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Antiphospholipid Syndrome Misdiagnosed as Infective Endocarditis: A Case Report

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Abstract: This article presents a retrospective study of a case that was initially misdiagnosed as infective endocarditis but was later diagnosed as antiphospholipid syndrome (APS) upon further evaluation. The study aims to explore the clinical manifestations of APS and increase clinicians' awareness of its non-specific manifestations. The ultimate goal is to provide effective treatment as early as possible and prolong patients' survival.

Keywords: Antiphospholipid syndrome; Heart valves; Misdiagnosis

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1. Introduction

APS is a non-inflammatory autoimmune disease characterized by recurrent arterial and venous thrombosis, spontaneous abortions, and thrombocytopenia based on positive serum antiphospholipid antibodies. In recent years, the incidence and prevalence of APS have been overlooked, while its poor prognosis has always attracted much attention. Studies have shown that the 10-year mortality rate of APS patients is approximately 10% [1–3]. Despite a relatively high survival rate, the 30% rate of permanent organ damage and disability cannot be ignored. Therefore, the diagnosis and treatment of APS have always been the focus of clinicians' work.

2. Medical records

A 42-year-old female patient presented to the emergency department of Yanbian University Hospital on October 17, 2023, with the chief complaint of "intermittent chest tightness and shortness of breath for 2 weeks, worsened by dyspnea for 2 days." The results of the cardiac color ultrasound indicate left heart enlargement, diffuse weakening of left ventricular (LV) systolic function, reduced LV diastolic function, severe aortic valve stenosis with insufficiency, and isoechoic area near the right coronary valve, possibly indicative of vegetation. The EF is 33%, the left atrial (LA) diameter is 43 mm, MPG is 77 mmHg, and the peak pressure gradient is 109 mmHg (**Figure 1**). Valvular heart disease with heart failure will cause the patient to experience occasional coughing and produce sputum. Additionally, the patient experienced a low-grade fever in the morning.

The patient has a history of hypertension and underwent two cesarean sections in 2018 and June 2023. On admission, physical examination revealed: temperature: 37.5℃; heart rate: 100 beats/min; respiratory rate: 15 breaths/min; blood pressure: 107/76 mmHg; no precordial bulge, apex beat located at 0.5cm to the left of the midclavicular line in the fifth intercostal space, no palpable thrills over the valve areas, regular rhythm, normal heart sounds, A2 > P2, systolic ejection murmur heard in the aortic valve area. Laboratory tests conducted after admission showed: cardiac markers: CK-MB 4.58 ng/mL, cTNI 0.62 ng/mL, MYO 35.62 ng/mL, NT-proBNP 14626.05 pg/mL, D-dimer 0.78 ug/mL, PCT 0.15 ng/mL. Coagulation time, blood routine, liver and kidney function, thyroid hormones, and tumor markers were all within normal ranges. The patient received treatment including nutritional support, vasodilators, and diuretics after admission. On October 20, 2023, a cardiovascular surgery consultation was requested to ascertain the cause. Considering the patient's recent cesarean section and occasional fever during illness, the possibility of "infective endocarditis" could not be ruled out. Blood cultures were negative. After improvement in the patient's condition, she was transferred to a higher-level hospital.

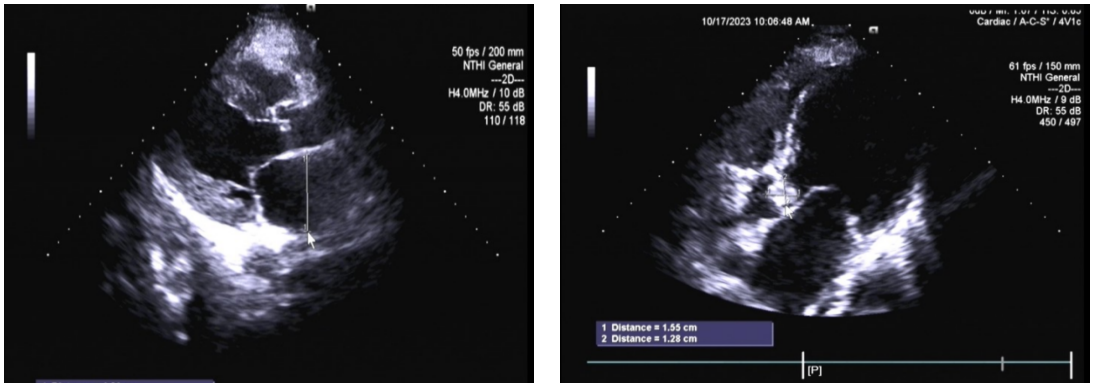

Figure 1. Cardiac color ultrasound.

On October 25, 2023, the patient underwent a cardiac color ultrasound at the Sixth Medical Center of the People's Liberation Army General Hospital. The results of the ultrasound showed that abnormal aortic valve function and elastic fibroma were considered, with possible vegetations not ruled out, severe aortic valve stenosis with moderate regurgitation was also observed, along with left heart enlargement and LV myocardial hypertrophy. Mildly reduced LV systolic function was noted, as well as moderate mitral valve regurgitation and mild tricuspid valve regurgitation. The LA measurement was 46 mm, the LV measurement was 54 mm, the interventricular septum was 14 mm, and the LV posterior wall was 14 mm. The patient sought treatment at Beijing Fuwai Hospital on October 26, 2023. Following admission, the medical team considered the possibility of infectious endocarditis based on the patient's symptoms and medical history. The Coronary CTA did not reveal any abnormalities. The transesophageal three-dimensional color ultrasound showed space-occupying lesions in the aortic valve, the nature of which is yet to be determined. The mitral valve showed small to moderate regurgitation, and there was left heart enlargement. Severe aortic valve stenosis and moderate regurgitation were also observed. The cardiac MRI scan revealed aortic valve nodules, which are more likely to be vegetations or thrombus. Additionally, severe aortic valve stenosis and mild to moderate regurgitation were observed. The cardiac MRI enhanced scan revealed the following:

(1) High possibility of vegetations and thrombus due to aortic valve nodules, severe aortic valve stenosis, and mild to moderate regurgitation.

(2) LV enlargement, left ventricular wall thickening, and decreased systolic function, which may indicate secondary changes.

(3) Small focal fibrosis was found scattered in the LV endocardium.

The results of the three-day blood culture were negative, indicating that infective endocarditis is not supported by current evidence. To further identify the underlying cause, comprehensive blood tests (**Table 1**) showed no abnormalities in blood routine, biochemistry, vasculitis markers, or antinuclear antibody spectrum. On November 9, 2023, consultation was sought from the Rheumatology and Immunology Department at Peking University People's Hospital due to abnormal indicators in the patient's medical history of rheumatic conditions and immune-related issues. Based on the patient's severe aortic valve stenosis, positive results for anticardiolipin antibodies, anti-β2 glycoprotein, and lupus anticoagulant, as well as a history of early pregnancy miscarriage and the presence of livedo reticularis on physical examination, combined with endocardial biopsy findings (**Figure 2**), the diagnosis of "antiphospholipid syndrome" was confirmed. The patient presented with fever and cough with sputum production, suggesting pulmonary inflammation secondary to antiphospholipid syndrome. Warfarin, heparin, and other anticoagulants are administered to prevent thrombosis, while prednisone is used to reduce inflammation. The blood tests were reviewed, and the lupus anticoagulant SCT standardized ratio (SCT-R) was found to be 1.82, anti-β2 glycoprotein 1IgG (β2GP1 IgG) was 101.00 AU/mL, and anti-β2glycoprotein 1IgM (β2GP1 IgM) was 28.70 AU/mL. The abnormal indicators were higher than before, but the recovery was effective.

To improve the patient's symptoms, cardiac surgery was performed on December 7, 2023. The procedure involved general anesthesia, hypothermia, and extracorporeal circulation to replace the aortic valve. The diseased valve was replaced with a Regent 19# aortic valve mechanical valve using interrupted sutures. The procedure was successful. Follow-up echocardiography showed an ejection fraction of 53%, an LV measurement of 50 mm, and an LA measurement of 34mm. The mechanical valve functioned normally after the aortic valve replacement. The postoperative pathology report (**Figure 3**) revealed chronic valvulitis (aortic valve) with non-infectious thrombotic vegetation formation. The patient was diagnosed with: (1) valvular disease, atypical verrucous endocarditis (Libman-Sacks), severe aortic valve stenosis, aortic valve vegetations; (2) heart failure; (3) APD. Treatment included oral prednisone 50 mg/d, low-molecular-weight heparin (warfarin added later, initial dose 3 mg/d), atenolol, torasemide, and irbesartan to improve cardiac remodeling and control blood pressure. The general condition of the patient improved and stabilized after the procedure. After discharge, the patient's condition remained stable and prednisone acetate dosage was reduced to 30 mg/d. The patient continued to take warfarin tablets 3 mg/d, atenolol 12.5 mg/d, torsemide 20 mg/d, and irbesartan 37.5 mg/d orally.

Table 1. Comprehensive blood tests

Subject	Result	Unit	Range
ASO	63.5	IU/mL	0–200
CRP	12.3	mg/L	0–8
RF	< 20.00	IU/mL	0–20
IgG	13.4	g/L	7.23–16.85
IgA	2.34	g/L	0.69–3.82
IgM	1.09	g/L	0.63–2.77
IgE	10.3	IU/mL	0–165
C3	0.95	g/L	0.85–1.93
C4	0.208	g/L	0.12–0.36
ACL IgG	> 120.00	GPLU/mL	negative: < 8; positive: ≥ 12

Table 1 (Continued)

Subject	Result	Unit	Range
ACL IgM	10.30	MPLU/mL	negative: < 8; positive: ≥ 12
β2GP1 IgG	162.00	AU/mL	negative: < 16; positive: ≥ 24
β2GP1 IgM	46.30	AU/mL	negative: < 16; positive: ≥ 24
SCT-S	3.99		
SCT-C	1.13		
SCT-R	3.54		0–1.16
DRVVT-S	2.03		
DRVVT-C	1.10		
DRVVT-R	1.85		0–1.2

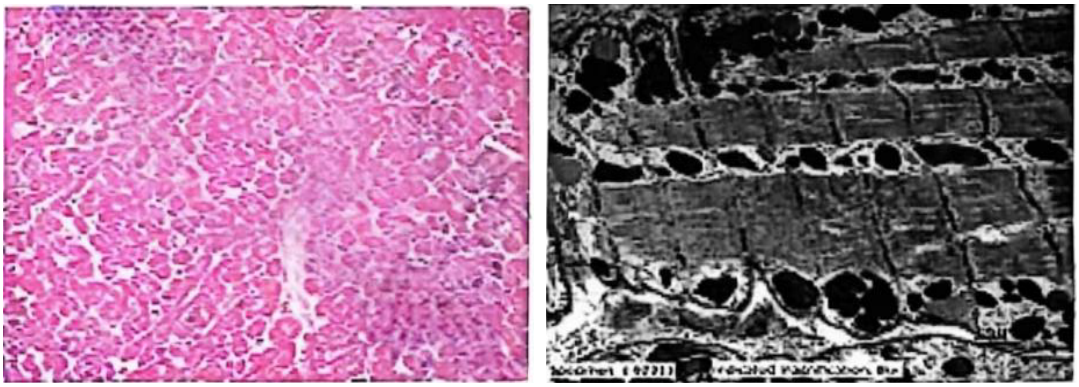

Figure 2. Endocardial biopsy.

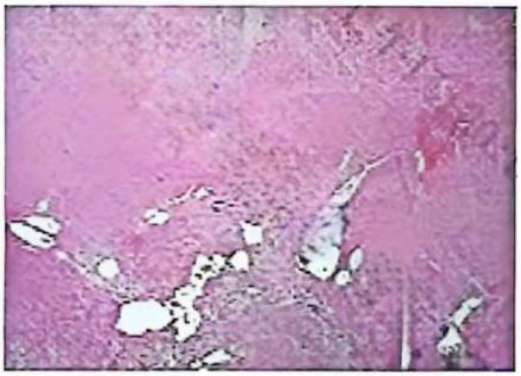

Figure 3. Postoperative pathology report**.**

3. Follow-up

The patient's six-month follow-up data after discharge showed no occurrence of thrombosis or thrombocytopenia.

4. Discussion

Studies have shown that patients with elevated antiphospholipid antibodies have an increased risk of developing

Libman-Sacks endocarditis [4]. As a result, when APS affects the heart, it is more likely to cause valvular disease, particularly on the left side of the heart, such as the mitral valve, while right coronary valve disease is less common [5–7]. The patient experienced a sudden onset of symptoms, including heart failure, vegetations on the right coronary valve, and Libman-Sacks endocarditis. The admission auxiliary examinations yielded positive results for anticardiolipin antibodies, anti-β2 glycoprotein, and lupus anticoagulant. The heart color prompts the formation of heart valve vegetation. The electrocardiogram and cardiac MRI did not show any obvious signs of myocardial ischemia. The coronary CTA showed no coronary vascular stenosis. The heart valve biopsy and postoperative pathology revealed the formation of chronic valvulitis and non-inflammatory thrombotic vegetations. The pathogenesis of this disease involves the linear deposition of low IgG anticardiolipin antibodies in cardiac valve endothelial cells. APS presents with an acute onset of cardiac involvement and severe symptoms. If examinations reveal unexplained intracardiac thrombus, valve involvement, myocardial ischemia, or other changes, APS should be considered, and further examinations should be performed to ensure timely diagnosis and treatment [8].

Female APS patients commonly experience morbid pregnancy symptoms such as recurrent miscarriage, eclampsia, preeclampsia, intrauterine distress, intrauterine growth retardation, stillbirth, or premature birth. Placental thrombosis is considered the main cause of APS in most cases, and its pathogenesis involves various cells and factors. Research indicates that APS has an incidence rate of 0.75/100,000 to 2.1/100,000 and a prevalence rate of 6.19/100,000 to 50/100,000. The highest incidence rate in women occurs between the ages of 30–39 and 70–79. APS is considered to be the cause of recurrent early miscarriage in 15% of patients [5]. In this case, the cause of the multiple failed pregnancies remains to be verified, and it is unclear whether APS is related. Therefore, patients who experience unexplained pregnancy loss should be tested for various autoantibodies, particularly antiphospholipid antibodies, before attempting another pregnancy. This will help determine if medication is necessary to improve their immune system and protect the health and well-being of both the mother and fetus.

Additionally, there are atypical manifestations that may be overlooked, such as skin rashes, redness, and reticular erythema. Damage to the lungs commonly includes pulmonary embolism and pulmonary infarction. Repeated pulmonary vascular thrombosis can lead to pulmonary hypertension, as well as rare conditions such as acute respiratory distress syndrome, intra-alveolar hemorrhage, pulmonary capillaritis, and alveolar fibrosis [6]. The patient exhibited reticular erythema and pneumonia during the disease. Several sputum tests revealed a small number of Gram-positive cocci. Although pulmonary inflammation is considered a likely factor, there is no direct evidence linking APS to pulmonary inflammation.

5. Conclusion

In summary, due to the ongoing advancements in medical technology, clinical subfields are becoming increasingly specialized. As a result, specialist doctors may lack knowledge of rare diseases in other disciplines, making it challenging to provide comprehensive diagnosis and treatment for complex cases. Furthermore, APS patients can experience rapid progression and damage to multiple systems. In this particular case, the patient's primary symptoms were chest tightness and shortness of breath. Clinicians typically only consider common causes of circulatory and respiratory issues, which can lead to misleading early diagnoses. The development and promotion of medical imaging and testing technology have played a significant role in advancing diagnosis and treatment methods [9,10]. The diagnosis of the disease in this case was based on the professional judgment of clinicians and supported by detection methods such as endocardial pathology and anticardiolipin antibodies.

Clinicians need to consider the possibility of autoimmune diseases in young patients with multi-system damage in the future, perform necessary laboratory examinations and thorough analysis promptly to attain early diagnosis and treatment, thereby reducing the incidence of missed diagnosis and misdiagnosis.

Disclosure statement

The authors declare no conflict of interest.

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