Successful Anticoagulation Therapy for Antiphospholipid Syndrome with Mobile Aortic Thrombi

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INTRODUCTION

Most systemic embolizations are caused by thrombi in the left side of the heart. Several hypercoagulable states have been associated with aortic thrombosis; indeed, Laperche et al. [1] reported that 17% of patients with thrombosis of the aortic arch had evidence of hematostatic disorders. Antiphospholipid syndrome (APS) is a disorder of coagulation that usually manifests as arterial and venous thromboses or pregnancy-related complications such as miscarriage, stillbirth, and severe preeclampsia. The most common site of arterial thrombosis in APS is the central nervous system, with half of the cases resulting in strokes and transient ischemic attacks [2]. The major source of arterial systemic emboli is the heart, whereas systemic thrombi originating from the aorta are much less common [3]. We hereby report the case of successful anticoagulation management in an APS patient with mobile thrombi within the aorta.

CASE

A 58-year-old male patient presented to the emergency department with vomiting, dysarthria, and right-sided upper and lower limb weakness. Of note, he had a history of cerebral infarction associated with left-sided weakness 4 years previously, that recovered fully on aspirin medication, but no history of diabetes, hypertension, or arrhythmias.
He was a smoker with a 30 pack-year history. There was no family history of thrombosis or malignancy. On examination, his chest X-ray and electrocardiogram was normal. However, magnetic resonance imaging of the brain revealed multiple acute embolic infarctions of the left frontal and parietotemporal lobes (Fig. 1). Diagnostic work-up to determine the cause of the infarctions included transthoracic echocardiography (TTE), transesophageal echocardiography (TEE), magnetic resonance angiography (MRA) of the brain and neck, and computed tomography angiography (CTA). Normal cardiac function was observed on TTE, with no atrial fibrillation or thrombus seen in the heart and ascending aorta. MRA revealed no thrombus, atheroma, or stenotic lesion in the carotid and intracranial arteries. However, TEE and CTA revealed multiple mobile thrombi within the ascending aorta and aortic arch (Fig. 2). Serological investigations for anti-cardiolipin, anti-double stranded DNA, anti-ssA/Ro, anti-ssB/La, lupus anticoagulant, and anti-phospholipid antibodies showed normal values. However, the protein S antigen level was decreased (37%), while anti-beta-2 glycoprotein 1 (anti-beta-2 GP 1) antibody level was increased (36.8 U/mL). In view of high risk of postoperative cerebral infarction, and given that the size of the thrombi were small, the patient was initiated on medical therapy instead of surgery. He initially received low-molecular-weight-heparin for 4 days before being switched to continuous heparin infusion, which maintained the activated partial thromboplastin time levels within a target range of 60-80 sec. On day 10 of admission, he was started on warfarin (on top of the heparin infusion), with daily monitoring of the prothrombin time (PT)/international normalized ratio (INR). A repeat TEE and CTA on day 12 of admission did not demonstrate any remaining thrombus (Fig. 3); the heparin infusion was therefore stopped and the warfarin dosage adjusted accordingly. The patient was discharged on day 13 of admission with maintenance warfarin, with a targeted PT/INR range of 3-4. A confirmatory diagnosis of APS was made when a second positive anti-beta-2 GP 1 antibody level was obtained during his outpatient clinic follow-up; he was then started on hydroxychloroquine as the management of APS. The patient recovered completely.
and remained well during his subsequent follow-up, with no symptoms of distal embolic event and no recurrence of aorta thrombi seen on CTA 3 months post-discharge.

DISCUSSION

APS occurs as a result of autoimmune production of antibodies against the cell membrane’s phospholipid. The Sapporo criteria require one clinical event (vascular thrombosis or pregnancy mortality before 10 weeks of gestation), and two antibody blood tests spaced at least 12 weeks apart that confirm the presence of either lupus anticoagulant, anti-cardiolipin, or anti-beta-2 GP 1 antibodies for the diagnosis of APS [4]. In the present case, APS was confirmed based on the presence of multiple thrombi within the aorta, as well as positivity of anti-beta-2 GP 1 antibodies on two occasions. In general, TTE, TEE, and CT scan can be used for the radiological diagnosis of an aortic thrombus. TTE visualizes the aortic root and proximal ascending aorta; in some patients, it can demonstrate the aortic arch from suprasternal notch views. However, most echocardiographers advocate the use of TEE for the diagnosis of mobile thrombi within the heart or aorta [5]; TEE is more accurate than TTE as the probe is located closer to the aorta and can be used at a higher frequency [1, 3]. CT scanning is an alternative modality used to evaluate aortic thrombus; it can sometimes detect thrombi in areas that are not visualized by TEE [6].

To the best of our knowledge, no randomized studies have evaluated the advantage of surgical approach compared to medical therapy with regards to management of aortic thrombosis. In medical treatment, anticoagulation and thrombolytic therapy are considered first-line attempts in preventing embolization of the aortic thrombus. Anticoagulation is not harmful in patients with aortic thrombi; in fact, there were fewer strokes in patients who received anticoagulation therapy [7]. On the other hand, there is a risk of thrombolytic agents selectively lysing a thrombus, and releasing the bulk of the lesion into the blood stream, leading to systemic embolization [8]. Reports of successful surgical therapy in cases of first or recurrent thrombi have been described. These reports suggested that surgical therapy is a better option for selected patients with acceptable surgery for cardiopulmonary bypass and medical treatment failure [7,8].

We report this rare case in which thrombi within the ascending aorta and aortic arch of a patient with APS was successfully-treated medically. The current recommendation for treatment of thrombosis in APS is long-term warfarin, of which the duration and intensity of treatment are still under debate [9]. Cohen et al. [10] suggested that the treatment of a first unprovoked venous thrombosis in patients with APS is long-term anticoagulation with a target PT/INR range of 2-3. However, the treatment of arterial thrombosis in patients with APS is controversial due to the lack of prospective studies. Most of the recommendations for treatment with higher intensity warfarin (PT/INR 3-4) in these patients comes from retrospective reviews of patient cohorts. These studies concluded that higher intensity warfarin is superior to standard treatment (whereby the target PT/INR range is 2-3) [11-13]. A recent systemic review of secondary thromboprophylaxis for arterial thrombosis in patients with APS showed that patients treated with higher intensity warfarin rarely experience recurrent events. Bleeding complications appear to be similar in patients on higher intensity warfarin in comparison to standard treatment.
Based on these reports, we initiated our patient on warfarin, with a target PT/INR range of 3–4. However, we agree that the treatment of arterial thrombosis in patients with APS continues to be a controversial subject; hence, more prospective studies are required.

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