Case Report

Diagnostic Challenges of Antiphospholipid Syndrome in Recurrent Pregnancy Loss: A Case Report

Ni Luh Lany Christina Prajawati, Artha Falentin Putri Susilo
[1]Department of Obstetrics and Gynecology, Dr. Hasan Sadikin General Hospital/Faculty of Medicine Universitas Padjadjaran, Bandung, Indonesia
Correspondence: Ni Luh Lany Christina Prajawati, Email: lanychrisrina1987@yahoo.com
Received: October 16, 2025 | Accepted: July 6, 2026 | Published: July 10, 2026

Abstract
Introduction: Recurrent pregnancy loss is a complex condition that affects a small number of women, with antiphospholipid syndrome being a well-recognized cause. Antiphospholipid syndrome is an autoimmune disorder associated with vascular thrombosis and pregnancy complications.
Case report: We present a 23-year-old woman with four consecutive pregnancy losses and cerebral venous sinus thrombosis. Despite an initial inability to fully confirm APS using the Sydney criteria due to resource limitations that hindered repeated laboratory testing, consultation with the rheumatology department led to a diagnosis based on the European Alliance of Associations for Rheumatology and American College of Rheumatology (ACR/EULAR) 2023 criteria. This case highlights the diagnostic challenges of antiphospholipid syndrome, especially in low-resource settings where repeat laboratory testing is often not feasible, underscoring the importance of alternative classification systems for confirming antiphospholipid syndrome when standard criteria cannot be met. Further research is necessary to validate the ACR/EULAR 2023 classification criteria and evaluate their impact on pregnancy outcomes in patients.
Conclusion: To optimize limited resources, improved diagnosis and pregnancy planning for patients with antiphospholipid syndrome and cerebral venous sinus thrombosis are achieved by applying current classification criteria along with multidisciplinary management, including anticoagulation and obstetric care.

Keywords: Recurrent pregnancy loss; antiphospholipid syndrome; autoimmune disorders; pregnancy complications; case report

Tantangan Diagnosis Sindrom Antifosfolipid pada Keguguran Berulang: Sebuah Laporan Kasus

Abstrak
Pendahuluan: Keguguran berulang adalah kondisi multifaktorial yang memengaruhi sebagian kecil wanita, dengan sindrom antifosfolipid sebagai salah satu penyebab yang dikenal. Sindrom antifosfolipid adalah gangguan autoimun yang berhubungan dengan trombosis vaskular dan komplikasi kehamilan.
Laporan kasus: Kami melaporkan seorang wanita berusia 23 tahun yang mengalami empat kali keguguran berturut-turut dan didiagnosis dengan trombosis sinus vena serebri. Meskipun pada awalnya konfirmasi penuh sindrom antifosfolipid, menurut kriteria Sydney tidak memungkinkan karena keterbatasan sumber daya yang menghambat pengulangan pemeriksaan laboratorium, konsultasi dengan bagian reumatologi menghasilkan diagnosis berdasarkan kriteria 2023 dari European Alliance of Associations for Rheumatology dan American College of Rheumatology (ACR/EULAR). Kasus ini menyoroti tantangan diagnostik sindrom antifosfolipid, terutama di lingkungan dengan sumber daya terbatas dengan pemeriksaan laboratorium berulang tidak selalu dapat dilakukan, serta pentingnya penggunaan sistem klasifikasi alternatif untuk menegakkan diagnosis ketika kriteria standar tidak dapat dipenuhi. Diperlukan penelitian lebih lanjut untuk memvalidasi kriteria klasifikasi ACR/EULAR 2023 dan menilai dampaknya terhadap hasil kehamilan pada pasien.
Kesimpulan: Untuk mengoptimalkan sumber daya yang terbatas, penggunaan kriteria klasifikasi saat ini bersama perawatan antikoagulasi dan obstetri secara multidisipliner memungkinkan diagnosis dan perencanaan kehamilan yang lebih baik bagi pasien dengan sindrom antifosfolipid dan trombosis sinus vena serebral.

Kata Kunci: Gangguan autoimun; keguguran berulang; komplikasi kehamilan; laporan kasus; sindrom antifosfolipid

Indonesian Journal of Obstetrics & Gynecology Science is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License (https://creativecommons.org/licenses/by-sa/4.0/) **DOI: 10.24198/obgynia.v9i2.1026**

Introduction

Recurrent pregnancy loss (RPL) is defined as the occurrence of two or more consecutive clinical pregnancy losses. It affects fewer than 5% of women, with only 1% experiencing three or more consecutive miscarriages. Studies on RPL have examined various contributing factors, including genetic abnormalities, maternal age, antiphospholipid syndrome (APS), uterine anomalies, thrombophilias, hormonal and metabolic disorders, infections, autoimmune conditions, sperm quality, and lifestyle factors.[1]

Antiphospholipid syndrome is a systemic autoimmune disorder linked to vascular thrombosis in arteries or veins and is a well-established cause of RPL. Its diagnosis relies on the Sydney clinical criteria (Table 1), which require at least one clinical symptom and positive laboratory tests for lupus anticoagulant (LA), anticardiolipin antibody (aCL), or anti-β2 glycoprotein I (aβ$_2$GPI).[1] However, as with other autoimmune diseases, some patients show clinical features of APS but do not fully meet the criteria, creating diagnostic uncertainty and treatment challenges.

APS can involve unusual sites of thrombosis, including cerebral venous sinus thrombosis (CVST).[2] However, CVST is rare in APS, occurring in about 0.7% of thrombotic APS cases, while APS accounts for only around 5–6% of all CVST cases.[3] Reported cases of APS-associated CVST mainly occur in young women (average age ~30), often triggered by pregnancy, the postpartum period, or estrogen exposure.[4] This suggests that in women of reproductive age with APS, pregnancy-related hypercoagulability may combine with antiphospholipid antibodies (aPL) to trigger CVST.

This case report underscores the challenges of diagnosing APS, particularly in resource-limited settings where access to advanced diagnostic tests might be limited, which

Table 1 Sydney Classification Criteria

	Vascular thrombosis
Clinical criteria	Pregnancy morbidity: 1. One or more unexplained deaths of morphologically normal fetuses after the 10th week of gestation, observed through ultrasound or direct examination of the fetus. 2. One or more premature births of a morphologically normal neonate before the 34th week of gestation due to eclampsia, severe pre-eclampsia, or signs of placental insufficiency. 3. Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomical or hormonal abnormalities and paternal and maternal chromosomal causes excluded.
Laboratory criteria	Lupus anticoagulant present in plasma on two or more occasions at least 12 weeks apart, or Anticardiolipin antibody of IgG or IgM isotype in serum or plasma present at medium or high titer (>40 GPL or MPL or >99th percentile), on two or more occasions at least 12 weeks apart, or Anti-b2 glycoprotein I antibody of IgG and/or IgM isotype in serum or plasma (at a titer greater than the 99th percentile), present on at least two occasions separated by a minimum of 12 weeks.

could impact patient outcomes.

Case Presentation

A 23-year-old woman (P0A4), married for one year, presented with a history of recurrent pregnancy loss and was diagnosed with APS. Over the past year, she has undergone multiple evaluations and seven months of treatment and is now planning for a future pregnancy. Her history of pregnancy losses includes an incomplete miscarriage at 8 weeks in 2017 (managed medically at Kasih Bunda Hospital) and another incomplete miscarriage at 10 weeks in 2018 (also treated medically). Later in 2018, she was diagnosed with a blighted ovum at 9 weeks, which required curettage.

Most recently, in 2023, she had an ectopic pregnancy at 10 weeks, which required a laparoscopic left salpingectomy at Cililin Regional Hospital. Her gynecological history notes menarche at age 13, with irregular menstrual cycles usually every 30 days lasting 4–5 days. She denied galactorrhea and used contraception for one month at the start of her marriage. There is no reported family history of chronic diseases or cancers.

During her physical exam, she measured 164 cm in height, weighed 79.2 kg, and had a body mass index (BMI) of 29.45 kg/m², which is classified as Class I obesity according to WHO standards. Her vital signs were stable, with a blood pressure of 126/87 mmHg, a pulse of 100 bpm, a respiratory rate of 20 breaths per minute, and a body temperature of 36.2°C. A comprehensive physical and ultrasound examination showed no abnormalities (Table 2).

On October 24, 2023, the patient underwent immunological, specific protein, and autoimmune tests to determine the cause of RPL (Table 3). She was diagnosed with APS based on positive aPL and her clinical history. After consulting with the rheumatology department at Dr. Hasan Sadikin General Hospital in Bandung, she was prescribed low-dose aspirin (LDA) 80 mg once daily, azathioprine 50 mg once daily, osteocal 500 mg twice daily, and methylprednisolone 4 mg once daily. Her response to therapy will be monitored, with a follow-up examination planned after six months.

A subsequent antinuclear antibody (ANA) test on November 21, 2023, using the indirect immunofluorescence method, showed a reactive result with a few nuclear dots (AC-7) pattern at a titer of 1:100. A follow-up ANA profile test on December 21, 2024, showed no evidence of systemic lupus erythematosus (SLE). After six months of therapy, a follow-up examination on May 7, 2024, revealed a significant decrease in IgG anti-beta-2 glycoprotein I levels from 54.1 GPL to 8.9 GPL. The ANA test was positive, but the ANA profile was negative for SLE, with unclear clinical significance.

On February 13, 2024, the patient presented with frequent headaches, leading to a referral to the neurology department, where she was prescribed warfarin 2 mg twice daily. Due to her history of APS and new neurological symptoms, further evaluation was conducted. A hypercoagulability panel, including fibrinogen and D-dimer levels, was recommended. An MRI on June 13, 2024, confirmed CVST in the transverse sinus (Figure 1)

On December 12, 2024, pelvic ultrasound showed an anteflexed, homogeneous uterus measuring 7.2 × 2.83 × 2.98 cm, with an endometrial thickness of 6.1 mm. No uterine structural abnormalities were seen. The right ovary measured 1.76 × 2.35 × 2.85 cm (volume 6.17 cm³), and the left ovary measured 1.96 × 2.96 × 2.08 cm (volume 6.32 cm³). Cervical length was 3.13 cm, and the sliding sign was negative (Figure 2).

Table 2 Patient Clinical Timeline

Year	Event / Diagnosis	Key Details & Management
2013	Menarche	Occurred at age 13.
2017	First Pregnancy Loss	Incomplete miscarriage at 8 weeks of gestation. Managed medically at Kasih Bunda Hospital.
2018	Second Pregnancy Loss	Incomplete miscarriage at 10 weeks, managed medically.
2018	Third Pregnancy Loss	Blighted ovum diagnosed at 9 weeks, managed with curettage.
2023	Fourth Pregnancy Loss	Ectopic pregnancy at 10 weeks, underwent laparoscopic left salpingectomy at Cililin Regional Hospital.

Table 3 Ultrasound Findings

Parameter	Findings
Uterus	Anteflexed, homogeneous, 7.2 x 2.83 x 2.98 cm, EL 6.1 mm
Uterine Abnormalities	None
Right Ovary	1.76 x 2.35 x 2.85 cm, Volume 6.172 cm^3
Left Ovary	1.96 x 2.96 x 2.08 cm, Volume 6.318 cm^3
Cervical Length	3.13 cm
Sliding Sign	Negative

Table 4 Immunological, Specific Protein, and Autoimmune Findings

Parameter	Result	Normal Value
ACA-IgG	52.3 GPL	Normal <10 Elevated >=10
ACA-IgM	0.6 MPL	Normal <7 Elevated >= 7
anti-B2-GP1 IgM	1.2	Normal <5 Borderline 5-8 Elevated >8
anti-B2-GP1 IgG	54.1	Normal <5 Borderline 5-8 Elevated >8
TSH	0.61	0.35-4.94
HbA1C	5.0	

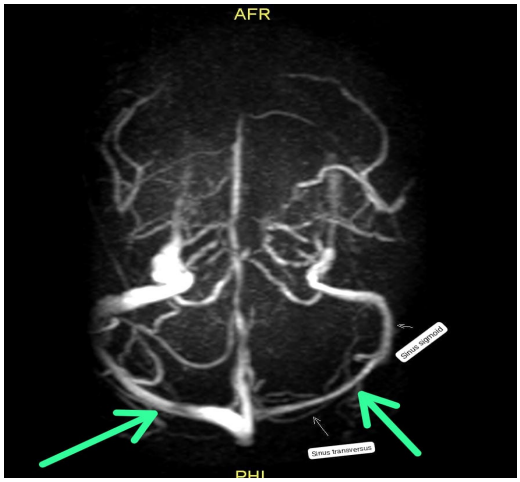


Figure 1 MRI Scan on June 13th, 2024 Showed Thrombosis at Transverse Sinus

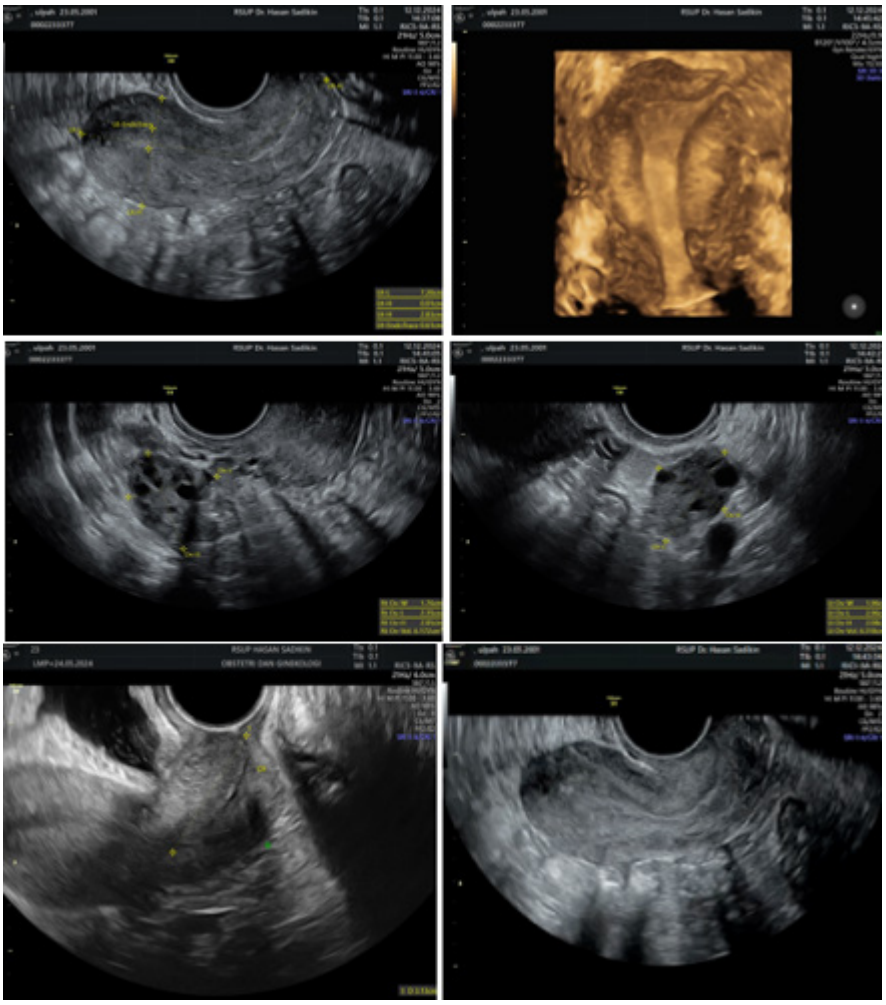


Figure 2. USG findings on December 12th, 2024, showed an anteflexed, homogeneous uterus (7.2×2.83×2.98 cm) with an endometrial thickness of 6.1 mm and no anatomical abnormalities; the right ovary measured 1.76×2.35×2.85 cm (6.17 cm³), and the left ovary was 1.96×2.96×2.08 cm (6.32 cm³); cervical length was 3.13 cm; sliding sign was negative

Discussion

zAntiphospholipid syndrome (APS) is considered a rare disease, with an estimated prevalence of about 0.05% in the general population. It is 3.5 times more common in women, who face a significantly higher risk of adverse pregnancy outcomes.[5] The management of women with obstetric APS requires a multidisciplinary approach before, during, and after pregnancy to optimize both maternal and fetal outcomes. A comprehensive assessment should include previous pregnancy complications and/or thrombotic events, the presence of non-criteria APS manifestations, related autoimmune diseases, potential genetic thrombophilia, major organ involvement linked to aPL, and additional comorbidities such as smoking, obesity, and diabetes. Additionally, risk stratification based on the aPL risk profile is crucial for tailoring management strategies.[6,7]

Lupus anticoagulant (LA) is the main predictor of adverse pregnancy outcomes after 12 weeks of gestation in aPL-positive pregnancies. In contrast, aCL and aβ₂GPI antibodies alone do not predict poor pregnancy outcomes in the absence of LA.[7,8] Studies have shown that patients testing positive for all three aPL subtypes have a significantly lower chance of live birth (odds ratio [OR] 0.33) and a higher risk of preeclampsia (OR 2.43) and small-for-gestational-age (SGA) neonates (OR 2.47). Similarly, patients with a laboratory APS category I profile have a lower likelihood of live birth (OR 0.66) and increased risk of delivering SGA neonates (OR 1.86) and preterm birth (OR 1.35). The presence of LA alone is linked to a higher risk of preeclampsia (OR 2.10), SGA neonates (OR 1.78), and preterm birth (OR 3.56). Additionally, a history of thrombosis is associated with a decreased chance of live birth (OR 0.60), increased neonatal mortality (OR 15.19), and a greater risk of antenatal or postpartum thrombosis (OR 6.26) 5 The risk of obstetric complications in women with positive aPL without prior events remains uncertain, although one study showed a higher 12-year thrombosis rate in those with obstetric APS (19.3%) compared to aPL-negative women (4.8%).[6,7]

A major diagnostic challenge was the inability to perform the required laboratory tests twice, which is necessary to confirm APS according to the Sydney criteria. When referred to the rheumatology department, the patient was reevaluated using the updated ACR/EULAR 2023 classification criteria (Figure 3).[9] Based on this system, our patient scored 4 points for clinical factors (cerebral venous thrombosis and subsequent pregnancy loss) and 4 points for laboratory findings (moderate IgG positivity), confirming the APS diagnosis despite the limitations in laboratory testing.

The EUROAPS initiative proposed Obstetric Morbidity Antiphospholipid Syndrome (OMAPS) and Non-Criteria Obstetric Antiphospholipid Syndrome (NC-OAPS) classifications to identify obstetric antiphospholipid syndrome cases that are missing by the strict laboratory criteria of the Sydney guidelines. This aims to close diagnostic and treatment gaps. OMAPS denotes cases in which clinical criteria are met, but there is no definitive laboratory confirmation; NC-OAPS denotes cases with positive laboratory tests but insufficient clinical events.[10]

CVST occurs in about 11% of patients with APS, highlighting its link to this autoimmune disorder.[11] Headache was the most common symptom, and the transverse and superior sagittal sinuses were frequently affected, often with multiple sinuses involved. Although rare, APS-related CVST has serious clinical consequences that require careful monitoring.[12]

Although rare, CVST in APS has been reported in the literature, mostly as case series. For example, in a series of 1,000

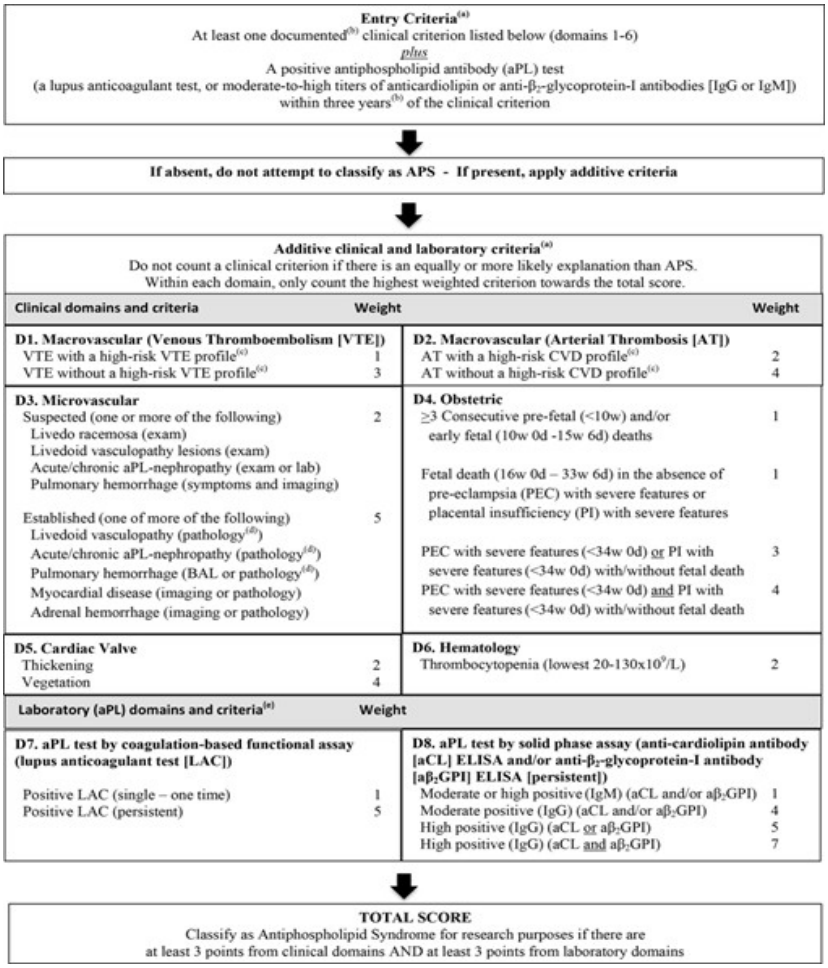


Figure 3 ACR/EULAR 2023 Classification Criteria

Inflammation in APS also disrupts normal trophoblast function, which is essential for placental development. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α), have been implicated in this process. Inflammatory cytokines in APS interfere with angiogenesis and increase anti-angiogenic factors, leading to placental insufficiency and complications such as preeclampsia, fetal growth restriction, and fetal distress, which may elevate the risk of postpartum CVST.[10,14] In APS-related CVST, the mechanism is similar to general APS thrombosis but is intensified by pregnancy. Antiphospholipid antibodies promote thrombosis via endothelial activation, and complement provides a first hit, while pregnancy offers a second hit through hypercoagulability and placental inflammation.[15,16]

The pelvic ultrasound reveals a normal-appearing, anteflexed uterus without structural defects, ovarian volumes within expected ranges, a relatively thin endometrium (6.1 mm), and a negative sliding sign. Taken together, these imaging results suggest that a primary uterine anatomic cause of recurrent loss is less likely, thereby supporting the prioritization of systemic causes such as APS with multidisciplinary preconception risk modification and anticoagulation planning over immediate surgical intervention interventions.[8,17]

The combination of low-molecular-weight heparin (LMWH) and LDA significantly reduces the risk of thrombosis

in pregnant women with APS. This is due to the anticoagulant properties of LMWH and the antiplatelet effects of aspirin, which together help manage the hypercoagulable state associated with APS. A meta-analysis showed that combination therapy improves coagulation by lowering D-dimer and platelet levels, indicating reduced thrombosis risk. The combination therapy has been demonstrated to significantly increase live birth rates. A study reported an odds ratio of 4.54 for live births in patients receiving both LMWH and aspirin compared to those receiving either treatment alone.[18–20]

For treatment considerations in our case, warfarin will be discontinued before conception due to the risk of fetal warfarin syndrome. The patient will transition to LDA and either LMWH or unfractionated heparin (UFH) at therapeutic doses as soon as pregnancy is confirmed, in accordance with international guidelines. LDA may also be initiated before conception as a primary therapy to reduce the risk of pregnancy complications in APS.[6,7] If the patient develops severe preeclampsia, eclampsia, or placental insufficiency, delivery before 34 weeks of gestation may be necessary, warranting further aPL testing to reassess thrombotic risk.[1]

Management of CVST in APS aligns with general CVST guidelines, with specific adaptations for APS. Acute treatment involves prompt anticoagulation followed by long-term oral anticoagulation.[15] Because APS patients face a high risk of recurrence, indefinite anticoagulation is often recommended after an initial CVST.[15] In APS–associated CVST, patients are typically switched from vitamin K antagonists to LMWH plus LDA once pregnancy is planned or confirmed, in consultation with a multidisciplinary team; endovascular thrombectomy or thrombolysis is reserved for severe cases that do not respond to anticoagulation. Most patients recover with minimal deficits, but significant morbidity and approximately 10% mortality have been reported.[4] Our patient's positive neurological recovery is therefore reassuring, but this case highlights the importance of vigilant follow-up and preconception risk management in APS.

This case report highlights unique clinical and practical strengths. It illustrates a rare progression of APS from recurrent pregnancy loss to cerebral venous sinus thrombosis, emphasizing the syndrome's diverse presentation. Additionally, it shows the real-world usefulness of the ACR/EULAR 2023 classification criteria in addressing diagnostic challenges in resource-limited settings where repeated laboratory testing is often not feasible. The study is limited by ongoing follow-up and uncertain long-term outcomes. Further prospective research is essential to validate the ACR/EULAR 2023 classification in clinical practice and to understand how laboratory profiles influence maternal and neonatal outcomes such as small-for-gestational-age, preterm birth, preeclampsia, thrombosis, and neonatal mortality.

Conclusions

This case highlights the diagnostic and therapeutic challenges of APS presenting with recurrent pregnancy loss and cerebral venous sinus thrombosis in a resource-limited setting. When standard Sydney laboratory confirmation was not feasible, applying the ACR/EULAR 2023 classification along with multidisciplinary management enabled a pragmatic diagnosis and obstetric planning. Further prospective studies are needed to validate newer classification criteria and improve care pathways for APS in low-resource environments.

References

1. American Society for Reproductive

Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril [Internet]. 2012 Nov;98(5):1103–11.
2. Arachchillage DJ, Platton S, Hickey K, Chu J, Pickering M, Sommerville P, et al. Guidelines on the investigation and management of antiphospholipid syndrome. Br J Haematol [Internet]. 2024 Sep 19;205(3):855–80.
3. Xu L, Wu J, Wang H, Yang B. Case Report: Primary catastrophic antiphospholipid syndrome in a pediatric patient with cerebral venous sinus thrombosis as the first manifestation. Front Pediatr [Internet]. 2024 Dec 11;12.
4. Jerez-Lienas A, Mathian A, Aboab J, Crassard I, Hie M, Cohen-Aubart F, et al. Cerebral Vein Thrombosis in the Antiphospholipid Syndrome: Analysis of a Series of 27 Patients and Review of the Literature. Brain Sci [Internet]. 2021 Dec 13;11(12):1641.
5. Walter IJ, Klein Haneveld MJ, Lely AT, Bloemenkamp KWM, Limper M, Kooiman J. Pregnancy outcome predictors in antiphospholipid syndrome: A systematic review and meta-analysis. Autoimmun Rev [Internet]. 2021 Oct;20(10):102901.
6. Arslan E, Branch DW. Antiphospholipid syndrome: Diagnosis and management in the obstetric patient. Best Pract Res Clin Obstet Gynaecol [Internet]. 2020 Apr;64:31–40.
7. Kaneko K, Ozawa N, Murashima A. Obstetric anti-phospholipid syndrome: from pathogenesis to treatment. Immunol Med [Internet]. 2022 Apr 3;45(2):79–93.
8. Garcia D, Erkan D. Diagnosis and Management of the Antiphospholipid Syndrome. Longo DL, editor. N Engl J Med [Internet]. 2018 May 24;378(21):2010–21.
9. Barbhaiya M, Zuily S, Naden R, Hendry A, Manneville F, Amigo M-C, et al. 2023 ACR/EULAR antiphospholipid syndrome classification criteria. Ann Rheum Dis [Internet]. 2023 Oct;82(10):1258–70.
10. Alijotas-Reig J, Esteve-Valverde E, Anunciación-Llunell A, Marques-Soares J, Pardos-Gea J, Miró-Mur F. Pathogenesis, Diagnosis and Management of Obstetric Antiphospholipid Syndrome: A Comprehensive Review. J Clin Med [Internet]. 2022 Jan 28;11(3):675.
11. Orion D, Itsekson-Hayosh Z, Peretz S, Mendel R, Yaniv G, Attia M, et al. Janus Kinase-2 V617F Mutation and Antiphospholipid Syndrome in Cerebral Sinus Venous Thrombosis: Natural History and Retrospective Bicenter Analysis. Front Neurol [Internet]. 2022 Apr 14;13.
12. Shen H, Huang X, Fan C. Clinical Characteristics and Management of Cerebral Venous Sinus Thrombosis in Patients With Antiphospholipid Syndrome: A Single-Center Retrospective Study. Clin Appl Thromb [Internet]. 2021 Jan 1;27.
13. Misasi R, Longo A, Recalchi S, Caissutti D, Riitano G, Manganelli V, et al. Molecular Mechanisms of "Antiphospholipid Antibodies" and Their Paradoxical Role in the Pathogenesis of "Seronegative APS." Int J Mol Sci [Internet]. 2020 Nov 9;21(21):8411.
14. Vrzić Petronijević S, Vilotić A, Bojić-Trbojević Ž, Kostić S, Petronijević M, Vićovac L, et al. Trophoblast Cell Function in the Antiphospholipid Syndrome. Biomedicines [Internet]. 2023 Sep 30;11(10):2681.
15. Zhang B, Lang Y, Zhang W, Cui L, Deng F. Characteristics and Management of Autoimmune Disease-Associated Cerebral Venous Sinus Thrombosis. Front Immunol [Internet]. 2021 Jul 22;12.
16. Yang L, Guo R, Liu H, Chen B, Li C, Liu R, et al. Mechanism of antiphospholipid antibody-mediated thrombosis in

antiphospholipid syndrome. Front Immunol [Internet]. 2025 Mar 13;16.
17. Atik RB, Christiansen OB, Elson J, Kolte AM, Lewis S, Middeldorp S, et al. ESHRE guideline: recurrent pregnancy loss: an update in 2022. Hum Reprod Open. 2023;2023(1).
18. Yin M, Qin X. Meta-Analysis of the Efficacy of Low Molecular Weight Heparin and Aspirin in the Treatment of Thrombosis During Pregnancy and Effects on Coagulation Function. Discov Med [Internet]. 2023;35(175):104.
19. Shi T, Gu Z-D, Diao Q. Meta-analysis on aspirin combined with low-molecular-weight heparin for improving the live birth rate in patients with antiphospholipid syndrome and its correlation with d-dimer levels. Medicine (Baltimore) [Internet]. 2021 Jun 25;100(25):e26264.
20. Eid MI, Abdelhafez MS, El-refaie W, El-Zayadi AA, Samir K, Abdelrazik MM, et al. Timing of initiation of low-molecular-weight heparin administration in pregnant women with antiphospholipid syndrome: a randomized clinical trial of efficacy and safety. Int J Womens Health [Internet]. 2019 Jan;Volume 11:41–7