Primary Antiphospholipid Antibody Syndrome Complicated with Cerebellar Hemorrhage and Aortic Dissection: A Case Report

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Conflict of interest: None declared

Patient: Female, 42-year-old
Final Diagnosis: Primary antiphospholipid antibody syndrome
Symptoms: Coma
Medication: —
Clinical Procedure: Evacuation of the intracranial hematoma • suboccipital decompression • intraventricular catheter placement
Specialty: Neurosurgery

Objective: Rare co-existence of disease or pathology

Background: Antiphospholipid antibody syndrome (APS) is a systemic autoimmune disease associated with arterial and venous thromboembolism and pregnancy complications. There have been several reports of APS with systemic lupus erythematosus (SLE) complicated with aortic dissection. However, none of them has been primary APS, which is APS without SLE.

Case Report: A 42-year-old woman with primary APS and APS nephropathy on warfarin and aspirin therapy presented with coma due to cerebellar hemorrhage. The effect of warfarin was immediately reversed with prothrombin complex concentrate. We performed emergent evacuation of the hematoma, and her level of consciousness improved to normal on postoperative day (POD) 1. She had acute hypertension on arrival, which was resistant to multiple antihypertensives and was stabilized on POD 3. She also had exacerbation of chronic kidney disease after using contrast and prothrombin concentrate complex, and was on temporary renal replacement therapy from POD 3. Aortic dissection was found accidentally on echocardiography on POD 7, and she was subsequently treated medically. She was transferred to the rehabilitation hospital with mild dysarthria and truncal ataxia on POD 59.

Conclusions: We report the first case in the English literature of primary APS complicated with cerebellar hemorrhage and aortic dissection. Acute hypertension following hemorrhage and exacerbation of APS nephropathy likely triggered the dissection of the aortic wall, the integrity of which might have been compromised by longstanding antiphospholipid antibody and vasa vasorum thrombosis.

MeSH Keywords: Antiphospholipid Syndrome • Aortic Diseases • Intracranial Hemorrhages

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Background

Antiphospholipid antibody syndrome (APS) is characterized by venous or arterial thromboses or pregnancy morbidity in the presence of persistent laboratory evidence of antiphospholipid antibodies. APS is well known to be associated with systemic lupus erythematosus (SLE), although approximately half of APS cases are diagnosed as primary APS without SLE [1]. Patients with APS continue to have significant morbidity and mortality despite current treatment. According to a multi-center prospective study of 1000 patients, the survival probability at 10 years was 91% [2]. In this study, the vast majority of patients were under antithrombotic treatment, and the causes of death were thrombosis, including myocardial infarction, stroke, and pulmonary embolism (37% of total deaths), as well as hemorrhages (11%) [2]. Valvular heart disease and coronary artery disease are the most frequent cardiac manifestations of APS [3]. However, APS complicated with aortic dissection is extremely rare [4–6], and no such case in primary APS has previously been reported in the English literature.

Case Report

A 42-year-old woman was diagnosed with primary APS 16 years ago following an unexplained abortion in the 24th week of her first pregnancy combined with pulmonary embolism and a confirmed so-called “triple-positive” antibody test result (positive test results for lupus anticoagulant, anticardiolipin antibody, and anti-beta-2-glycoprotein-I antibody test). She was treated with prednisolone for 5 years, cyclophosphamide for 1 year, and warfarin except during pregnancy. During her second pregnancy, which occurred 4 years after the diagnosis, she was given aspirin, but the pregnancy resulted in intrauterine fetal death, with thrombosis confirmed in the placenta. During her third pregnancy, which occurred 9 years after the diagnosis, she was placed on continuous intravenous heparin therapy and gave birth to her first child by Cesarean section without any major complications. She was then given warfarin again in addition to aspirin. She subsequently had no hemorrhagic or thrombotic events until hypermenorrhea at 15 years after the initial diagnosis. Warfarin was suspended, but her serum creatine level then gradually increased to 1.43 mg/dl, with an estimated glomerular filtration rate (eGFR) of 33 mL/min/1.73 m², which was normal before the suspension. She was diagnosed with APS nephropathy and was re-administered warfarin, which resulted in slight and gradual improvement in her eGFR.

She woke up in the morning of the day of presentation, 16 years after the initial diagnosis of primary APS, with a severe headache, nausea, and dizziness and soon lost consciousness. She was carried to our emergency room (ER) by ambulance, with a Glasgow coma scale (GCS) score of 3 and pinpoint pupils. Her heart rate was 49 beats per minute, and her blood pressure was 198/65 mmHg. Noncontrast computed tomography (CT) revealed right cerebellar hemorrhage with brainstem compression and intraventricular hematoma (Figure 1). No intracranial arteriovenous malformation or arterial aneurysm was detected on contrast-enhanced CT. The prothrombin time-international normalized ratio (PT-INR) was 2.16 with a normal platelet count, and the eGFR was 36 mL/min/1.73 m². The effect of warfarin was immediately reversed with prothrombin complex concentrate. Then, an emergent evacuation of the hematoma, suboccipital decompression, and intraventricular catheter placement were performed (Figure 2). She had severe hypertension on presentation despite no previous history of chronic hypertension. She needed high doses of multiple antihypertensives until discharge.

On postoperative day (POD) 1, she improved to GCS 15 and was extubated. Her blood pressure was 167/70 mmHg on POD 1, 170/58 mmHg on POD 2, and stabilized to within normal range after POD 3. She resumed warfarin on the same day. Additionally, pleural effusion was detected on chest X-ray and was confirmed for the next 1 month. The eGFR decreased from admission and was 11 mL/min/1.73 m² on POD 3. The patient was diagnosed with contrast-induced nephropathy based on the contrast-enhanced CT scan performed on the first day. She was
on temporary renal replacement therapy from POD 3. On POD 7, an echocardiography was performed to evaluate her cardiac function and volume status and accidentally showed a flap in the descending aorta. A contrast-enhanced CT scan revealed a communicating aortic dissection (Stanford type-B, De Bakey type-IIIb) with an entry in the lesser curvature of the aortic arch (Figure 3). All of the major organ arteries originating from the aorta were supplied from the true lumen with no organ damage. She was treated medically, and her systolic blood pressure has been maintained between 100 and 120 mmHg since then. She developed contrast-induced nephropathy again, and her eGFR decreased to 13 mL/min/1.73 m² on POD 11. She kept receiving temporary renal replacement therapy until POD 21, and her renal function then improved to the same level as that observed at baseline on admission. No major organ complications related to the dissection or the extension of the false lumen was confirmed until discharge. She was transferred to the rehabilitation hospital due to mild dysarthria and truncal ataxia on POD 59. She was able to walk short distances with a walker at the time of discharge.

Discussion

We hypothesize that aortic dissection occurred after cerebellar hemorrhage for the following reasons. First, serum C-reactive

Figure 2. Noncontrast CT scan in the transverse plane soon after the operation. The arrow indicates that the hematoma was evacuated.

Figure 3. Contrast-enhanced CT in the sagittal plane on POD 7. The arrow indicates a communicating aortic dissection with an entry into the lesser curvature of the aortic arch.
Some patients present with hypertensive emergencies without a previous history of hypertension [11]. GFR also decreases with APS nephropathy, although it did not necessarily reflect the exacerbation of APS nephropathy in this case since she had contrast-induced nephropathy in the same period. The reversal and discontinuation of antithrombotics might have accelerated small vessel thrombus formation, leading to exacerbation of the existing APS nephropathy, which likely contributed to postoperative hypertension in this patient.

We also propose that the APS itself caused aortic fragility in this patient. Medial necrosis was confirmed in all 3 pathological reports that showed aortic dissection with APS, and old thrombosis in the veins in aortic wall was also confirmed in one of them [4–6]. The patient’s history of pulmonary embolism, thrombosis in the placenta, and APS nephropathy suggests longstanding multiple microthrombosis in this patient. It was previously demonstrated in a dog model that the impairment of vasa vasorum blood flow leads to necrosis in the aortic media [12]. We assume that in this case, vasa vasorum thrombosis might have led to medial necrosis, which contributed to aortic wall fragility. Moreover, some studies have suggested that antiphospholipid antibodies accelerate atherosclerosis [13], which can impair resistance of the aortic wall to pressure. It is widely accepted that long-term corticosteroid use induces discontinuation of the connective tissue of the media [14], although this was not the primary cause of wall fragility in this case considering the relatively short history of steroid therapy.

The combination of anticoagulation therapy with aspirin and warfarin is highly likely to have contributed to the cerebellar hemorrhage observed in this patient. Warfarin increases the risk of intracranial bleeding, and adding aspirin to warfarin further increases this risk [15]. The target range for PT-INR was 1.6 to 2.0 before hospitalization in this patient. A target range of 2.0 to 3.0 is recommended in some guidelines in the US and EU [16,17]. However, the risk of intracranial hemorrhage caused by anticoagulation is far higher in Asian individuals than in whites [18]. There are no widely accepted guidelines suggesting the optimal target range for Asian patients with APS.

**Conclusions**

Here, we report the first case in the English literature of primary APS complicated with cerebellar hemorrhage and aortic dissection. Acute hypertension following hemorrhage and exacerbation of APS nephropathy likely triggered the dissection of the aortic wall, the integrity of which might have been compromised by longstanding antiphospholipid antibody and vasa vasorum thrombosis.
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Conflicts of interest
None.

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