



## Anticoagulant therapy and TEVAR in a patient with antiphospholipid syndrome presenting with pulmonary embolisms and multiple arterial embolisms due to thoracic aortic mural thrombosis



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### ABSTRACT

We often observe patients with antiphospholipid syndrome (APS) presenting with both venous and arterial thrombi. Anticoagulant therapy is effective for venous and peripheral arterial embolisms in these patients; however, it has opposite effects when applied for thoracic aortic mural thrombosis because of the risk of new arterial embolisms. Recently, thoracic endovascular aortic repair (TEVAR) has been used to prevent arterial embolisms due to aortic thrombosis. However, we generally hesitate to implant artificial materials in patients in a hypercoagulable state because this can cause new thrombi to develop. Here, we present a case of successful treatment by anticoagulant therapy and TEVAR in an APS patient presenting with pulmonary embolisms (PEs) and multiple arterial embolisms due to thoracic aortic mural thrombosis.

A 46-year-old man was referred to our hospital due to dyspnea and leg pain. Since contrast-enhanced computed tomography revealed PEs, thoracic aortic mural thrombosis, and lower limb arterial embolisms, we administered anticoagulation therapy. Three days later, contrast-enhanced computed tomography revealed new arterial embolisms in the right kidney. To prevent further arterial embolisms due to thoracic aortic mural thrombosis, we performed emergent TEVAR in addition to anticoagulant therapy. Thereafter, no venous or arterial embolisms recurred during the 13-month follow-up period.

**<Learning objective:** An optimal therapy has not been established for patients in a hypercoagulable state who are threatened by venous thrombi and multiple arterial embolisms due to thoracic aortic mural thrombosis. In such patients, in addition to anticoagulant therapy, thoracic endovascular aortic repair for thoracic aortic mural thrombosis can be a promising option to prevent further arterial embolisms.>

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### Introduction

We often observe patients with antiphospholipid syndrome (APS) presenting with both arterial and venous thrombi. Anticoagulant therapy is effective in treating venous and peripheral arterial embolisms in these patients [1]; however, it has opposite effects when applied to treat thoracic aortic mural thrombosis because of the risk of new arterial embolisms developing within

2 to 4 weeks after initializing therapy [2]. Therefore, an optimal therapy has not been established for such cases.

Thoracic endovascular aortic repair (TEVAR) has been used for treating aortic dissection, abdominal aortic aneurysms, and thoracic aortic aneurysms [1]. Because TEVAR can prevent arterial embolisms due to large aortic thrombi [2], applying TEVAR to treat thoracic aortic mural thrombosis can be a promising option for preventing secondary arterial embolisms. However, we generally hesitate to implant artificial materials in patients in a hypercoagulable state, such as those patients with APS, because the implantation of artificial materials can cause new thrombi to develop. To the best of our knowledge, there have been no reports on the use of TEVAR in patients with multiple arterial embolisms due to thoracic aortic mural thrombosis in the hypercoagulable state of APS.

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## Case report

A 46-year-old man was referred to our hospital due to dyspnea on exertion and leg pain at rest. A laboratory examination showed that the patient's C-reactive protein level was 6.27 mg/dl; the white blood cell count was 13,480 cells/ $\mu$ l, and the D-dimer level was 10.6  $\mu$ g/ml. The level of anti-cardiolipin antibody was high (52.9 U/ml). Contrast-enhanced computed tomography revealed pulmonary embolisms (PEs) in the bilateral pulmonary arteries, thoracic aortic mural thrombosis (Fig. 1A, B), and peripheral arterial embolisms in the left internal iliac arteries, peroneal artery, and posterior tibial artery (Supplementary Fig. S1). Since the PEs and acute limb ischemia were symptomatic, we started unfractionated heparin.

Three days later, the patient experienced sudden back pain. Emergent contrast-enhanced computed tomography revealed new embolisms in the right kidney, along with a reduction in the thoracic aortic mural thrombus (Supplementary Figs. S2 and S3). Because we could not permit the risk of new embolisms developing during treatment with the single anticoagulation therapy of unfractionated heparin, we decided to perform emergent TEVAR to prevent the recurrence of embolisms with the approval of the Institutional Review Board of Kagawa University. To prevent a thrombus shift toward the cranial side, we needed to extend the stent graft from that side. Furthermore, to prevent new peripheral artery embolism by excessive pressure on the thrombus, we needed to select the tapered type stent graft. For these reasons, we have decided to apply the Relay plus® (28/24 155 mm, Bolton Medical, Sunrise, FL, USA). Furthermore, to prevent new peripheral artery embolism, we placed the filter catheter (Neuhaus Protect®, TORAY, Tokyo, Japan) from the right femoral artery at the level of the diaphragm during procedure. The stent graft was deployed just distal to the origin of the left subclavian artery and completely covered the thoracic aortic mural thrombus. After removal of the filter catheter, no thrombus could be confirmed visually. On the second day after surgery, warfarin therapy, targeting a prothrombin time-international normalized ratio (PT-INR) of 2.5–3.5, and clopidogrel at 75 mg was started. Seven days after the surgery, contrast-enhanced

computed tomography demonstrated an appropriate graft position, reduced pulmonary and kidney embolization, and no new thrombi (Fig. 1C, D). Ten days after the surgery, treatment with unfractionated heparin was ended because warfarin therapy reached the optimum PT-INR. Although antibiotic treatment was required for a catheter infection, the patient was discharged from the hospital on the 49th day. Three months later, increased levels of anti-cardiolipin antibody (16.5 U/ml) were noted twice, and the patient was definitively diagnosed with APS. We continued to prescribe warfarin at 5 mg and clopidogrel at 75 mg and the D-dimer level decreased to a normal level (1.0  $\mu$ g/ml). We used contrast-enhanced computed tomography to confirm an appropriate graft position and that no new thrombi had formed at 13 months after discharge.

## Discussion

The present study demonstrates that treatment with anticoagulant therapy and TEVAR for thoracic aortic mural thrombosis can be a promising option for preventing further arterial embolisms in patients in the hypercoagulable state of APS.

First, we selected unfractionated heparin as an initial anticoagulation therapy; however, new arterial embolisms in the kidney occurred along with a reduction in thoracic aortic mural thrombosis. This case indicates the importance and difficulty of preventing arterial embolisms due to thoracic aortic mural thrombosis, even in the case of symptomatic PEs and acute limb ischemia.

Recently, TEVAR has been used to prevent arterial embolisms due to large aortic thrombi [2]; however, stent graft placement in patients in the hypercoagulable state of APS should be carefully considered. Perl and colleagues reported remarkably high rates of target vessel revascularization (hazard ratio: 6.45) in patients with APS who had undergone a percutaneous coronary intervention [3], suggesting that stent placement in coronary arteries in APS patients should be carefully considered. On the other hand, Scantlebury and colleagues reported an interesting case regarding recurrent mitral valve thrombosis in a patient with APS [4]. They concluded that APS causes valvular thrombosis in both native and

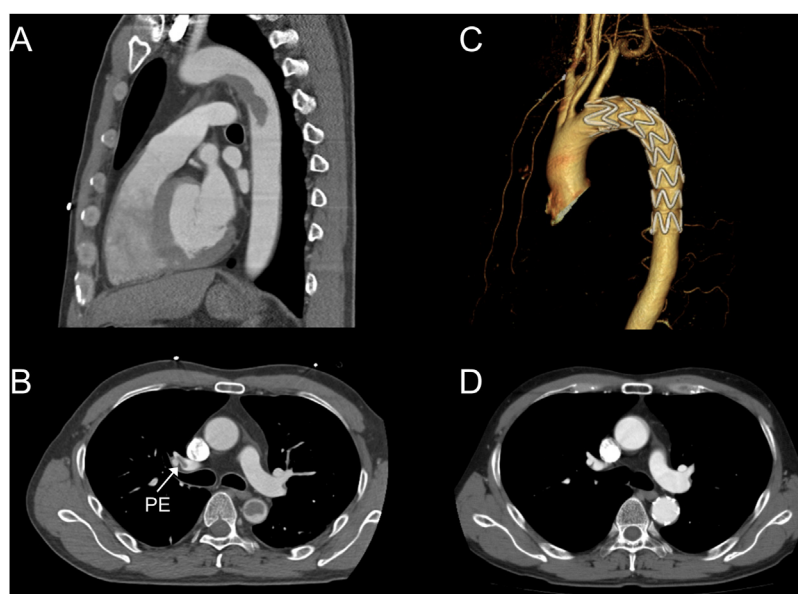


Fig. 1.

(A) Thoracic aortic mural thrombus at the end of the aortic arch. (B) Pulmonary embolism (PE) in bilateral pulmonary arteries. (C) Thoracic endovascular aortic repair for the prevention of embolization. (D) Reduced volume of PE after anticoagulant therapy.

prosthetic valves, including bioprostheses; however, the resolution of thrombosis in bioprostheses can be achieved by sustained anticoagulant therapy. Their study suggests that the implantation of artificial materials, such as stent grafts, could be available even to patients in the hypercoagulable state of APS through adequate and continuous anticoagulant therapy. As a point to be noted, when we measure PT-INR in APS patients, we need to be cautious because point of care devices sometimes show incorrect values of PT-INR [5].

Importantly, Meyermann and colleagues reviewed the cases of patients who initially underwent TEVAR; 93.1% of them had no signs of recurrence and no evidence of repeated phenomena [2]. TEVAR has become a feasible and safe treatment for aortic disease, with high procedural success and low incidences of postprocedural complications and short-term mortality [6]. Therefore, we performed TEVAR in addition to anticoagulant therapy in the current patient in the hypercoagulable state of APS patient. Thereafter, we continued anticoagulant therapy even after the PEs disappeared and prevented new thrombosis and arterial embolisms. To the best of our knowledge, this is the first report of TEVAR applied in the case of a patient in the hypercoagulable state of APS who was threatened by venous thrombi and multiple arterial embolisms due to thoracic aortic mural thrombosis.

We have dealt with a particular case and had successful treatment with applying the Relay plus® and the filter catheter (Neuhaus Protect®). When the thrombus is small, and the risk of a thrombus shift toward the cranial side is low, expanding stent graft initially in the caudal side or the middle part would be a beneficial procedure. We must carefully select the stent graft depending on the size and location of aortic mural thrombosis. In addition, we should have further considered ways to reduce the risk of embolism during deployment. Rapid pacing or caval occlusion could be effective to reduce the risk of embolism in the case of hemodynamic stability. However, this patient presented with bilateral pulmonary embolisms. Since we were concerned about the risk of hemodynamic instability, we selected distal protection to reduce the risk of embolism instead of rapid pacing or caval occlusion.

When should we have performed TEVAR in the present case? Boufi and colleagues reported that the recurrence rate of thoracic aortic mural thrombosis after anticoagulant therapy was 39% [7]. This case also suggests that anticoagulant therapy can cause an aortic embolism in cases of thoracic aortic mural thrombosis. If we had performed TEVAR before starting anticoagulant therapy, it might have been possible to prevent new embolisms in the right kidney. Therefore, we should carefully consider the optimal timing of TEVAR for treating thoracic aortic mural thrombosis.

In the present study, we report a case of the successful treatment with anticoagulant therapy and TEVAR of a patient in

the hypercoagulable state of APS. Anticoagulant therapy and TEVAR can prevent secondary arterial embolisms in patients in the hypercoagulable state of APS. Although there were several case reports and systematic reviews to demonstrate that TEVAR is promising to prevent the aortic thromboembolism in hypercoagulable states [8], no randomized study was conducted. A clinical study is warranted to determine the optimal timing of TEVAR and its effectiveness compared with medical therapy alone in patients with hypercoagulable states.

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None.

## Conflict of interest

The authors have no conflict of interest to report.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jccase.2019.08.002>.

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