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Native Aortic Valve Thrombosis: What's Behind?

ABSTRACT

KEY WORDS: native aortic valve, thrombosis, cancer, transesophageal echocardiography

Native aortic valve thrombosis is an exceptionally rare and serious condition characterized by the formation of a thrombus on the native aortic valve. It presents a significant clinical challenge and can lead to severe complications, including heart failure or cardiogenic shock due to a heart attack or aortic valve dysfunction, neurological issues such as stroke, and peripheral embolisms affecting the arteries of the arms, legs, kidneys, and other organs. Given the numerous potential causes of peripheral embolism, native aortic valve thrombosis is an extremely rare source. Due to its low incidence, there is limited data on its aetiology, treatment, complications, and clinical outcomes, with most information derived from individual case reports. It is imperative to identify the underlying cause, which frequently poses a significant clinical challenge. We present the case of a 55-year-old patient with a pronounced prothrombogenic condition, which manifested as a venous thromboembolism and thrombosis of the native aortic valve. This condition led to a repeated embolism into the central nervous system and peripheral arteries of the arms and legs. The underlying cause of the prothrombogenic state was a newly diagnosed lung carcinoma.

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CASE REPORT

A previously healthy 55-year-old woman, a non-smoker, presented to the angiology outpatient clinic with a three-week history of left swelling. Her medical history was notable only for asthma. Clinical examination revealed no abnormalities other than left leg calf swelling. An ultrasound of the left leg veins indicated acute popliteal and posterior tibial deep vein thrombosis and treatment with therapeutic doses of dalteparin was initiated.

Baseline laboratory tests, including complete blood count, troponin level, screening rheumatological examinations, liver and kidney function, were normal, except for an elevated D-dimer level of 21,114 µg/L. There was no clinical evidence of infections. A chest X-ray showed thickening in the left hilum but no other pathological changes. One week later, the patient reported tingling and weakness in her right arm and leg. A head CT revealed two acute ischemic lesions. Anticoagulant therapy was immediately discontinued, and a filter was inserted into the inferior vena cava. Despite this, hemiparesis recurred the next day, and a follow-up head CT revealed another ischemic lesion measuring 2 × 1 cm.

Suspecting paradoxical embolism, a transthoracic echocardiography (TTE) was performed, which showed a thickening of the right and non-coronary aortic valve leaflets, mild aortic valve insufficiency, no shunt, and otherwise normal findings. A transesophageal echocardiography (TEE) confirmed a mass on the right and non-coronary aortic valve leaflets (figure 1). To further characterize the mass, a cardiac CT angiography was performed, revealing hypodense changes measuring 11 × 11 × 6 mm on the non-coronary leaflet, 7 × 7 × 6 mm on the right coronary leaflet, as well as a smaller hypodense change on the left coronary leaflet. These lesions did not enhance convincingly after contrast administration and were most likely thrombi. According to the cardiosurgical council, surgical treatment of the aortic valve thrombosis was not indicated. The patient was treated conservatively, initially with subtherapeutic doses of dalteparin due to a recent ischemic stroke, and after ruling out the haemorrhagic trans-

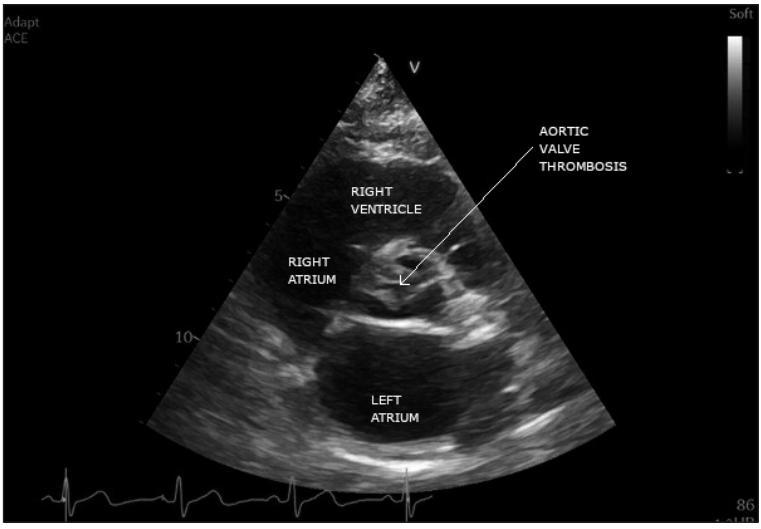

Figure 1. Transthoracic echocardiography (parasternal window, short axis) showing mass (thrombosis) on the right and non-coronary aortic valve leaflets.

formation of ischemic lesions by a head CT, therapeutic doses were resumed.

A contrast-enhanced chest CT showed a 6.5 cm consolidation in the lingula suspicious for pulmonary malignancy, signs of lymphangitic carcinomatosis, bilateral pleural effusion, and a small pulmonary thromboembolism. The preliminary radiological stage was assessed as T3 N2 M1a. An abdominal CT showed no signs of malignancy in the abdomen. A head MRI revealed multiple small acute ischemic lesions consistent with microembolisms. A pleural puncture confirmed a malignant exudate, cytomorphological indicating non-small cell carcinoma, most likely adenocarcinoma of the lung. Molecular genetic testing revealed the presence of a proto-oncogene tyrosine-protein kinase-1 (ROS-1) gene fusion.

The thoracic-oncology council recommended systemic immunotherapy with entrectinib. However, before systemic targeted therapy could be initiated, the patient's condition rapidly deteriorated despite therapeutic doses of dalteparin with recurrent emboli affecting both the central nervous system and peripheral arteries of the arms and legs. She developed tetraparesis, and acute ischemia of the fingers and toes, and experienced severe pain. Unfortunately, only palliative treatment was possible for the patient, a palliative mobile unit was activated, and the patient died two months after the first symptoms appeared.

DISCUSSION

Unlike thrombosis on an artificial, mechanical aortic valve, thrombosis on a native aortic valve is extremely rare, resulting in very limited data in the literature. However, the number of published cases of thrombosis on native valves has increased with each decade, primarily due to improved imaging techniques. By 2020, 74 cases had been described. That is why this condition poses significant diagnostic and therapeutic challenges *(1)*.

The most common clinical presentations of aortic valve thrombosis are myocardial infarction, acute limb ischemia, cerebrovascular incidents, and heart failure *(1)*. In our clinical case, the first manifestations were tingling and weakness in patient's right arm and leg due to an embolism into the central nervous system, followed by several embolisms into the peripheral arteries of the arms and legs, resulting in acute limb ischemia.

The diagnostic work-up typically relies on an echocardiography, particularly TEE, due to its superior temporal and spatial resolution compared with TTE *(2)*. A TTE with 59% and a coronary angiography with 29% sensitivity are not sufficiently sensitive examinations for detecting aortic valve thrombosis. Therefore, it is essential to perform either TEE or aortic root angiography, which achieves 100% sensitivity. Other imaging modalities, such as cardiac CT, can also be useful but may yield false negatives, especially in cases involving mobile thrombi *(1)*. In our clinical case, in addition to TEE, we also performed a CT angiography of the heart to obtain additional information regarding the aetiology of the mass on the valve.

Given the rarity of native aortic valve thrombosis, it is essential to investigate underlying causes thoroughly. In most described cases, native aortic valve thrombosis occurs in hypercoagulable conditions, with antiphospholipid syndrome being the most common, in systemic connective tissue disease, alternatively formed on a diseased valve (calcifications), followed by aortic root/valve structural abnormalities such as a bicuspid aortic valve, degenerative aortic valve, left ventricular assist device, hypoplastic left heart syndrome or as a consequence of trauma (surgery catheterization) *(1, 3)*. Therefore, in the absence of structural abnormalities of the aortic valve and endothelial lesions, it is reasonable to check autoantibodies

(anti-cardiolipin, lupus anticoagulants, anti-b2GPI antibodies), tumour markers, and coagulopathy markers (prothrombin gene mutation, C-S protein deficiency, antithrombin III, resistance to activated protein C). We must also always consider the possibility of an underlying malignancy and conduct a thorough screening for cancer *(4)*.

In our case, we observed simultaneous deep vein thrombosis and thrombosis on the native aortic valve. Suspecting an occult malignancy, we performed a CT scan of the abdomen and chest, which revealed a tumour in the lingula. This tumour was diagnosed as non-small cell carcinoma, most likely adenocarcinoma of the lung. We have found another case report in the literature describing thrombotic masses on the native aortic and mitral valves in a patient with lung cancer *(5)*.

Differentiating native aortic valve thrombosis from tumours, particularly papillary fibroelastoma, which is the most common valvular tumour, can be challenging. Both native valve thrombus and papillary fibroelastoma can cause systemic embolic events *(6)*. The definitive diagnosis is made histologically.

The risk of in-hospital clinical deterioration in patients with native aortic valve thrombosis is 38%, and the overall in-hospital mortality is 20% *(1)*. Therefore, native aortic valve thrombosis predicts an unfavourable prognosis. Some authors advocate for the prompt surgical resection of this valvular disease, regardless of its size and shape, not only to confirm the pathology but also due to the potential for life-threatening complications from a left-sided mass and for representing a poor prognosis *(5)*.

Due to the lack of evidence, decision-making regarding the treatment approach is often based on individualized care, the recommendations of a heart team, or expert opinion. Anticoagulation treatment decisions are complex, especially when central nerve system embolisms prevent treatment with therapeutic doses of anticoagulant drugs. The optimal treatment approach is unclear; there are no guidelines to definitively recommend thrombectomy accompanied with anticoagulation versus anticoagulation alone.

Our patient was treated conservatively with anticoagulation and supportive therapy. Based on the systematic review, patients who were not treated with thrombectomy and those who experienced clinical deterioration or recurrence during hospitalization had worse outcomes with statistically significant increased in-hospital mortality *(1)*. In our case, a neurological complication (hemiparesis) recurred during hospitalization and, according to the cardio surgery council, she was treated conservatively without surgery, which was somehow understandable given the newly discovered metastatic malignant disease *(2)*. However, thrombectomy is worth considering in patients who are otherwise reasonable candidates for surgery.

In our patient, following conservative treatment, the condition rapidly deteriorated due to recurrent central and peripheral embolisms, resulting in critical limb ischemia. Consequently, only palliative therapy could be administered, and the patient passed away two months after the onset of the initial symptoms. This case underscores the severity and extremely poor prognosis associated with aortic valve thrombosis. In any case, serious consideration of operative treatment would be necessary in the absence of disseminated malignancy. The literature review indicates that surgical intervention has a better outcome in these cases *(1)*.

CONCLUSIONS

A thrombosis on the native aortic valve is an extremely rare, urgent, and dangerous condition with a poor prognosis and high mortality. It is essential to investigate underlying causes thoroughly. Rapid action

and treatment are necessary, though challenging, as decisions often must be made on a case-by-case basis. Due to the rarity of the disease and the consequent lack of data, there are no established guidelines. There is a need to report cases that can enhance knowledge about this condition. Our report represents a rare case of spontaneous native aortic valve thrombosis in a patient with newly discovered pulmonary carcinoma, who was treated conservatively.

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