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FUNGAL MYCOTIC VEGETATION IN THE ASCENDING AORTA

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Background

In most clinical scenarios, the appropriate diagnostic methodology and treatment plan can be determined in a timely manner. However, complex clinical cases with obscure etiology can be deceptive, and a multidisciplinary approach can help to clarify things. At the Methodist DeBakey Heart & Vascular Center, we encountered a huge progressive mass in the ascending aorta in a 50-year-old chronic hemodialysis patient after mechanical aortic valve replacement. In addition to initial image diagnosis and consultation workups, a transcranial Doppler (TCD) study identified continuous generation of microemboli that suggested the need for urgent surgical resection instead of conservative heparin IV therapy. Histopathology showed the huge friable mass to be hyphenated fungal mycosis (Aspergillus or Fusarium) and necrotic tissue surrounded by fresh thrombus. The postoperative course was uneventful, and the patient was discharged home.

Preoperative Clinical Course

A 49-year-old African American man with a history of end-stage renal disease on chronic hemodialysis, hypertension, and hyperlipidemia underwent aortic valve replacement (SJM Regent 23 mm mechanical valve prosthesis, St. Jude Medical Inc., St. Paul, Minnesota, USA) due to aortic valve stenosis and insufficiency with quadricuspid aortic valve (Figure 1). The postoperative course was uneventful, and the patient returned to his regular hemodialysis cycle and was maintained on antihypertensive and anticoagulation therapy. There was no postoperative paravalvular leakage and no sign of sepsis or active infective endocarditis. Nine months after the surgery, he presented to the emergency room with headache, nausea, and visual field disturbance.

Upon hospital admission, vital signs showed arterial blood pressure at 158/99 mmHg, heart rate of 86 bpm, body temperature of 98.7° F, and no physical signs of heart failure. A head computed tomography (CT) scan demonstrated bilateral occipital stroke (left <right) and a small amount of post-infarct hemorrhage around the same stroke areas (Figure 2). There was no significant carotid disease by duplex scanning. Laboratory blood work-up indicated slight increase of WBC count (11,780/μL) and mild fever, but other than that there was no remarkable abnormality. A TEE showed a normally functioning mechanical aortic valve and no intracardiac mass. However, TEE revealed a large pedunculated mobile mass (1.9 cm x 1.5 cm) within the intraluminal space of the ascending aorta that arose just 1–2 cm above the aortic mechanical valve (Figure 3). The appearance was suggestive of mobile thrombus perhaps associated with an atheromatous plaque. Intravenous heparin was initiated while carefully monitoring the potential risk of bleeding against existing bilateral occipital hemorrhages.

Despite heparin administration, follow-up TEE one week later demonstrated rapid growth of the mass (maximal diameter was 2.5 cm), and cardiac MRI showed marked obstruction of the blood flow at the ascending aorta (Figure 4). Furthermore, a transcranial Doppler (TCD) study detected two remarkable high-intensity transient signals (HITS), which strongly suggested generation of microemboli released from the growing mobile mass at the ascending aorta (Figure 5). These emboli signals are differentiated from

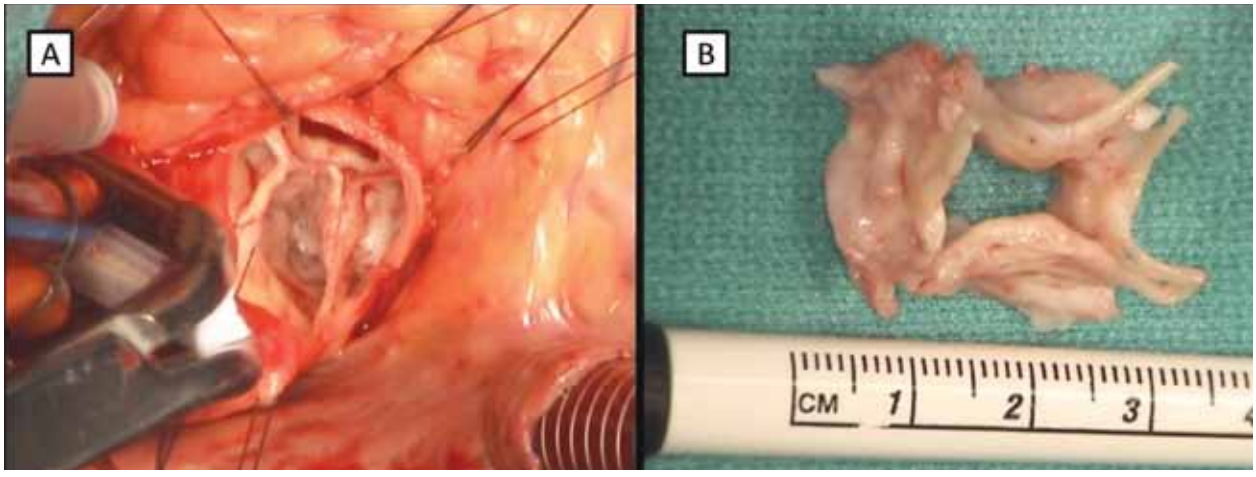


Figure 1. Quadricuspid aortic valve. A: surgical view of the calcified quadricuspid valve before resection; B: general appearance of the resected aortic valve.

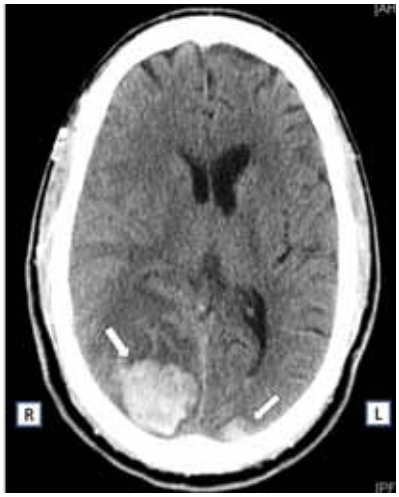
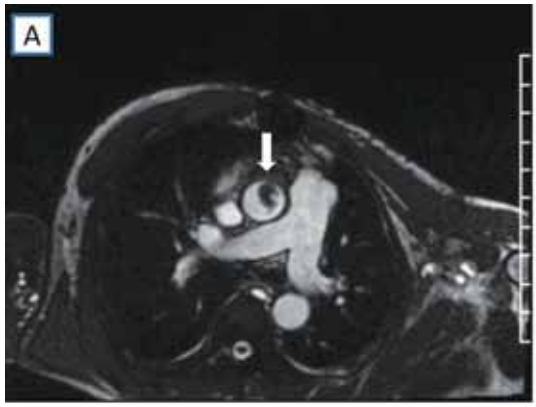


Figure 2. Head CT. Arrows: intracranial hemorrhage at bilateral occipital lobes.



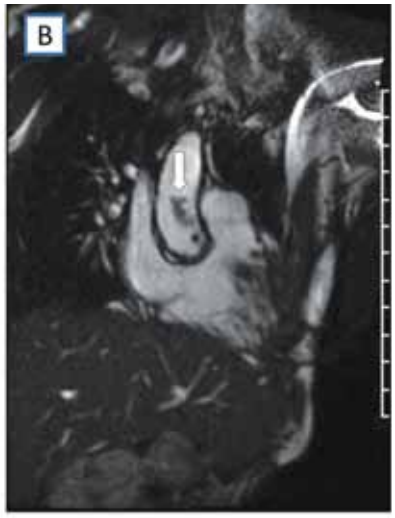


Figure 4. Cardiac MR imaging study shows irregular mobile mass that has a pedunculated attachment to the anterior wall of the ascending aorta, just above the aortic root. Arrows indicate mobile mass. A: transverse view of the ascending aorta; B: sagittal section view.

mechanical valve-related HITS by administration of 100% oxygen.[1] Head CT scan showed a reduction in the size of the occipital lesions in spite of the patient being on heparin. The patient remained afebrile, and blood cultures were negative. Due to the mass's rapid growth refractory to intravenous anticoagulation therapy and the continuous generation of microemboli, a multidisciplinary clinical team comprised of cardiac surgeons, a cardiac imaging specialist, and a neurologist determined that the most appropriate therapy was a surgical resection of the mass. With the patient's consent, the surgery was planned.

Surgical Findings

Preoperatively, it was noted that moderate mitral valve regurgitation and stenosis (10.8 mmHg pressure gradient) with significant calcification of the leaflets was present. Since this was not considered significant, only surgical resection of the mass was planned; the mitral valve would be left intact to reduce time on cardiopulmonary bypass and thus minimize the risk.

After a median sternotomy and establishment of cardiopulmonary bypass, cardiac arrest was achieved with only retrograde cardioplegia to avoid damaging the mass and the possible consequent coronary embolization that could be caused by insertion of the antegrade cardioplegia catheter. An aortic cross-clamp was placed at the distal ascending aorta far enough from the expected location of the mass. An aortotomy was made at the mid-ascending aorta, just above the previous aortic aortotomy suture line. From the aortotomy opening view, the large mass was observed to originate from the anterior side of the aorta around the previous suture line with a tan-gray, lobulated appearance, like a small bunch of grapes surrounded by fresh soft thrombus (Figure 6). The resected mass was very friable and measured about 2.5 cm in length. It was located about 2 cm distal to the mechanical aortic valve, which was found to be in pristine condition. After removing the mass, the ascending aorta was carefully inspected, and loose atherosclerotic plaques and small debris were thoroughly removed. The aortotomy was closed with 3-0 Prolene running suture. Weaning of the cardiopulmonary support was smooth and the chest was closed after appropriate hemostasis.

Pathophysiology Finding and Postoperative Course

The entire specimen consisted of numerous hyphenated fungi with areas of necrotic fungi in thrombus. Gomori methenamine silver (GMS) stain revealed that this fungus was suspected to be a Fusarium species or possibly Aspergillus. However, culture of the sample specimen was fungus-negative, thus no specific species of fungus could be identified (Figure 7). Blood culture results for gram stain, anaerobic culture, and acid-fast bacterium (AFB) were all negative. No fungus was even detected from the blood culture specimen. However, as a result of consultation with the infectious disease group, broad-spectrum antifungal drugs such as micafungin,

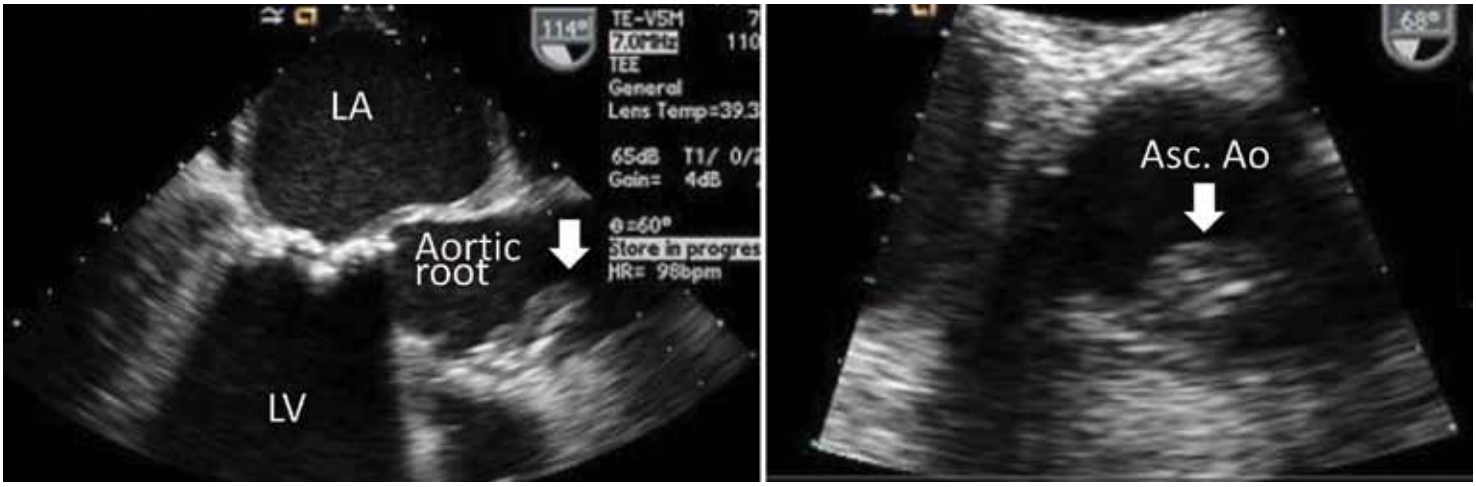


Figure 3. TEE. White arrows indicate pedunculated mobile mass arose at the ascending aorta. Asc. Ao: ascending aorta; LA: left atrium; LV: left ventricle.

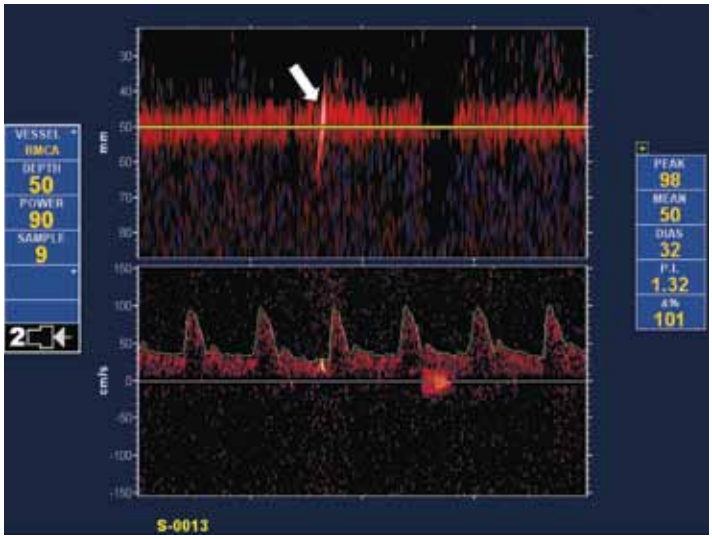


Figure 5. Transcranial Doppler results; microembolic signal detected on TCD screening. The right middle cerebral artery was monitored by TCD system for 15 minutes and captured 2 embolic signals. One of two emboli signals is indicated by a white arrow.

voriconazole, and terbinafine were administered for prophylactic purposes along with postoperative antibiotic therapy. Hemodialysis was continued as scheduled, and erythropoietin was given to correct the nephrogenic anemia. The patient initially suffered visual defects and exhibited some abnormal visual symptoms before and right after the surgery. However, these symptoms gradually improved. Coumadin was temporarily discontinued after surgery, but it was restarted after reconfirmation of the head CT scan and did not exacerbate neurological symptoms.

Discussion

Systemic fungal mycosis is a typical infectious disease in patients with immunodeficient status due to immunosuppressive therapy, chronic hemodialysis treatment, implantation of vascular graft prosthesis, and other immunodeficiency syndromes.[2-5] However, development of fungal mycotic vegetation at the ascending aorta is a very rare clinical manifestation.[6,7] Since blood culture tends to be fungus-negative and no disease-specific imaging findings are available, it was difficult to diagnose the mass as "fungal mycotic vegetation" preoperatively.[7] In our case and in the other literature, definitive diagnosis was made by postoperative pathological studies.[7]

There are several differential diagnoses for mass formation in the aorta, as follows:

1. **Mobile plaque and thrombus.** A mobile mass at the ascending aorta is often identified by TEE screening in patients with cerebral stroke. In the elder population, extended atherosclerosis of the aorta causes mobile atheromatous plaque, and this can be a nidus of thrombus formation, which are both associated with stroke and transient ischemic attack (TIA).[8] Various clinical reports alerted that mobile plaque greater than 4 mm with a noncalcified appearance significantly increases the risk of ischemic stroke and mortality.[8-10] Unlike mobile plaque that has an irregular margin, thrombus at the aorta commonly forms a relatively smooth mural attachment or ball-shaped mass. The intramural aortic thrombus can be treated by anticoagulation therapy, and this approach often results in shrinkage or complete disappearance of the thrombus.[8] G. Piffaretti et al. reported that the ascending aorta mural thrombus comprises only 5% of thoracic aortic thrombi, whereas most of the thoracic aortic thrombi are observed at the descending aorta (28%) and the aortic arch (16%).[11] This may be implicated in a degree of aortic atherosclerosis. However, some groups of aortic thrombi, i.e., those which form a pedunculated shape, are associated with a high risk of thromboembolic events. Therefore, it may require a surgical intervention or other aggressive alternative therapy in order to avoid a possible embolic event.[12]
2. **Primary aortic tumor.** Primary aortic tumor is a rare disease compared to other cardiac tumors such as cardiac myxoma and cardiac malignant tumors.[13] According to a worldwide literature review, 135 cases have been reported for patients with a primary tumor in the aorta.[8,14] Most of the aortic primary tumors were sarcomas; these primarily arose in the aortic arch (11%) and in the descending aorta (35%). Most importantly, there have been a few reports of benign primary aortic myxoma. If the aortic primary tumor was a sarcoma, the patient had a dismal prognosis.
3. **Fungal mycotic aneurysm.** Systemic fungal infection rarely causes an aortic mycotic aneurysm. Mycotic aneurysms are a rare disease identified in only 0.9% of aortic aneurysms overall.[15] It is defined as a localized artery dilatation due to small septic emboli, obstructing the entire vascular lumen or the feeding vasa vasorum, and causing destruction of the arterial wall. In turn, disruption of blood flow and the local inflammatory response cause vascular wall destruction, which results in dilatation of the

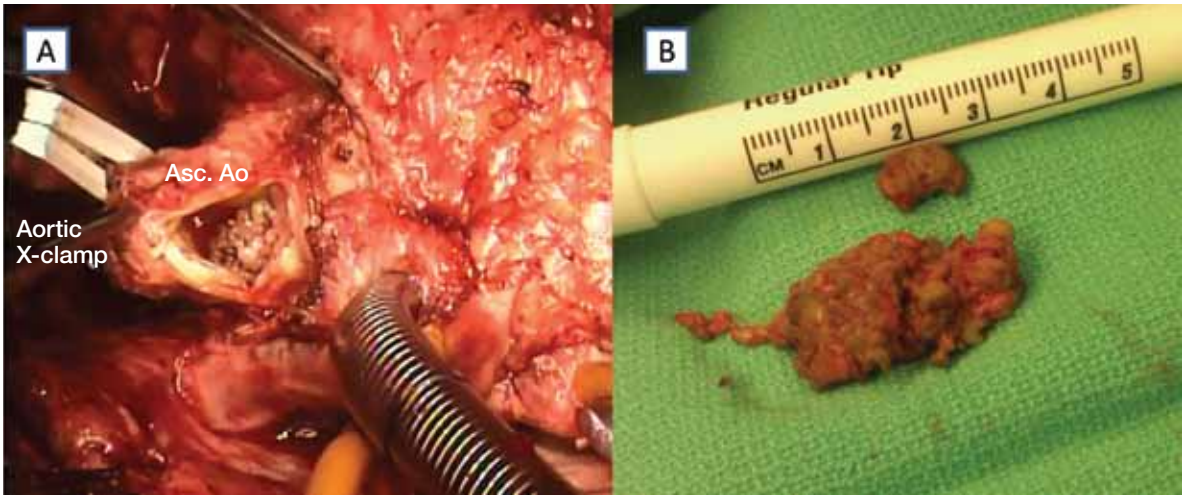


Figure 6. Surgical view (A) and appearance of the resected friable mass in the ascending aorta (B).

artery. The aneurysm structure is manifested as a true aneurysm or sometimes as a pseudoaneurysm. Mycotic aneurysm occurs in the femoral artery (38%), abdominal aorta (31%), the superior mesenteric artery (8%), the brachial artery (7%), the iliac artery (7%), and the carotid artery (5%).[16] Mycotic aneurysm rarely arises at the ascending aorta. Chen et al. reported that in their 2,585 series of aortic aneurysm patients, only two patients were identified as having an ascending aorta mycotic aneurysm.[15]

4. **Fungal mycotic vegetation in the intraluminal aortic system.** Unless the patient has had previous cardiac surgery, particularly implantation of a vascular graft prosthesis, development of fungal mycotic vegetation at the ascending aorta is an unusual clinical manifestation. In our case, the TEE study utilized over the course of anticoagulation therapy was effective in following the progression of mass size. Furthermore, the detection of a high HITS count with TCD and the dialogue among the multidisciplinary clinical team enabled the timely conversion of our treatment plan from one of conservative heparin IV therapy to more aggressive open-heart surgery. In fact, the resected fungus ball was pedunculated as visualized on TEE and cardiac MRI and very friable with lobulated characteristics, which appeared to have a high probability of causing a life-threatening embolic event. The etiology of the fungus ball development is unknown. However, since the fungus mass originated around the previous surgery suture line of the aortotomy, intraoperative contamination may be one putative cause.

One interesting finding during surgery was that there was a 4-0 Prolene suture hanging down from the old suture aortotomy line into the aortic lumen. It is speculated that this old suture may have triggered the fungi deposition and developed the vegetation as a nidus in combination with turbulent jet passing through the mechanical aortic valve. Another possible cause may be fungal infection through chronic hemodialysis shunt puncture.[4] As described in the other literature, blood culture studies tend to be negative for fungus, thus it is difficult to nail down definite etiology prior to surgery. However, Huang et al. of University of Louisville mentioned that fungal endaortitis is associated with high mortality if the clinician hesitates in developing a treatment plan and delays the initiation of aggressive treatment such as broad-spectrum antifungal drug therapy and surgical intervention.

A strong clinical acumen and decision making are required to capture several key phenomena: (1) previous cardiac or aortic surgery, (2) the presence of aortic atherosclerosis or comorbidity of high-risk atherosclerosis, (3) evidence of a mobile mass at the ascending aorta by TEE, and (4) episodes of repeating or concurrent embolic events. We would like to especially emphasize that prompt clinical judgment, particularly determination of appropriate therapeutic timing, is the most important element not only for improving mortality but also for high quality of life after treatment. TCD is the most useful noninvasive diagnostic tool to determine whether a mobile mass requires urgent surgical treatment. Regardless of the etiology, as soon as the ascending aortic mass is found to be a nidus of microembolization, the clinician may need to consider early surgical intervention rather than conservative therapies.

Conclusion

We successfully rescued a high-risk patient with rare fungal mycotic vegetation that had developed in the ascending aorta. In addition to TEE and cardiac MRI, TCD was an effective tool to detect ongoing microembolization. These comprehensive diagnostic methodologies, cooperation among a multidisciplinary medical team, and optimization of therapeutic timing are essential for the treatment of complex rare diseases such as this.

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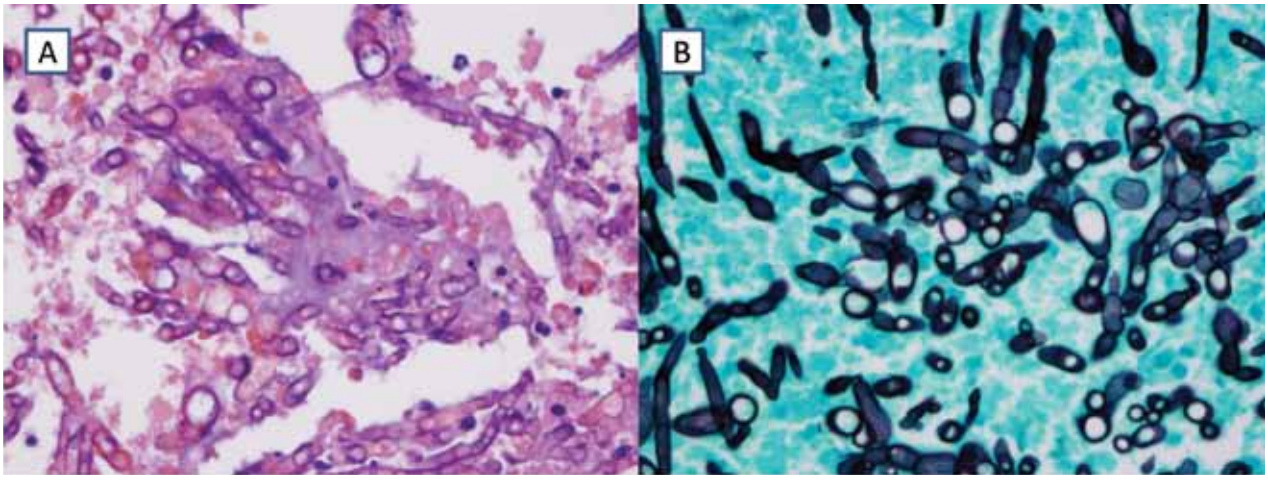

Figure 7. Pathological findings. A: HE stain/x40 magnification; B: GMS stain/x40 magnification.

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