CASE REPORT
Acute ischemia of bilateral lower extremities as a presenting feature of disseminated mucormycosis endocarditis: A case report

Niranjan Tachamo, MD1*, Priya Rajagopalan, MD1, Salik Nazir, MD1, Saroj Lohani, MD1, Brian Le, MD2 and Nitin Patel, MD1

1Department of Medicine, Reading Health System, West Reading, PA, USA; 2Department of Pathology, Reading Health System, West Reading, PA, USA

Disseminated mucormycosis endocarditis is extremely rare, and only a few cases have actually been reported in the literature. It is almost universally fatal despite aggressive surgical and medical management. In this article, we present the case of a 48-year-old immunocompromised male with mucormycosis endocarditis, who presented with acute bilateral lower extremity ischemia and passed away due to subsequent multi-organ failure. To our knowledge, this is the first case report of disseminated mucormycosis native valve endocarditis presenting as acute bilateral lower extremity ischemia.

Keywords: acute lower extremity ischemia; disseminated; fungal endocarditis; native valve; mucormycosis

*Correspondence to: Niranjan Tachamo, Department of Medicine, Reading Health System, Sixth Avenue and Spruce St, West Reading, PA 19611, USA, Email: niranjantachamo@gmail.com

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Fungal endocarditis is uncommon. However, it is considered to be the most severe form of infective endocarditis (1). Predisposing factors include diabetes mellitus, hematologic malignancies, long-term steroid therapy, prosthetic valves, trauma with infected wounds, and other immunocompromising conditions (1, 2). Disseminated mucormycosis endocarditis of native valve is uncommon and associated with high mortality (2). Management invariably requires surgical intervention along with optimal medical therapy, but the outcome is usually poor (1).

Case presentation
A 48-year-old male with past medical history of intravenous (IV) drug abuse on methadone treatment, untreated chronic hepatitis C infection, and poorly controlled diabetes mellitus presented to the emergency department with 2-3 h of acute bilateral lower extremity pain which started while he was watching television. The pain was severe and continuous with no aggravating or relieving factors. He denied any history of trauma, fever, chills, skin rashes, or joint pain. Past history was negative for atrial fibrillation, peripheral artery disease, blood clots, or malignancies. He was a non-smoker and his last IV drug use was several months ago.

On physical examination, he was alert, oriented, afebrile, and hemodynamically stable. His vitals were BP 152/84 mm Hg, heart rate (HR) 112/min and regular, temperature (T) 97.9 F. Both feet were pale and cold but with normal range of motion. The bilateral femoral pulses were 2+; however, the pedal pulses were absent. Gross motor and sensory function were intact.

Pertinent labs included white blood count of 12,900/μL, hemoglobin of 10 g/dL, platelet count of 144,000/μL, blood glucose of 345 mg/dL with normal renal function test, liver function test, thyroid function test, and coagulation profile. Electrocardiogram showed sinus tachycardia with prolonged QTc of 556 but no atrial fibrillation. Computed tomogram (CT) angiogram of abdomen revealed multiple splenic and bilateral renal infarctions. CT angiogram of the pelvis showed occlusion of left common iliac, left popliteal tibial, right common femoral and right popliteal tibial arteries (Fig. 1). The patient was taken to operating room for emergency embolectomy. He underwent embolectomies involving multiple arteries (right common femoral and deep femoral, right popliteal and tibial, left common iliac, and left popliteal-tibial arteries) along with bilateral lower extremity arterial tissue plasminogen activator (tPA) infusion. Intra procedure patient developed hypoxic respiratory failure and could not be extubated. He was transferred to the intensive care unit on ventilator support for further care.

Transthoracic echocardiogram (TTE) performed to evaluate the source of multiple emboli revealed a large
1.2 cm highly mobile vegetation attached to the anterior mitral valve leaflet with associated eccentric posteriorly directed severe mitral regurgitation (Figs. 2 and 3). Transesophageal echocardiogram revealed additional small pulmonary valve vegetation with a patent foramen ovale. Blood cultures were sent and the patient was started on broad spectrum antibiotics. CT of the brain demonstrated a 10-mm area suspicious for cerebral infarct in the right frontal lobe. Bilateral carotid duplex was unremarkable. HIV 1 and 2 antibodies and Rapid Plasma Reagin (RPR) were non-reactive. Antiphospholipid and Beta-2 glycoprotein antibodies came back negative. Emergency cardiac catheterization done due to troponin elevation showed 100% embolic occlusion of the mid left posterior descending artery. Preliminary blood cultures were negative for any bacterial growth.

The embolectomy specimen was examined histologically, showing organizing blood clot with abundant fungal organisms arranged in parallel arrays (Fig. 4). On high power magnification, the fungal elements were characterized by wide hyphae, with lack of distinctive septa (Fig. 5). The morphologic features were interpreted as most consistent with Mucorales. Fungal cultures were sent and
empiric liposomal amphotericin B for fungal endocarditis was added to his regimen. Cardiothoracic surgery was consulted for mitral valve replacement and pulmonic valve repair. Unfortunately, clinical course was complicated by acute upper gastrointestinal bleeding requiring an urgent gastroenterology evaluation delaying the surgical course. He underwent an esophagogastroduodenoscopy which revealed a 3-cm friable pedunculated polypoid mass within the gastric antrum with diffuse gastritis/gastropathy but no active bleeding. The mass was biopsied due to concern for malignancy. During this period, the patient continued to deteriorate with ventilator-dependent respiratory failure and multi-organ dysfunction. Biopsy of the gastric mass was negative for malignancy, but reconsideration of valve replacement surgery was not entertained as he was felt to be a high-risk candidate because of his comorbidities and multiple organ failure. Bacterial and fungal cultures remained persistently negative.

With aggressive medical management, the patient was transiently weaned off of ventilator support; however, he developed recurrent respiratory distress requiring reintubation. Repeat TTE showed increased mitral valve vegetation size now measuring 2.2 × 1.6 cm on the anterior mitral valve leaflet along with an additional vegetation on the posterior valve leaflet. Because of the critical condition of the patient with refractory shock and multi-organ failure, the family decided to go on comfort care. The patient continued to deteriorate and passed away on the 18th day of hospitalization.

Discussion

Mucormycosis is a rare opportunistic fungal infection caused by Mucorales fungi (3). It occurs almost exclusively in persons with immunosuppression (1, 3, 4). Although rhinocerebral mucormycosis is the commonest presentation, it may present as pulmonary, cutaneous, gastrointestinal, or disseminated infection (3). Our patient presented with acute bilateral lower limb ischemia and also had multiple septic emboli in spleen and kidneys, which, to the best of our knowledge, has never before been reported in the literature.

Fungal endocarditis is characterized by large vegetations with increased propensity for prosthetic heart valves and risk for embolization (1). Very rarely it can infect the native valves (2, 4). Fungal endocarditis should always be considered in patients with large vegetations and negative routine blood cultures (1). Our patient had large vegetations in native mitral and pulmonic valves, which by itself is rare. Bacterial and fungal blood cultures were negative in our patient.

Surgical debridement of necrotic tissue along with early administration of antifungal agent is the mainstay of treatment (1–3, 5). Despite adequate and aggressive surgical and medical management, outcome is usually dismal (1). Liposomal amphotericin B has been the agent of choice; however, anecdotal reports suggesting posaconazole may be effective for refractory or intolerant cases (2, 5). All successfully treated cases reported in the literature had undergone aggressive surgical debridement along with antifungal treatment (1). Our patient could not undergo surgical management due to multiple comorbidities and eventually died of multi-organ failure.

Teaching points

1. In acute limb ischemia in high-risk patients (intravenous drug abuse, diabetes mellitus, chronic steroid use, malignancies, and other immunocompromising conditions), fungal endocarditis leading to embolic phenomena should be considered.
2. Combined early surgical and medical management is the standard treatment, but the outcome is usually poor.

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