloroquine or corticosteroids.

In the literature, a case report has described a rare presentation of systemic lupus erythematosus (SLE) with massive bilateral pleural effusions as the initial manifestation in a previously healthy 20-year-old soldier. Initial investigations were inconclusive; however, within three months, the patient developed the full clinical features of SLE and showed marked improvement following treatment with corticosteroids and cyclophosphamide, leading to complete resolution of the pleural effusions (22). A case series documented four cases of systemic lupus erythematosus (SLE) presenting with pleuritis as the initial disease manifestation; surprisingly, all of them were men (23). Another case was reported of a 31-year-old Black male who presented with recurrent pleural effusions secondary to active systemic lupus erythematosus (SLE**)** (24). A case report described a 38-year-old male with antiphospholipid syndrome (APS) who presented with deep vein thrombosis (DVT) and pleural effusion (8).

CONCLUSION

This case illustrates that SLE with secondary APS can present in males with isolated venous thrombosis and pleural effusion. The presentation emphasizes the need for autoimmune screening in young patients with unprovoked DVT or serositis. Early immunological evaluation and timely initiation of anticoagulation

are key to preventing recurrence and improving outcomes. Clinicians should remain vigilant for atypical presentations of autoimmune thrombotic disease, especially in high-risk environments where infectious etiologies are common mimickers and can delay diagnosis and thus treatment.

Abbreviations

APS
Antiphospholipid Syndrome
SLE
Systemic Lupus Erythematosus
DVT
Deep Vein Thrombosis
ESR
Erythrocyte Sedimentation Rate
CRP
C-Reactive Protein
LDH
Lactate Dehydrogenase
ANA
Antinuclear Antibody
IgA
Immunoglobulin A
IgM
Immunoglobulin M
IgG
Immunoglobulin G
LMWH
Low Molecular Weight Heparin

Declarations

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and publication was obtained from the head of the department

Availability of data and material: All data relevant to this case are contained within the manuscript.

Code availability: Not applicable

Compliance with Care Guidelines:

This report was prepared in accordance with the CARE (Consensus-based Clinical Case Reporting) guidelines; the completed CARE checklist is available upon request.

Contributorship: **SR** contributed to the conception and design of the study, acquisition of clinical data, and drafting of the manuscript. **AA** contributed to literature review, data interpretation, and manuscript drafting. **HK** contributed to data collection, literature review, and manuscript preparation.
MTA contributed to critical revision of the manuscript for important intellectual content.
SMK contributed to supervision, data interpretation, and critical review of the manuscript. **UY** contributed to the conception of the study, overall supervision, critical revision, and final approval of the manuscript.

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Written informed consent for participation and publication of anonymized clinical details was obtained from the patient.

References

1. Wysokinska E, Ortel TL. Antiphospholipid syndrome. In: *Elsevier eBooks* [Internet]. 2019 [cited 2026 Feb 12]. pp. 374–95. Available from: https://doi.org/10.1016/b978-0-323-46202-0.00020-0
2. Ivan GP. An insight into the pathophysiology of thrombosis in antiphospholipid syndrome. Frontiers in Bioscience [Internet]. 2007 Jan 1 [cited 2026 Feb 12];12(8–12):3093. Available from: https://doi.org/10.2741/2297
3. Rodríguez-Pintó I, Espinosa G, Cervera R. The catastrophic antiphospholipid syndrome. In: Rare diseases of the immune system [Internet]. 2014 [cited 2026 Feb 12]. pp. 249–62. Available from: https://doi.org/10.1007/978-3-319-11044-8_20
4. Agmon-Levin N, Shoenfeld Y. The spectrum between antiphospholipid syndrome and systemic lupus erythematosus. Clinical Rheumatology [Internet]. 2014 Jan 16 [cited 2026 Feb 12];33(3):293–5. Available from: https://doi.org/10.1007/s10067-014-2486-5
5. Singhal S, Jotwani P, Gupta S, Srikaram P, Desai D, Styler M. Prevalence, demographics, and mortality/morbidity of thrombotic events: A nationwide study of SLE patients in the United States. Journal of Thrombosis and Thrombolysis [Internet]. 2025 Oct 25 [cited 2026 Feb 12]; Available from: https://doi.org/10.1007/s11239-025-03200-4

6. Specker C, Becker A, Lakomek HJ, Bach D, Grabensee B. [Systemic lupus erythematosus in men–a different prognosis?]. Z Rheumatol. 1994;53(6):339–45. PMID: 7871906.
7. Thomas R, Jawad AS. Systemic lupus erythematosus: rarer in men than women but more severe. Trends in Urology & Men S Health [Internet]. 2022 Sep 1[cited 2026 Feb 12];13(5):11–4. Available from: https://doi.org/10.1002/tre.876
8. Bhutda S, Acharya S, Taori B, Bhutda S, Sharma R, OF CLINICAL AND DIAGNOSTIC RESEARCH [Internet]. Antiphospholipid syndrome complicated by unilateral pleural effusion and deep vein thrombosis: a case report. JOURNAL. 2023 Jan 1[cited 2026 Feb 12]; Available from: http://dx.doi.org/10.7860/jcdr/2023/65303.18624
9. Amarnani R, Yeoh SA, Denneny EK, Wincup C. Lupus and the lungs: The assessment and management of pulmonary manifestations of systemic lupus erythematosus. Frontiers in Medicine [Internet]. 2021 Jan 18 [cited 2026 Feb 12];7:610257. Available from: https://doi.org/10.3389/fmed.2020.610257
10. Gupta V, Singla T, Singh B, Mohan B. Antiphospholipid antibody syndrome presenting as pulmonary embolism in a young male. Journal of the Practice of Cardiovascular Sciences [Internet]. 2020 Jan 1[cited 2026 Feb 12];6(1):75–7. Available from: https://doi.org/10.4103/jpcs.jpcs_66_19
11. Wang DY, Chang DB, Kuo SH, Yang S, Shiah DC, Chou HT, Luh KT. Systemic lupus erythematosus presenting as pleural effusion: report of a case. J Formos Med Assoc. 1995;94(12):746–9. PMID: 8541737. [cited 2026 Feb 12].
12. Chaturvedi S, McCrae KR. Diagnosis and management of the antiphospholipid syndrome. Blood Reviews [Internet]. 2017 Jul 30 [cited 2026 Feb 12];31(6):406–17. Available from: https://doi.org/10.1016/j.blre.2017.07.006
13. Arreola-Diaz R, Majluf-Cruz A, Sanchez-Torres L, Hernandez-Juarez J. The Pathophysiology of the antiphospholipid Syndrome: A perspective from the blood coagulation system. Clinical and Applied Thrombosis/Hemostasis [Internet]. 2022 Jan 1[cited 2026 Feb 12];28:10760296221088576. Available from: https://doi.org/10.1177/10760296221088576
14. Cervera R, Piette J, Font J, Khamashta MA, Shoenfeld Y, Camps MT et al. Antiphospholipid syndrome: Clinical and immunologic manifestations and patterns of disease expression in a cohort of 1,000 patients. Arthritis & Rheumatism [Internet]. 2002 Apr 1[cited 2026 Feb 12];46(4):1019–27. Available from: https://doi.org/10.1002/art.10187
15. Capelusnik D, Ramiro S, Nikiphorou E, Maksymowych WP, Magrey M, Marzo-Ortega H, AB0198 THRESHOLDS OF PRESENTEEISM MEASUREMENT INSTRUMENTS FOR UNACCEPTABLE WORK PARTICIPATION AND FUTURE ADVERSE WORK OUTCOMES IN RA. Annals of the Rheumatic Diseases [Internet]. 2023 Jun 1[cited 2026 Feb 12];82:1281–2. Available from: https://doi.org/10.1136/annrheumdis-2023-eular.2823
16. Garcia-Diaz J, Escudero-Salamanca M, Alvarez-Santana R, Espinola-Zavaleta N. Catastrophic Antiphospholipid Syndrome Associated With Systemic Lupus Erythematosus: A case-based Review.

Future Cardiology [Internet]. 2020 Nov 3[cited 2026 Feb 12];17(6):985–90. Available from: https://doi.org/10.2217/fca-2020-0145

17. Specker C, Becker A, Lakomek HJ, Bach D, Grabensee B. [Systemic lupus erythematosus in men — a different prognosis?]. Z Rheumatol. 1994;53(6):339–45. PMID: 7871906. [cited 2026 Feb 12].
18. Pierangeli SS, Vega-Ostertag M, Liu X, Girardi G. Complement activation: a novel pathogenic mechanism in the antiphospholipid syndrome. Annals of the New York Academy of Sciences [Internet]. 2005 Jun 1[cited 2026 Feb 12];1051(1):413–20. Available from: https://doi.org/10.1196/annals.1361.083
19. Mulherin D, Bresnihan B. Systemic lupus erythematosus. Baillière S Clinical Rheumatology [Internet]. 1993 Feb 1[cited 2026 Feb 12];7(1):31–57. Available from: https://doi.org/10.1016/s0950-3579(05)80267-5
20. Koike T. Anticardiolipin Antibodies in NZW x BXSB F1 Mice. Lupus [Internet]. 1994 Aug 1[cited 2026 Feb 12];3(4):241–6. Available from: https://doi.org/10.1177/096120339400300407
21. Hewagama A, Richardson B. The genetics and epigenetics of autoimmune diseases. Journal of Autoimmunity [Internet]. 2009 Apr 6 [cited 2026 Feb 12];33(1):3–11. Available from: https://doi.org/10.1016/j.jaut.2009.03.007
22. Stamm E. Die Insulinempfindlichkeit des nichtdiabetischen Menschen und ihre Beziehung zum vegetativen Nervensystem. Digestion [Internet]. 1930 Jan 1[cited 2026 Feb 12];48(1–2):104–24. Available from: https://doi.org/10.1159/000195982
23. Edahiro Y, Ando J, Suzuki T, Fukumura Y, Masuda A, Sakayori S et al. Multiple Placental Infarcts in a Pregnant Woman with Essential Thrombocythemia. Internal Medicine [Internet]. 2018 Aug 9 [cited 2026 Feb 12];57(24):3647–50. Available from: https://doi.org/10.2169/internalmedicine.1311-18
24. Kaine JL. Refractory massive pleural effusion in systemic lupus erythematosus treated with talc poudrage. Annals of the Rheumatic Diseases [Internet]. 1985 Jan 1[cited 2026 Feb 12];44(1):61–4. Available from: https://doi.org/10.1136/ard.44.1.61

Figures

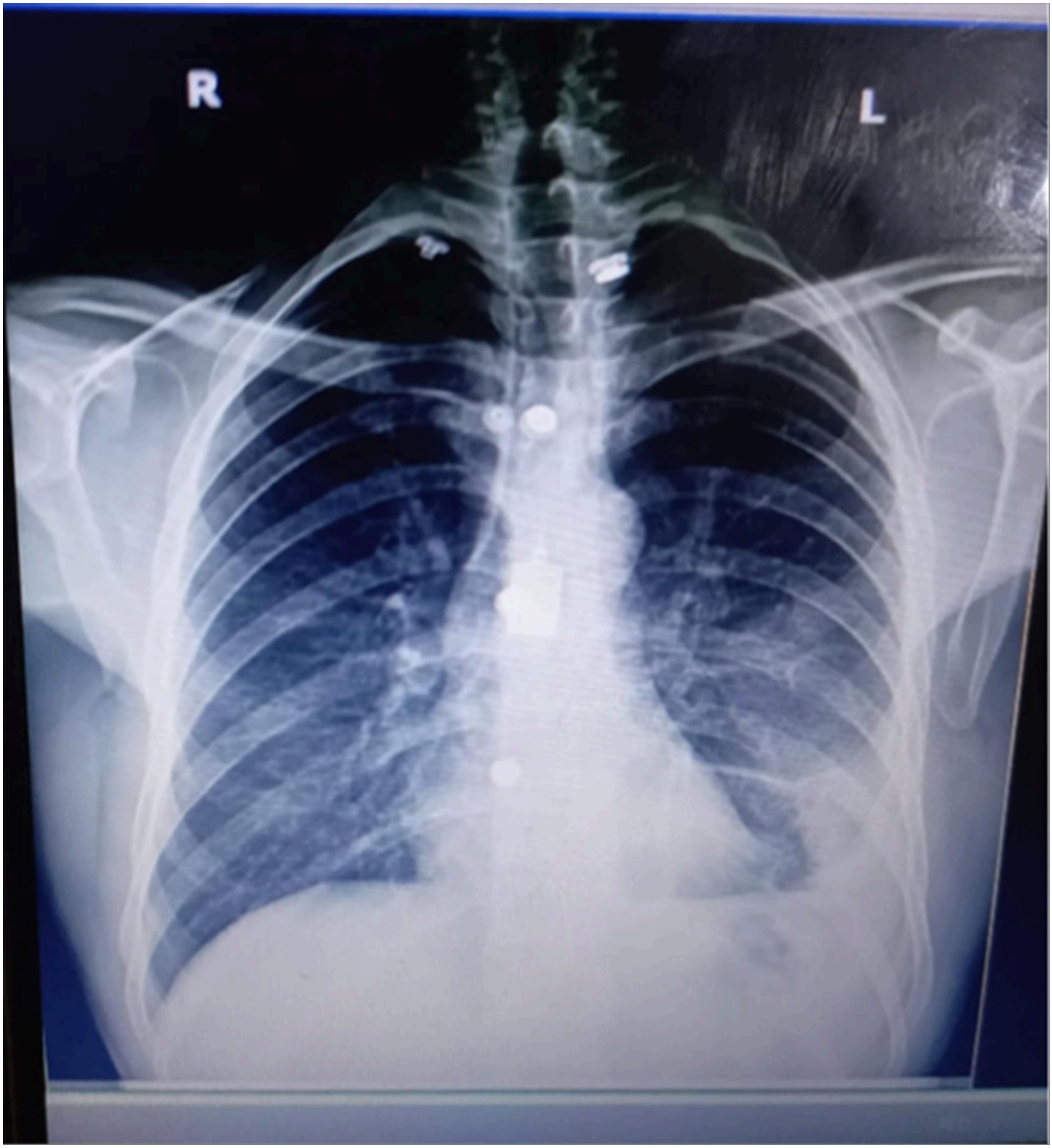


Figure 1

Chest X-ray demonstrating homogeneous opacity in the left lower lung zone with blunting of the left costophrenic angle and obscuration of the left hemidiaphragm, consistent with a left-sided pleural effusion.