RESEARCH PAPER

A Tempest of the Immune System: Primary Antiphospholipid Antibody Syndrome Presenting as Evans Syndrome, Pulmonary Embolism, Tricuspid Valve Mass, and Hypocomplementemia in an Adolescent Female: A Case Report

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ABSTRACT

We report a diagnostically challenging case of acute respiratory distress in a 17-year-old girl with primary antiphospholipid antibody syndrome (APLA). This patient presented with Evans syndrome (immune cytopenia due to autoimmune hemolytic anemia [AIHA] plus immune thrombocytopenia [ITP]), an acute bilateral pulmonary embolism and a mobile mass on the tricuspid valve per ultrasound at initial assessment. Multiple laboratory investigations revealed she had three antiphospholipid antibody positives: lupus anticoagulant (LA), anti-cardiolipin IgG (aCL), and anti-(β2-glycoprotein I [anti-(β2GPI)] thus fulfilling revised Sydney criteria for APLA. Additionally, hypocomplementemia was present suggesting possible complement cascade activation that may have contributed to disease severity. The severe blood-related and clotting-related findings in this child without systemic lupus erythematosus (SLE) demonstrate the aggressive and various manifestations of primary APLA. The findings in this report create a more extensive understanding of adolescent-onset primary APLA with concurrent Evans' syndrome, thromboembolic events and cardiac valve involvement; they stress the importance of early identification of the disease through a multi-disciplinary approach and continued follow-up over time.

Keywords: Primary Antiphospholipid Antibody Syndrome; Evans Syndrome; Autoimmune Haemolytic Anaemia; Pulmonary Embolism; Tricuspid Valve; Hypocomplementemia; Adolescent

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INTRODUCTION

Antiphospholipid antibody syndrome (APLA) is a systemic autoimmune thrombophilia characterised by the persistent presence of antiphospholipid antibodies (aPL) and associated clinical manifestations including arterial and venous thromboses and, in women of reproductive age, recurrent pregnancy morbidity [1]. When occurring in the absence of an identifiable underlying autoimmune disease such as systemic lupus erythematosus (SLE), it is classified as primary APLA. The revised Sapporo (Sydney) classification criteria require at least one clinical criterion vascular thrombosis or pregnancy morbidity and at least one laboratory criterion: lupus anticoagulant (LA), anticardiolipin antibodies (aCL) of IgG or IgM isotype, or anti-β2-glycoprotein I antibodies (anti-β2GPI) of IgG or IgM isotype, confirmed on two occasions at least 12 weeks apart [2].

The clinical spectrum of APLA is broad and may involve virtually any organ system. Beyond thrombosis, haematologic manifestations, most notably immune thrombocytopenia (ITP) and autoimmune haemolytic anaemia (AIHA) occur in a significant subset of patients [3]. Evans syndrome, defined by the simultaneous or sequential occurrence of AIHA and ITP, is a well-recognised but uncommon association with APLA and has been described both in secondary APLA (in the context of SLE) and, more rarely, in primary APLA [4]. The pathogenesis of haematologic cytopenias in APLA likely involves direct antibody-mediated destruction of red cells and platelets, as well as complement-dependent mechanisms [5].

Cardiac manifestations of APLA include valvular abnormalities, most classically Libman–Sacks

endocarditis, which typically involves the mitral valve but has been described on all four cardiac valves [6]. Valvular lesions in APLA are characterised as sterile non-bacterial thrombotic endocarditis (NBTE) and may serve as a source of systemic emboli, thereby perpetuating the thrombotic milieu. Pulmonary embolism is among the most common venous thrombotic events in APLA and may occur even in the setting of thrombocytopenia, reflecting the paradoxical pro-thrombotic nature of this disorder [7].

Hypocomplementemia, though classically associated with SLE, has been increasingly recognised in primary APLA, particularly in patients with severe or catastrophic manifestations. Complement activation through the classical and alternative pathways has been implicated in the amplification of thrombosis and endothelial injury in aPL-positive patients [8]. Adolescent-onset primary APLA presenting with the full constellation of Evans syndrome, venous thromboembolism, valvular mass, and hypocomplementemia is extremely rare, with only isolated reports in the literature.

We report such a case, emphasising the diagnostic challenges inherent in multi-systemic presentations of primary APLA in young patients and the importance of a structured, multidisciplinary approach to diagnosis and management.

CASE REPORT

A 17-year-old female with no prior medical history was referred to our tertiary care centre with a three-day history of progressive breathlessness and productive cough, and one day of acute chest pain with palpitations. There was no personal or family history of autoimmune disease, prior thrombosis, or pregnancy-related complications. The patient attained menarche at 13 years of age with regular menstrual cycles occurring every 28–30 days, lasting 4–5 days with normal flow. There was no history of menorrhagia or intermenstrual bleeding. There were no prior documented episodes of cytopenias, bleeding tendencies, or thrombotic events .Family history was negative for autoimmune diseases, thrombophilia, or hematological disorders. Written informed consent was obtained from the patient's guardian for the publication of anonymised data.

The emergency department did an initial evaluation of the patient to assess for acute ischemic changes on ECG and none were identified. They performed a transthoracic echocardiogram (TTE) and demonstrated with the 2D imaging that there were no wall motion abnormalities, normal left ventricular ejection fraction, right atrium and right ventricle were enlarged, and demonstrated a small trace pericardial effusion and no evidence of thrombus in the atrium. The patient was experiencing respiratory distress that had not improved; therefore, the pulmonologist was consulted and a CT pulmonary angiogram (CTPA) was completed. The patient was transferred to the medical intensive care unit for monitoring.

Upon transferring to the ICU, the patient was alert, orientated with vital signs including a heart rate of 100 beats per minute, blood pressure of 130/60mmHg, respiratory rate of 28 breaths per minute, and oxygen saturation of 98% room air. Physical exam findings are included in Table 1. On examination, the patient was pale with mild icterus. There was no lymphadenopathy.

Abdominal examination revealed mild splenomegaly (spleen palpable 2 cm below left costal margin).

Cardiovascular examination showed tachycardia with normal heart sounds and no murmurs.

Respiratory examination revealed bilateral basal crepitations.

No peripheral edema or signs of deep vein thrombosis were noted. Thrombocytopenia: Laboratory investigations revealed a severe level of thrombocytopenia at 19400/μL, with reference to a thorough chronological summary of the patient's clinical events and laboratory investigation results being made available (Table 1). The continued presence of thrombocytopenia necessitating repeated platelet transfusions. Direct Antiglobulin Test (DAT/Coombs test): Positive (IgG type)

Peripheral smear: Normocytic normochromic anemia with spherocytes and polychromasia

Reticulocyte count: 6.5% (elevated) ,LDH: 780 U/L (elevated; normal <250 U/L),Serum haptoglobin: <10 mg/dL (reduced),Indirect bilirubin: 2.4 mg/dL (elevated) ,Serial hemoglobin trend: Day 1: 8.2 g/dL , Day 3: 7.4 g/dL ,Day 5: 9.1 g/dL (post steroids) .

Cardiovascular findings: Another 2D TTE was done on day +1 of ICU admission revealing a pedunculated mass (1.6 × 0.9 cm) free floating off the tricuspid valve leaflet raising concern for thrombus vs vegetation. Mild right ventricular dysfunction with continuing dilation of the right atrium and right ventricle was also seen (Figure 1). Infective endocarditis was ruled out based upon the presence of negative blood cultures, as well as the absence of typical Duke criteria. Cardiac MRI was planned for further characterisation of the tricuspid valve mass; however, it could not be performed during the acute phase due to clinical instability and resource limitations. This remains a limitation of the present case.

CTPA identified an acute pulmonary embolism in the bilateral lower lobe pulmonary arteries and segmental branches that was classified as intermediate risk. There were diffuse ground-glass opacities in the bilateral upper lobes, the right middle lobe and the superior segment of the right lower lobe with evidence of patchy changes that appeared as subtle bilateral basal patches that likely

represent pulmonary edema or aspiration pneumonia (as seen in Figure 2). The main and right pulmonary arteries were described as being dilated, which could suggest that pulmonary hypertension exists. An uncertain or questionable thrombus was present in the IVC-right atrium junction. Deep vein thrombosis was ruled out by Doppler examination of the lower limbs bilaterally.

Immunological findings: Antinuclear antibody (ANA) screening was weakly positive at 1:100 with cytoplasmic fluorescence. Anti-dsDNA antibodies: Negative (<10 IU/mL) and Anti-Smith (anti-Sm) antibodies: Negative **.**The antiphospholipid antibody profile demonstrated triple positivity: lupus anticoagulant (positive), anticardiolipin IgG (positive), and anti-β2-glycoprotein I IgG (positive), meeting laboratory criteria for APLA syndrome [2]. Complement levels were reduced - C3: 58 mg/dL (normal: 90–180 mg/dL) and C4: 9 mg/dL (normal: 10–40 mg/dL).A full laboratory summary is provided in Table 2.

Ophthalmological assessment: Fundoscopic examination revealed no evidence of retinopathy or thrombotic ocular manifestations.

Management and Clinical Course

The patient's acute management prioritised treatment of intermediate-risk pulmonary embolism with therapeutic anticoagulation using low-molecular-weight heparin (enoxaparin). Given concurrent severe thrombocytopenia, platelet transfusions were administered to maintain haemostasis. The detection of the tricuspid valve mass initially prompted empirical antibiotic coverage for infective endocarditis pending blood culture results; however, all cultures remained sterile and antibiotics were subsequently discontinued.

High-dose corticosteroid therapy was initiated with intravenous dexamethasone (40 mg/day for 4 days), followed by pulse methylprednisolone (1 g/day for 3 consecutive days). This was subsequently transitioned to oral prednisolone (1 mg/kg/day) with gradual tapering over 6–8 weeks based on clinical response. Hydroxychloroquine was initiated at a dose of 200 mg twice daily as adjunctive therapy in view of high-risk triple-positive APLA.

Cardiology recommended continuation of anticoagulation with a planned transition to warfarin with a target INR of 2–3. A target INR of 2–3 was initially selected due to concurrent severe thrombocytopenia and bleeding risk. However, escalation to a higher INR target (3–4) or addition of low-dose aspirin is planned upon stabilization of platelet counts, in accordance with EULAR 2019 recommendations for high-risk APLA.

The patient showed significant clinical improvement with resolution of dyspnoea and stabilization of vital parameters. Platelet counts improved from 19,400/μL to 110,000/μL over 7 days. Hemoglobin improved to 10.2 g/dL.

Repeat echocardiography after 2 weeks demonstrated a reduction in the size of the tricuspid valve mass to 0.8 × 0.4 cm and was discharged on Oral warfarin with INR monitoring (target 2–3 initially) , Oral prednisolone (tapering dose) , Hydroxychloroquine 200 mg twice daily, Calcium and vitamin D supplementation. Follow-up was advised with rheumatology, cardiology, and hematology. Regular monitoring of INR, platelet counts, and hemoglobin was planned. Repeat APLA antibody testing at 12 weeks post-initial testing is required to confirm persistent positivity per Sydney criteria [2].

Repeat antiphospholipid antibody testing at 12 weeks confirmed persistent positivity:Lupus anticoagulant: Positive , Anticardiolipin IgG: 78 GPL units (positive >40), Anti-β2 glycoprotein I IgG: 65 SGU (positive >40) .This confirmed the diagnosis of definite antiphospholipid antibody syndrome as per revised Sydney criteria.

DISCUSSION

This case illustrates a rare and clinically formidable presentation of primary APLA syndrome in a young female, combining Evans syndrome, acute bilateral pulmonary embolism, a tricuspid valve mass, and hypocomplementemia. Each individual feature has been described in association with APLA, but their simultaneous occurrence at disease onset in an adolescent without underlying SLE is exceptionally uncommon and warrants detailed discussion.

Primary APLA in adolescents. Primary APLA is predominantly a disease of young to middle-aged women, but paediatric and adolescent-onset cases are increasingly recognised. A large European cohort study found that approximately 2.8% of APLA patients have onset before the age of 18 years, with venous thromboembolism being the most frequent presenting event [3]. Adolescent-onset cases tend to present with a higher burden of thrombotic events and a greater likelihood of triple positivity, which carries the highest risk of recurrent thrombosis and mortality [9]. Triple positivity - defined as simultaneous positivity for LA, aCL, and anti-β2GPI - confers a substantially elevated thrombotic risk compared to single or double positivity, and its identification in this patient underscores the urgency of aggressive anticoagulation and long-term immunomodulation [10].

Evans syndrome as an initial manifestation of primary APLA. Evans syndrome - the co-occurrence of AIHA and immune thrombocytopenia - has traditionally been associated with SLE and common variable immunodeficiency, but its occurrence as an initial manifestation of primary APLA is distinctly uncommon [4]. Michel et al. reported that approximately 12% of patients with Evans syndrome harbour antiphospholipid

antibodies, though the full clinical overlap with primary APLA is not always evaluated [4]. Mechanistically, aPL antibodies can coat erythrocytes and platelets, promoting complement-mediated lysis and reticuloendothelial clearance, thereby inducing cytopenias even in a pro-thrombotic milieu [5]. This paradox - simultaneous haemorrhagic risk from thrombocytopenia and thrombotic risk from aPL - represents a unique therapeutic challenge, as anticoagulation must be balanced against the bleeding risk imposed by low platelet counts. In our patient, thrombocytopenia was severe (nadir 19,400/μL), yet the thrombotic burden necessitated anticoagulation.

Pulmonary embolism and right heart strain in APLA. Pulmonary embolism is one of the most common venous thrombotic events in APLA, occurring in up to 14% of APLA patients in large registry studies [3]. In this patient, bilateral lower lobe PE with right heart strain and possible IVC thrombus at its right atrial junction indicates a significant clot burden consistent with the high-risk antibody profile. The presence of right ventricular dilatation and dysfunction, along with contrast reflux into the intrahepatic IVC on CTPA, denotes haemodynamic compromise and classifies this as intermediate-high risk PE according to ESC 2019 guidelines [7]. The management with anticoagulation alone was appropriate. Although systemic thrombolysis could be considered in intermediate-high risk pulmonary embolism, it was deferred in this case due to severe thrombocytopenia and the associated high bleeding risk

Tricuspid valve mass and non-bacterial thrombotic endocarditis. Valvular lesions are well-recognised cardiac manifestations of APLA, occurring in up to 30–40% of patients on echocardiographic screening in some series [6]. Libman–Sacks endocarditis (LSE), the prototypical valvular manifestation, classically involves the mitral and aortic valves. Isolated tricuspid valve involvement is less commonly described but has been reported in APLA patients, usually presenting as non-bacterial thrombotic endocarditis (NBTE) [6]. The mobile, pedunculated morphology and negative blood cultures in our patient are consistent with NBTE rather than infective endocarditis. Although LSE is most frequently described in SLE-associated APLA, isolated reports document similar lesions in primary APLA, supporting a direct role of aPL antibodies in endothelial injury and thrombus formation on valve leaflets [11]. The recommended investigation to definitively characterise valvular masses in this context-cardiac MRI- was planned but could not be performed, which represents a limitation of the present report

Hypocomplementemia in primary APLA. The presence of low complement levels in a patient without SLE is noteworthy and pathophysiologically significant. Complement activation has emerged as a key mechanism in the amplification of aPL-mediated thrombosis. Girardi et al. demonstrated in animal models that complement activation - particularly generation of C5a - is essential for aPL-induced fetal loss and thrombosis, and that complement inhibition can abrogate these effects [8]. In human studies, complement consumption (low C3 and/or C4) has been documented in primary APLA patients during acute thrombotic events, suggesting active complement utilisation [12]. The severity of multi-system involvement in this patient may reflect complement-amplified endothelial damage superimposed on direct aPL-mediated thrombophilia.

Exclusion of SLE and classification as primary APLA. The distinction between primary and secondary APLA has important prognostic and therapeutic implications. In our patient, ANA was weakly positive at 1:100 - a finding that can be seen in up to 25–30% of primary APLA patients and does not, in isolation, indicate SLE [13]. However, rigorous exclusion of SLE requires assessment of all 2019 EULAR/ACR classification criteria, including anti-dsDNA and anti-Sm antibodies, complement levels, full blood count interpretation, renal and skin involvement, serositis, and haematologic criteria [14]. **Management considerations and guideline alignment.** Current EULAR 2019 recommendations for APLA advocate indefinite anticoagulation with vitamin K antagonists (VKA) for patients with confirmed APLA and thrombotic events [15]. For high-risk patients - particularly those with triple positivity or arterial thrombosis - a target INR of 3.0 or higher may be preferable, and hydroxychloroquine is recommended as an adjunctive agent due to its anti-thrombotic and immunomodulatory properties [15]. The rationale for choosing a target INR of 2–3 in a triple-positive patient with life-threatening VTE and valvular involvement should be explicitly justified by the authors. Additionally, the use of direct oral anticoagulants (DOACs) is not recommended in high-risk triple-positive APLA, and the manuscript should confirm that warfarin rather than a DOAC was chosen for long-term anticoagulation. The corticosteroid regimen for Evans syndrome was appropriate; however, discussion of steroid-sparing agents (e.g., rituximab for refractory AIHA/ITP, mycophenolate mofetil for immunosuppression) should be included, as long-term corticosteroid use carries significant morbidity in a young patient.

Limitations and future directions. This case report has several important limitations. The diagnosis of Evans syndrome rests on clinical inference without complete documentation of AIHA markers. Quantitative complement data are absent. The cardiac MRI to characterise the tricuspid valve mass has not yet been performed or reported. Although repeat APLA positivity was confirmed at 12 weeks, long-term follow-up data on clinical response, platelet recovery, and resolution of thrombotic events are lacking. Despite these limitations, this case raises important clinical questions regarding the

pathophysiological interplay between complement activation, aPL-mediated thrombosis, and immune cytopenia in adolescent-onset primary APLA, and highlights the need for prospective registries and longer follow-up in this rare patient population.

CONCLUSION

This case describes an exceptionally rare multi-systemic presentation of primary APLA syndrome in a 17-year-old female, encompassing Evans syndrome, bilateral pulmonary embolism with right heart strain, a tricuspid valve mass consistent with non-bacterial thrombotic endocarditis, and hypocomplementemia. Triple-positive antiphospholipid antibodies were confirmed, meeting diagnostic criteria for primary APLA. Management required a multidisciplinary approach involving rheumatology, haematology, cardiology, pulmonology, and critical care. This case underscores the importance of maintaining a high index of suspicion for primary APLA in young patients with overlapping thrombotic and haematologic presentations and emphasises the need for systematic workup including complete AIHA markers, SLE exclusion serologies, complement quantification, cardiac MRI, and rigorous long-term follow-up.

Figure Legends

Figure 1. (A and B) Two-dimensional transthoracic echocardiogram demonstrating a mobile, pedunculated mass measuring 1.6 × 0.9 cm attached to the tricuspid valve leaflet, consistent with non-bacterial thrombotic endocarditis in the context of primary antiphospholipid antibody syndrome. Right atrial and right ventricular dilatation with mild right ventricular dysfunction are also noted.

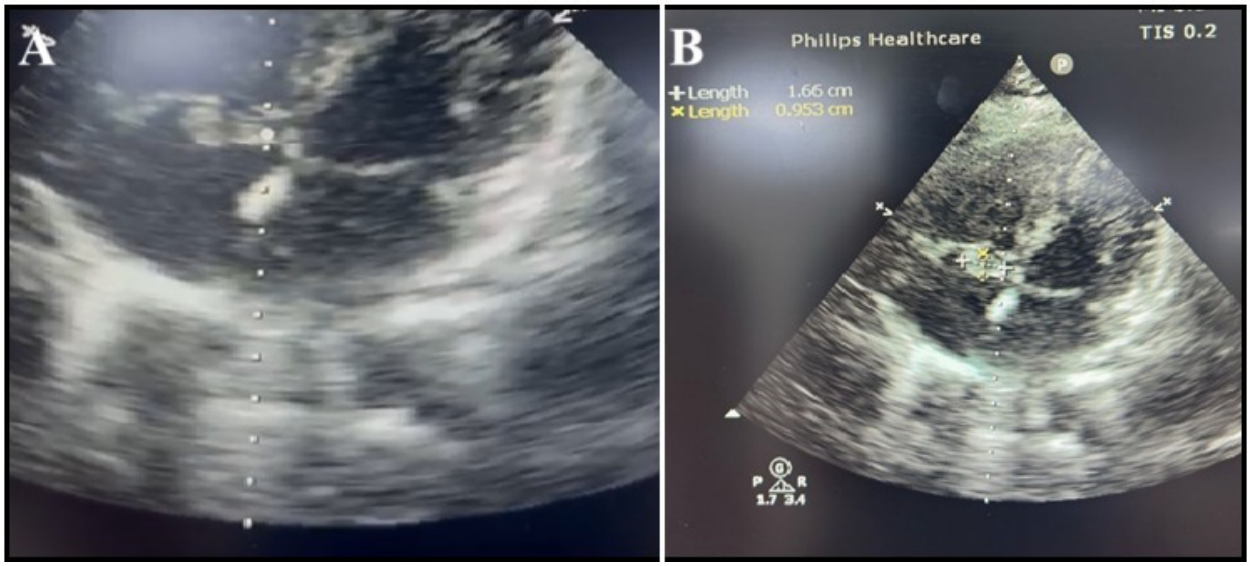

Figure 2. (A and B) Computed tomography pulmonary angiography (CTPA) demonstrating acute thromboembolism involving bilateral lower lobe pulmonary arteries and segmental branches. Diffuse ground-glass opacities in the

bilateral upper lobes and right middle lobe are also visible, consistent with pulmonary oedema or aspiration pneumonitis. Dilatation of the main and right pulmonary arteries suggests secondary pulmonary hypertension.

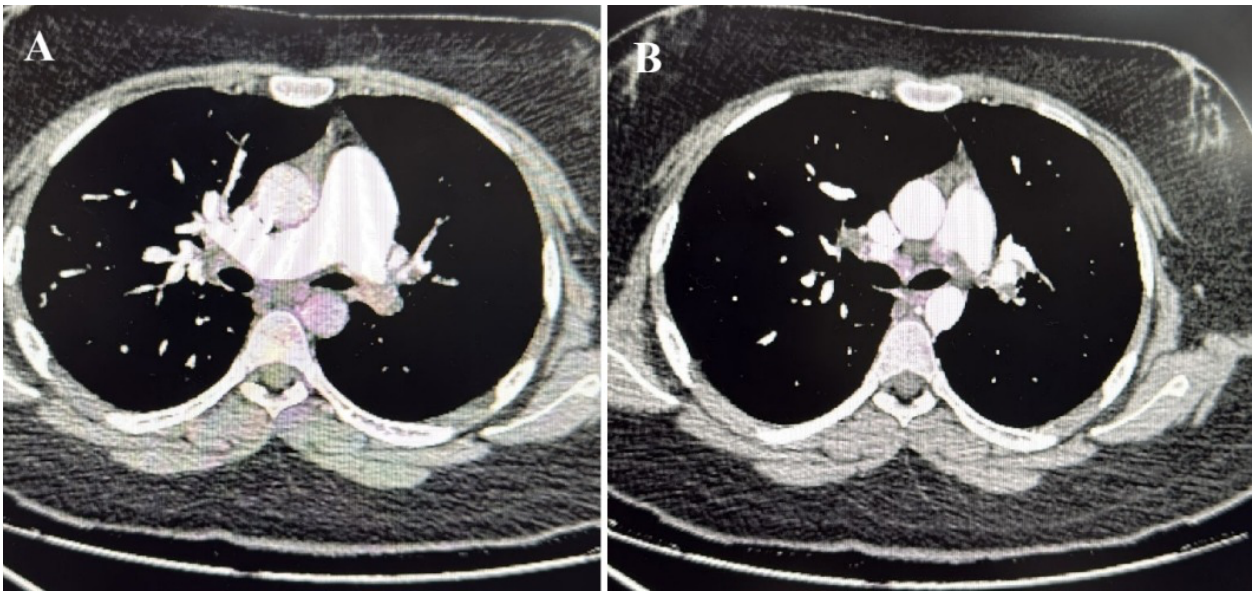

Table 1. Timeline of Clinical Events

Day	Event / Clinical Status	Investigations / Imaging	Management
Day -3	Onset of breathlessness, cough with expectoration	-	-
Day -1	Onset of chest pain and palpitations	-	-
Day 0	Presentation to emergency department; hemodynamically stable; no ischemic changes on ECG	2D Echo: Dilated RA/RV, preserved EF, no intracardiac thrombus	Pulmonology consult; CTPA advised
Day +1	Transferred to ICU; respiratory distress persists	CBC: Platelets 19,400/µL	Platelet transfusions initiated
Day +2	Persistent respiratory distress	CTPA: Bilateral pulmonary embolism, ground-glass opacities, suspicious thrombus at IVC–RA junction	Therapeutic enoxaparin initiated; oxygen monitoring
Day +3	Ongoing symptoms	Repeat 2D Echo: Pedunculated tricuspid valve mass (1.6 × 0.9 cm)	Infective endocarditis considered; cardiology evaluation
Day +4	Autoimmune workup initiated	ANA weakly positive; APLA profile: triple positivity (LA, aCL IgG, anti-β2GPI IgG)	Intravenous dexamethasone initiated (40 mg/day)
Day +5–7	Persistent thrombocytopenia; Evans syndrome confirmed	DAT positive; LDH elevated (780 U/L); indirect bilirubin elevated (2.4 mg/dL); reticulocytosis present; low complement levels (C3 58 mg/dL, C4 9 mg/dL)	Pulse IV methylprednisolone (1 g/day × 3 days), followed by oral prednisolone

Day +8	Clinical stabilization	-	Transition to warfarin planned (bridging therapy); cardiac MRI advised
Day +10–14	Clinical improvement	Platelets improved to >100,000/µL; hemoglobin improving	Continued anticoagulation and steroid therapy
2 weeks	Follow-up imaging	Repeat 2D Echo: Reduction in tricuspid valve mass (0.8 × 0.4 cm)	Continued medical management
12 weeks	Follow-up evaluation	Repeat APLA profile: persistent triple positivity	Diagnosis of definite APLA confirmed

Table 2: Laboratory investigations

Parameter	**Result**	**Interpretation**
Hemoglobin	8.2–10.2 g/dL (trend: 8.2 → 7.4 → 9.1 → 10.2)	Anemia with improvement post-treatment
Platelets	19,400/µL (initial) → 110,000/µL	Severe thrombocytopenia, improving
WBC	10,710/µL	Within normal limits
Reticulocyte count	6.5%	Elevated (hemolysis)
Peripheral smear	Normocytic normochromic anemia with spherocytes and polychromasia	Suggestive of hemolysis
Direct Coombs test (DAT)	Positive (IgG type)	Confirms autoimmune hemolysis
LDH	780 U/L	Elevated (hemolysis marker)
Indirect bilirubin	2.4 mg/dL	Elevated (hemolysis)
Serum haptoglobin	<10 mg/dL	Reduced (hemolysis)
ANA	Positive (1:100, cytoplasmic)	Suggests autoimmune process
Anti-dsDNA	Negative (<10 IU/mL)	SLE unlikely
Anti-Smith (anti-Sm)	Negative	SLE unlikely
Lupus anticoagulant	Positive	APLA laboratory criterion
Anticardiolipin IgG	Positive (78 GPL units)	APLA laboratory criterion
Anti-β2 glycoprotein I IgG	Positive (65 SGU)	APLA laboratory criterion
Complement C3	58 mg/dL	Low (hypocomplementemia)
Complement C4	9 mg/dL	Low (hypocomplementemia)
D-dimer	Elevated	Consistent with thrombosis
Blood cultures	No growth	Infective endocarditis excluded

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