

## Case report

# Spontaneous regression of severe aortic stenosis after massive embolization in a patient with antiphospholipid syndrome

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### Summary

We present a case of probably unreported aortic stenosis evolution in a patient with primary antiphospholipid syndrome (APS). A female patient, 54 years old, with a history of recurrent deep venous thrombosis, an episode of pulmonary embolism and was positive for APS antibodies. She was kept on warfarin and aspirin. The patient was admitted with acute pulmonary edema and severe aortic stenosis. While preparing for aortic valve surgery, the patient developed acute stroke, and a week later developed concurrent acute ischemia of both lower limbs. Emergency surgery salvaged the lower limbs and follow up transthoracic echocardiography showed marked regression of the thickening of the aortic valve leaflets, only mild aortic stenosis and moderate aortic regurgitation. Aortic valve surgery was cancelled, and the patient was kept on warfarin and aspirin.

### Conclusion

Development of severe aortic stenosis is uncommon in primary APS, and this scenario of spontaneous improvement from a severe to a mild aortic stenosis, is probably unreported before.

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**Keywords:** antiphospholipid syndrome, aortic stenosis, embolization

### Introduction

Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by venous or arterial thrombosis and/or pregnancy loss, in the presence of persistent expression of antiphospholipid antibodies (aPL). APS can occur as a primary condition, or in the presence of systemic lupus erythematosus (SLE) or another systemic autoimmune disease [1].

Local deposition of platelets and inflammatory molecules produces nonbacterial thrombotic endocarditis (NBTE) [2], a form of noninfectious endocarditis, that mostly affects the mitral and aortic valves, essentially as valvular regurgitation. The development of valvular stenosis is rare [3]. Also, long term follow-up of SLE and APS cases had reported potential improvement of se-

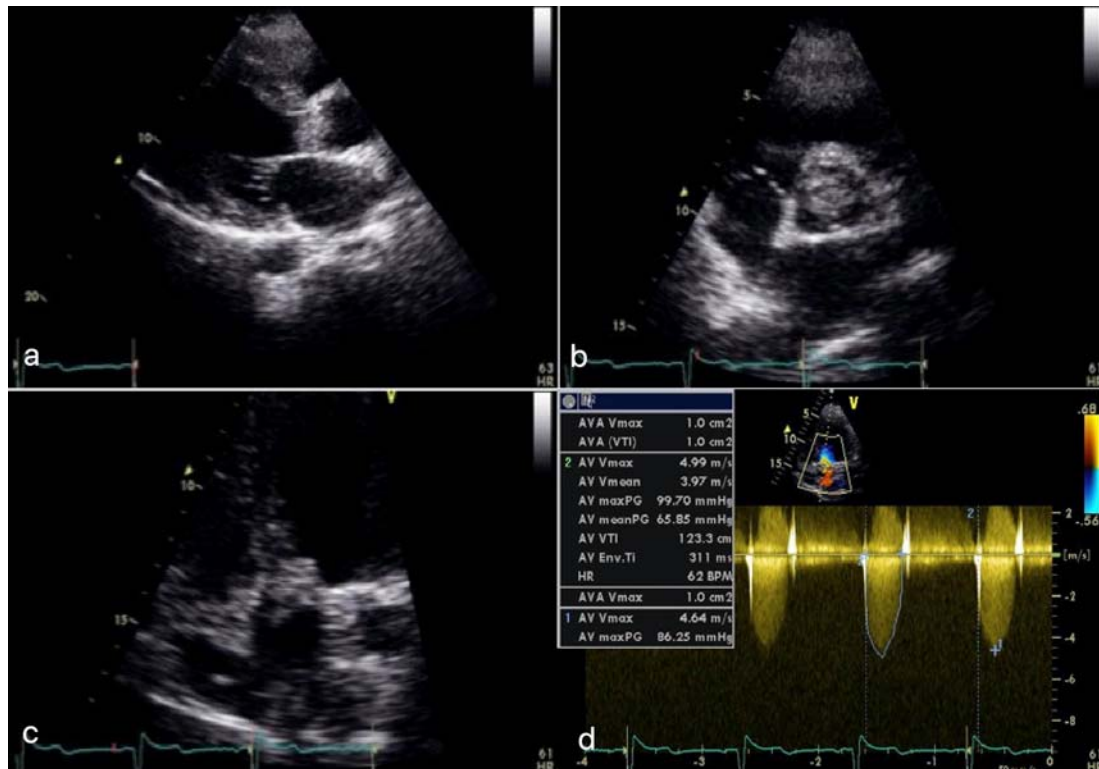
vere valvular regurgitation, but none reported for stenosis [3,4].

### Case presentation

A female patient, 54 years old, mother of a single child, with no history of maternal adverse events. She is known to have hypertension, bronchial asthma and hypothyroidism. She had recurrent deep venous thrombosis and got a manifest pulmonary embolism once. She had been diagnosed to have APS after laboratory results for persistent positive APS antibodies. Work-up had ruled out SLE. The patient achieved good time in therapeutic range with warfarin, however, she was referred to our center after acute pulmonary edema complicating severe aortic stenosis. Echocardiography showed markedly thickened aortic valve leaflets, structurally bicuspid valve, with severely limited systolic excursion, mild aortic regurgitation, transvalvular gradient of 99/65 mmHg and calculated aortic valve area of 0.65 cm<sup>2</sup> (Fig. 1). Other cardiac valves were un-

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**Figure 1.** Parasternal long axis views (a) showing markedly thickened aortic valve leaflets, markedly reduced systolic excursion and impression of degenerated bicuspid morphology (b). The aortic valve leaflets are thickened in the apical views (c). Continuous wave Doppler (d) showed aortic gradient of 99/65 mmHg, denoting severe stenosis.

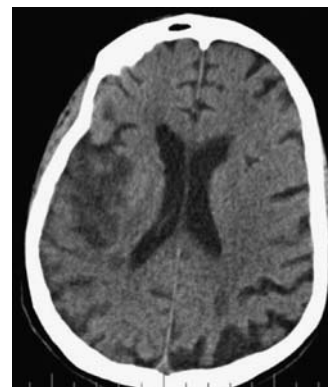
remarkable and left ventricular systolic function was preserved.

The patient was fully active despite shortness of breath on effort, she had history of dysfunctional uterine bleeding but no history of fever. Her blood pressure was controlled with medications and she had stable sinus rhythm.

Here blood picture was normal apart from hemoglobin of 8.1 gm/dL, and her chemistry was unremarkable. Abdominal ultrasound was normal apart from mild hepatomegaly, she had mild antral gastritis upon endoscopy. Preoperative coronary angiogram showed normal coronaries.

The patient was cleared from gynecology, started on proton pump inhibitors and got 2 units of blood transfusion. She was dentally sanitized and follow up hemoglobin was stable around 10.5 g/dL and was discharged on warfarin (INR range 2–3) and aspirin (81 mg/d).

While waiting for elective aortic valve surgery, the patient developed acute stroke (Fig. 2), and one week later, developed concurrent acute ischemia of both lower limbs. Emergency surgery salvaged the lower limbs. Transthoracic echocardiography showed trileaflet aortic valve, marked regression of the thickness of valve leaflets, with almost normal systolic excursion, transvalvular gradient of 40/21 mmHg (Fig. 3) and moderate aortic regurgitation (Fig. 4).

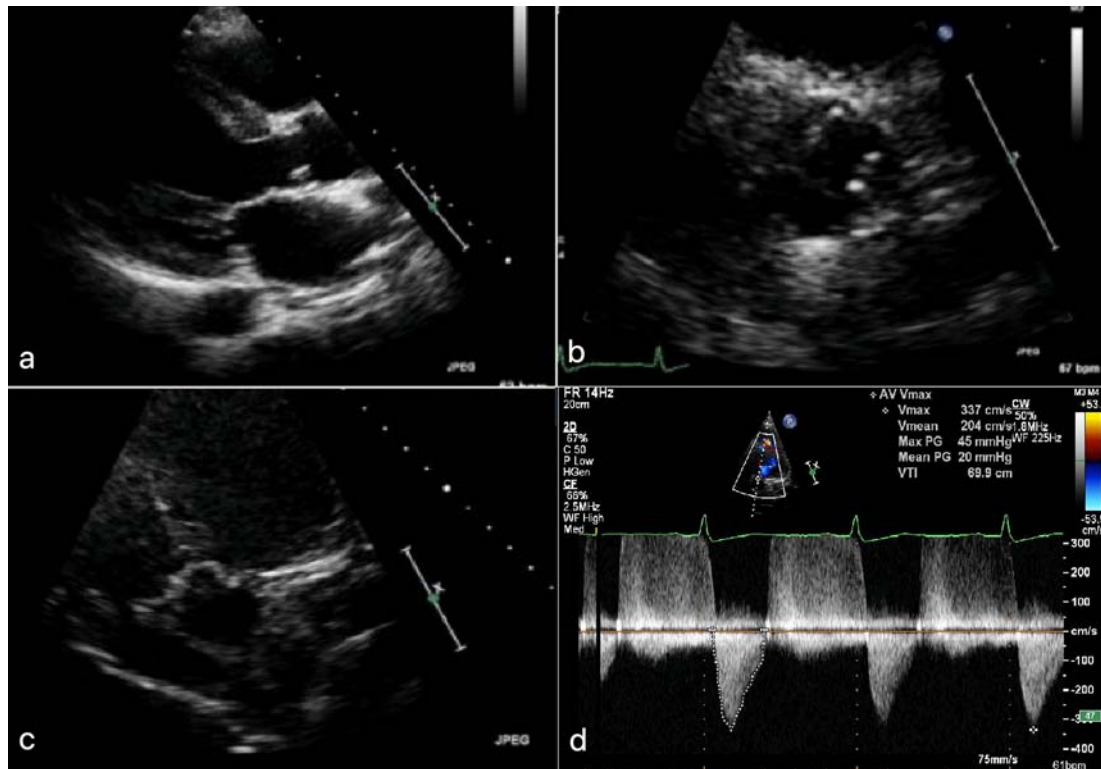


**Figure 2.** Brain computed tomography showed large infarction of the right temporo-parietal region.

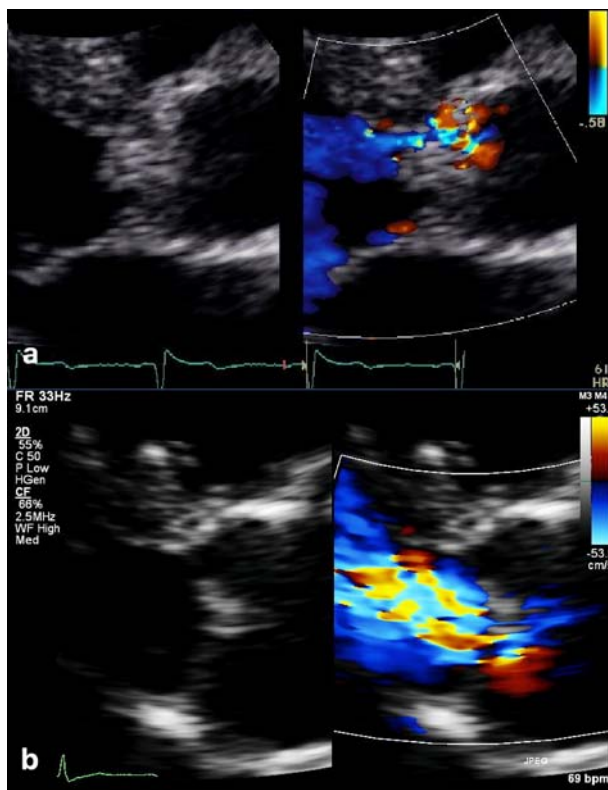
Given these changes, aortic valve surgery was cancelled, and the patient was kept on warfarin (INR range 2.5–3.5) and aspirin (81 mg). She showed good recovery of her motor power with poor recovery of her concentration and memory. Rheumatology referral and follow up echocardiography were considered.

## Discussion

The vegetations in NBTE consist of thrombi interwoven with strands of fibrin, immune complexes and mononuclear cells (“white throm-



**Figure 3.** Parasternal long axis views (a) and the parasternal short axis view (b) showing mildly thickened aortic valve leaflets, with good systolic excursion. The aortic valve leaflets are mildly thickened, with no more bulk attachment in the apical views (c). Continuous wave Doppler (d) showed aortic gradient of 41/20 mmHg, denoting mild stenosis.



**Figure 4.** Color compare, parasternal long axis view, zoomed, showing the evolution of marked aortic valve thickening and mild regurgitation (a), into mildly thickened leaflets with moderate regurgitation (b) after detachment of the nonbacterial thrombotic endocarditis mass from the leaflets.

bus”). When thrombi are large, the term verrucous endocarditis is used (also known as Libman-Sacks endocarditis). Patients with advanced malignancy or SLE are the most common populations affected by NBTE [5].

Compared to vegetations in infective endocarditis, vegetations in NBTE are easily dislodged since there is little inflammatory reaction at the site of attachment [6]. Our patient was first interpreted as structurally bicuspid aortic valve, with severe degeneration. However, NBTE causing severe aortic stenosis, which is rarely reported [7] was not ruled out. Unloading these bulky masses of NBTE from the aortic valve leaflets in our patient produced these unusual, massive systemic showering. Embolization from NBTE can happen anywhere in the body, however, emboli to the central nervous system and coronary arteries are more likely to reveal the diagnosis due to the presence of more worrisome symptoms [8].

Cardiac manifestations of APS most commonly involve the valves, including valvular thickening and valve nodules [9]. The mitral valve is most frequently involved, followed by the aortic valve [4,10]. Cases with all four valves affected by NBTE have also been reported [11,12]. Involvement of the mitral and aortic valves can lead to valvular regurgitation and, rarely, to stenosis [10–13]. Valve lesions, especially aortic nodules, are highly

associated with the risk of stroke [14]. In our case, shedding of the bulky NBTE masses from the leaflets, revealed the aortic trileaflet morphology, reduced the leaflets' thickness, improved their excursion, markedly reduced the transvalvular gradient and added one grade to the aortic regurgitation severity.

The frequency, clinical course, and complications of valvular disease were studied in patients with SLE and primary APS using transesophageal echocardiography, most of whom underwent a second study at a mean of 29 months later [15, 16]. Valvular stenosis, which was not progressive, was found in 4 percent at baseline evaluation and 3 percent at follow up. Also, some valvular abnormalities resolved with time, others appeared for the first time, and some changed their appearance.

Such aggressive valvular evolutionary changes and recurrent thromboembolism in our patient with primary APS, who is being treated with an anticoagulant is relatively rare.

Management strategies in our case is a clinical dilemma; the patient was therapeutically anticoagulated with warfarin at the time of the event (INR; range, 2 to 3), one approach is to increase the target INR (e.g., range 3 to 4). An alternative approach is switching from warfarin to a low-molecular-weight heparin. This approach may be more appropriate for an individual who had a recurrent event when the INR was in the higher end of the target range. This is largely based on data from a small series [17]. Some experts may add another medication, such as low dose aspirin, hydroxychloroquine and/or statin. However, there is a lack of high-quality data to guide practice and there is no good-quality evidence to guide selection of a specific immunomodulatory agent for the treatment of APS [18,19]. It is also important to evaluate for other possible reversible thrombosis risk factors.

There has been an interest in the use of direct oral anticoagulants (DOACs) for APS due to their convenience, lack of need for laboratory monitoring, and decreased risk of bleeding [20]. However, there are no high-quality data demonstrating equivalent efficacy or safety of DOACs in individuals with APS [21].

Despite this high prevalence of valvular affection in APS, only 4–6% of aPL-positive patients with valve disease will require surgical treatment [22]. The indications for surgery (vegetation excision or valve replacement) are the same as for infective endocarditis, but reports suggest that prevention of recurrent embolization is the most common reason for surgery. Due to the high risk of recurrence, most case studies also report the use of postoperative anticoagulation when feasi-

ble, especially in those with a systemic reason for embolization (e.g., APS). A study that involved 32 patients with APS underwent cardiac valve surgery, first month morbidity was 21.8%, most of them major bleeding or thrombosis, and the later overall mortality and/or morbidity was 50%, with mortality 9.6% after the first month [23]. Importantly, as the NBTE are frequently detached to the systemic circulation, one might recommend valve surgery sooner for such cases with bulky mass on the valve [24].

## Declarations

- This case report had been reviewed by our institutional research and ethics committee.
- The patient involved in this report was notified of this publication and her consent is retained.
- All the data, materials and videos related to this case are available.
- None of the authors have financial and non-financial competing interests related to this case report.
- This case report has no funding.
- All authors had contributed almost equally in this case report.

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