Aspergillus thromboembolism from a mycotic ascending aortic pseudoaneurysm

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This case report describes an immune-competent patient with acute upper extremity ischemia caused by thromboembolism from an *Aspergillus*-infected ascending aortic pseudoaneurysm. Efforts to identify the source of an acute arterial thromboembolic occlusion should be made, and a high index of suspicion for mycotic infection should be maintained in patients with an atypical presentation, such as fevers of unknown origin. Additional measures, such as pathologic examination of thromboembolic debris, blood cultures, and positron emission tomography, should be performed to identify the etiology in these unexplained situations. (J Vasc Surg Cases 2015;1:94-6.)

Mycotic thromboembolization is a rare cause of acute large-vessel arterial occlusion. This case report describes an immune-competent patient with acute upper extremity ischemia caused by embolization from an *Aspergillus*infected ascending aortic pseudoaneurysm. Signed consent was obtained from the patient for publication.

CASE REPORT

A 57-year-old man, who had undergone coronary artery bypass grafting (CABG) 5 years prior to presentation, was admitted to an outside facility with a 4-day history of fevers and a 24-hour history of numbness and tingling in his right upper extremity. The patient was noted to have an absent radial pulse. Duplex ultrasound imaging demonstrated a brachial artery occlusion. The patient was transferred to our institution for further evaluation and treatment.

Upon arrival, the patient was taken emergently to the operating room for thromboembolectomy. A Fogarty catheter was used to remove ~ 5 cm of normal-appearing clot after multiple passes, with subsequent return of a strong radial pulse, a weak ulnar pulse, and brisk capillary refill in all fingers. The patient was maintained on intravenous systemic anticoagulation.

A postoperative electrocardiogram demonstrated sinus rhythm. A transthoracic echocardiogram was negative for an embolic source. A transesophageal echocardiogram with bubble

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- Author conflict of interest: none.
- This case report was presented at the Tennessee Chapter, American College of Surgeons 2014 Annual Meeting Plenary Session, Paris Tenn, August 8-10, 2014.
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The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

2352-667X

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http://dx.doi.org/10.1016/j.jvsc.2015.03.010

study likewise confirmed the absence of vegetation or clot within the heart. A computed tomography (CT) angiogram of the chest demonstrated a 7.2-cm saccular pseudoaneurysm of the ascending aorta, which had not been seen on either echocardiogram (Figs 1 and 2).

Pathologic examination of the clot using hematoxylin and eosin and Grocott methenamine silver stains unexpectedly found hyphae with parallel and acute angle branching, morphologically consistent with *Aspergillus* (Fig 3). Voriconazole systemic antifungal therapy was initiated.

Human immunodeficiency virus serologic testing was negative. The results of a complete blood count with differential were within expected limits, and blood cultures were negative for growth. A head CT was negative for disseminated infection, and the chest CT likewise had not shown pulmonary disease. An ophthalmologic examination was negative for fungal endophthalmitis.

The patient was transferred to a cardiac surgery unit with additional capabilities. A positron emission tomography (PET) scan confirmed localized infection to the ascending aortic pseudoaneurysm. After axillary cannulation and initiation of cardiopulmonary bypass, a sternotomy was performed under deep hypothermic circulatory arrest. Cardioprotection after aortic cross-clamping was achieved selectively through a proximal vein graft and the coronary ostia. The aortic pseudoaneurysm was opened primarily, and cavitary thrombectomy was performed. The infection and false aneurysm appeared to originate from a proximal vein graft anastomotic suture line. After extensive débridement and irrigation of the pseudoaneurysm, a large aortic patch repair using heterologous bovine pericardium was performed for complete exclusion.

The patient was discharged home in satisfactory condition. He had not demonstrated any signs of recurrence upon initial followup, and will be followed annually with contrasted CT scans of the chest. The patient has been maintained on life-long voriconazole antifungal therapy, aspirin, and warfarin.

DISCUSSION

This is a unique case of *Aspergillus* endoaortitis and aortic pseudoaneurysm producing acute limb ischemia secondary to thromboembolization in an immune-competent patient who did not have any cardiovascular prosthetic implants. Upon reflection, the patient recalled an event ~ 3 years prior

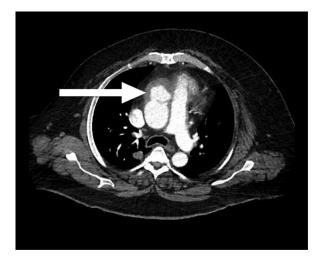


Fig 1. Axial view of ascending aortic pseudoaneurysm (*white arrow*).



Fig 2. Sagittal view of ascending aortic pseudoaneurysm (*white arrow*).

when he was placing mulch in his yard, which had caused mild respiratory symptoms. In the outside environment *Aspergillus* is known to be ubiquitous and can be internalized by inhalation.¹⁻⁴ The most common source for *Aspergillus* endoaortitis is pulmonary,^{5,6} which represents a possible source of infection in this patient. In addition, the patient had undergone CABG; thus, infection at the time of CABG represents another possible source. The presence of an *Aspergillus*infected aortic pseudoaneurysm after CABG is extremely rare but can occur at an anastomotic or aortic cannulation site.^{7,8} Indeed, some have suggested that, despite its rarity, aortic mycotic aneurysm and fungal endoaortitis be considered in any patient who presents with fevers of unknown origin who had previously undergone an invasive cardiovascular procedure.^{4,9,10}

Aspergillus is the most common cause of fungal endoaortitis,¹¹ and although Aspergillus endoaortitis is

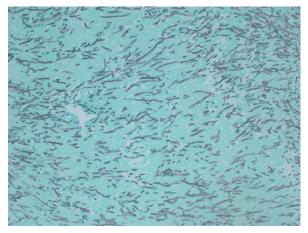


Fig 3. Grocott methenamine silver stain at original magnification $\times 20$ delineated hyphae with parallel and acute angle branching consistent with *Aspergillus*.

usually associated with an immunocompromised state,^{4,6} it can rarely occur in immune-competent patients.^{2,3} The most common source of immunocompromise associated with *Aspergillus* endoaortitis is chemotherapy,¹² with other common causes including immunosuppression,^{6,13,14} diabetes,¹⁵ and acquired immune deficiency syndrome.¹ This patient had no known history of cancer, immunosuppressive therapy, diabetes, or any other recognized cause of immunocompromise.

Acute arterial thromboembolic occlusion of the extremity is often associated with cardiac arrhythmias, left ventricular aneurysm, and valvular heart disease.¹ In this patient, however, the echocardiograms did not demonstrate any intracardiac abnormalities that could have produced an arterial embolism. Moreover, Aspergillus embolization from an aortic or cardiac source is usually associated with infection of prosthetic material, such as a prosthetic heart valve or an aortic graft,^{4,5} but this patient had no prior cardiovascular prosthetic implants of any kind. In the setting of embolization from an unknown source, pathologic examination of thromboembolic debris should be considered.¹⁶ After thromboembolectomy, if an aneurysm is discovered to be the source, then PET can confirm aneurysm infection based on uptake and can delineate other locations of active infection.¹⁷

Systemic anticoagulation after thromboembolism resulting in acute ischemia has been supported by level 1 evidence.¹⁸ This notion has been reiterated in current practice guidelines by the Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) and by the American College of Chest Physicians.^{19,20} Moreover, in the setting of arterial embolization, systemic anticoagulation reduces the chance of future embolization by up to 75% and can decrease long-term mortality.¹⁸ Although the combination of systemic anticoagulation with antiplatelet therapy has been questioned in symptomatic peripheral arterial disease,²⁰ administration of a combination of systemic anticoagulation with antiplatelet

therapy has been suggested after operations for acute thromboembolism, except in situations where specific contraindications exist.²¹

Upon diagnosis of a mycotic aortic pseudoaneurysm, prompt surgical intervention should be performed.⁸ Repair options include autologous pericardial patch, heterologous bovine pericardial patch, cryopreserved allograft, or a synthetic graft if the above are unavailable.^{8,12,22,23} Surgical intervention to remove the infected thromboembolic source is the treatment of choice,^{8,11,12,15} although *Aspergillus* endoaortitis is often fatal even with both medical and surgical intervention.^{2,11,13}

Even though patients with mycotic aneurysms of the aorta often present with fevers,⁹ blood cultures are often negative in cases of fungal infection, and cultures that are persistently negative should alert the clinician that a fungal rather than bacterial infection may be present.^{5,7,10} Indefinite systemic antifungal therapy plays a prominent role in the medical treatment of patients with *Aspergillus* endoaortitis.^{13,14} Voriconazole has been shown to have a superior response compared with amphotericin B, and if adverse effects develop, then voriconazole can be transitioned to itraconazole.²⁴ Once the diagnosis of invasive aspergillosis has been made, systemic antifungal therapy using voriconazole should be initiated.²⁴

CONCLUSIONS

Efforts should be made to identify the source of an acute arterial thromboembolic occlusion, and a high index of suspicion for mycotic infection should be maintained in patients with an atypical presentation, such as fevers of unknown origin. Additional measures, such as pathologic examination of thromboembolic debris, blood cultures, and PET, should be performed to identify the etiology in these unexplained situations. Surgical intervention to remove the infected thromboembolic source is the treatment of choice, although *Aspergillus* endoaortitis is often fatal even with both medical and surgical intervention. Indefinite systemic antifungal therapy plays a prominent role in the medical treatment of patients with *Aspergillus* endoaortitis, whether or not surgical intervention is possible.

We acknowledge Dr Elizabeth Arze, East Tennessee State University Department of Pathology, Dr Melanie Davidson, Mountain States Health Alliance Department of Cardiology, and Dr Dima Youssef, Mountain States Health Alliance Department of Infectious Disease.

REFERENCES

- Light JT Jr, Hendrickson M, Sholes WM, Portnoy DA, Bell WH 3rd, Kerstein MD. Acute aortic occlusion secondary to Aspergillus endocarditis in an intravenous drug abuser. Ann Vasc Surg 1991;5:271-5.
- Pasqualotto AC, Denning DW. Post-operative aspergillosis. Clin Microbiol Infect 2006;12:1060-76.
- Abenza-Abildua MJ, Fuentes-Gimeno B, Morales-Bastos C, Aguilar-Amat MJ, Martinez-Sanchez P, Diez-Tejedor E. Stroke due to septic embolism resulting from Aspergillus aortitis in an immunocompetent patient. J Neurol Sci 2009;284:209-10.
- Noordally SO, Sohawon S, De Bels D, Duttmann R, Gottignies P, Devriendt J. Late onset of Aspergillus aortitis presenting as femoral

artery embolism following coronary artery bypass graft surgery. Acta Medica (Hradec Kralove) 2011;54:175-6.

- Calcaterra D, Bashir M, Gailey MP. Ascending aortic graft thrombosis and diffuse embolization from early endoluminal Aspergillus infection. Ann Thorac Surg 2012;94:1337-9.
- Abderrahim E, Ben Abdallah T, Aouina H, Ben Maïz H, Kheder A. Aortic thrombus during invasive aspergillosis in a kidney transplant recipient. J Postgrad Med 2008;54:62-3.
- Gray R, Kaplan L, Matloff J, Uman S, Shachtman J. Aortic pseudoaneurysm with Aspergillus aortitis. An unusual complication of coronary bypass surgery. Chest 1986;89:306-8.
- Devbhandari MP, Balasubramanian SK, Campanella C, Brackenbury ET. Aortic pseudoaneurysm complicating sternal wound infection following CABG. Cardiovasc Surg 2003;11:243-5.
- Prech M, Grajek S, Cieśliński A, Jemielity M. Mycotic aneurysm of the ascending aorta following CABG. Heart 2000;83:E3.
- Duygu H, Nalbantgil S, Ozerkan F, Kirilmaz B, Yagdi T. Aspergillus niger aortitis after aortic valve replacement diagnosed by transesophageal echocardiography. Echocardiography 2006;23:405-6.
- Huang J, Bouvette MJ, Hagi Y, Subramanian S, Zhou J, Austin EH 3rd. Flow impeding fungal thrombus in the ascending aorta. Ann Thorac Surg 2008;86:1373-5.
- Hosono M, Hattori K, Shibata T, Sasaki Y, Hirai H, Suehiro S. Mycotic aneurysm of the distal aortic arch caused by Aspergillus. Jpn J Thorac Cardiovasc Surg 2006;54:160-3.
- Grothues F, Welte T, Grote HJ, Roessner A, Klein HU. Floating aortic thrombus in systemic aspergillosis and detection by transesophageal echocardiography. Crit Care Med 2002;30:2355-8.
- Ronco F, Simsir S, Czer L, Luo H, Siegel RJ. Incidental finding by two-dimensional echocardiography of a mycotic pseudoaneurysm of the ascending aorta after orthotopic heart transplantation. J Am Soc Echocardiogr 2010;23:580.e1-3.
- Rose HD, Stuart JL. Mycotic aneurysm of the thoracic aorta caused by Aspergillus fumigatus. Chest 1976;70:81-4.
- O'Connell JB, Quiñones-Baldrich WJ. Proper evaluation and management of acute embolic versus thrombotic limb ischemia. Semin Vasc Surg 2009;22:10-6.
- Murakami M, Morikage N, Samura M, Yamashita O, Suchiro K, Hamano K. Fluorine-18-fluorodeoxyglucose positron emission tomography-computed tomography for diagnosis of infected aortic aneurysms. Ann Vasc Surg 2014;28:575-8.
- Jackson MR, Clagett GP. Antithrombotic therapy in peripheral arterial occlusive disease. Chest 2001;119(1 Suppl):2838-995.
- Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG; TASC II Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg 2007;45(Suppl S):S5-67.
- 20. Alonso-Coello P, Bellmunt S, McGorrian C, Anand SS, Guzman R, Criqui MH, et al; American College of Chest Physicians. Antithrombotic therapy in peripheral artery disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141(2 Suppl):e6698-908.
- Magishi K, Izumi Y, Shimizu N. Short- and long-term outcomes of acute upper extremity arterial thromboembolism. Ann Thorac Cardiovasc Surg 2010;16:31-4.
- **22.** Zhou W, Lin PH, Bush RL, Terramani TT, Matsuura JH, Cox M, et al. In situ reconstruction with cryopreserved arterial allografts for management of mycotic aneurysms or aortic prosthetic graft infections: a multi-institutional experience. Tex Heart Inst J 2006;33:14-8.
- Dhadwal AK, Abrol S, Zisbrod Z, Cunningham JN Jr. Pseudoaneurysms of the ascending aorta following coronary artery bypass surgery. J Card Surg 2006;21:221-4.
- 24. Herbrecht R, Denning DW, Patterson TF, Bennett JE, Greene RE, Oestmann JW, et al; Invasive Fungal Infections Group of the European Organisation for Research and Treatment of Cancer and the Global Aspergillus Study Group. Voriconazole versus amphotericin B for primary therapy of invasive aspergillosis. N Engl J Med 2002;347:408-15.

Submitted Dec 9, 2014; accepted Mar 1, 2015.