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HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

BEGINNER

Prosthetic Valve Endocarditis From *Trichosporon asahii* in an Immunocompetent Patient

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ABSTRACT

Fungal endocarditis is a rare clinical entity. This report describes an unusual case of fungal endocarditis caused by infection with *Trichosporon asahii* in a 20-year-old immunocompetent man who received the diagnosis 1 year following biological aortic valve replacement. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:693–6)

Our patient is a 20-year-old man with a history of severe aortic stenosis who underwent biological aortic valve replacement (AVR) with an EPIC valve (St. Jude Medical, Minneapolis, Minnesota), with no immediate postoperative complications. His medical history was negative for human immunodeficiency virus infection, diabetes mellitus, neutropenia, malignant disease, or connective tissue diseases. One month following surgery, the patient noted drainage of serous fluid from his sternal wound. He was treated with topical antibiotics with resolution of the drainage. One year following AVR, he was admitted for low-grade fever and erythematous macules on his palms, soles, and conjunctiva. The initial workup included a negative transesophageal echocardiogram (TEE) and negative blood cultures. Because of the high clinical suspicion of bacterial endocarditis, he was subsequently treated with 2 weeks of intravenous vancomycin and gentamicin, followed by long-term oral antibiotics.

One month following initiation of antibiotics, our patient presented with recurrent fever, nausea, and severe headache. Vitals signs were stable on admission. Physical examination demonstrated small, erythematous, macular lesions consistent with Janeway lesions on bilateral palms and soles (**Figure 1A**). Cardiopulmonary examination was remarkable for a systolic ejection murmur and a diastolic decrescendo murmur. Neurologic examination was significant for right-sided weakness in upper and lower extremities

LEARNING OBJECTIVES

- To understand the risk factors for fungal endocarditis.
- To highlight the role of multidisciplinary management of fungal endocarditis.

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ABBREVIATIONS AND ACRONYMS

AVR = aortic valve replacement

MRI = magnetic resonance imaging

TEE = transesophageal echocardiogram

TTE = transthoracic echocardiogram

and right quadrantanopia. Laboratory examination was significant for leukocytosis (white blood count: 13.85 × 10 cells/mm^3) with eosinophilia (eosinophils: 25.41%).

1. HOW IS INFECTIVE ENDOCARDITIS DIAGNOSED?

The presentation of infective endocarditis is often variable and requires a high index of suspicion. The Duke criteria, which incorporate serological, physical, and imaging findings, is recommended to risk stratify patients into 3 categories of definite, possible, and rejected diagnosis (1). A minimum of 3 sets of blood cultures obtained from different sites with an interval of at least 1 hour between the first and last set is recommended (1). Echocardiography plays a crucial role in the diagnosis and must be performed expeditiously, ideally within 12 h of initial evaluation (1). If the clinical suspicion of endocarditis is high and the initial transthoracic echocardiogram (TTE) findings are negative, a repeat TTE or a TEE should be performed. The use of other imaging modalities such as computed tomography and cardiac magnetic resonance imaging (MRI) may also play an important role (1). Intraoperatively, immediate identification of the pathogen using polymerase chain reaction has also proven useful (1). **Figures 1A to 1E** show the various manifestations of endocarditis in our patient.

MRI of the brain showed multiple embolic lesions in the right occipital and left parietal lobes with hemorrhagic transformation (**Figures 1D and 1E**). The patient was restarted on vancomycin, gentamicin, and rifampin while further work-up was conducted. Findings on an initial TEE were negative. However, computed tomography of the chest demonstrated a lesion above the prosthetic aortic valve. A repeat TEE 2 days following admission showed large vegetations on the anterior wall of the aorta, and this finding was confirmed with MRI of the chest. The patient was subsequently taken to surgery for treatment of infective endocarditis. Following surgery, intravenous amphotericin was started.

2. WHAT ARE THE OPTIONS FOR VALVE REPLACEMENT IN FUNGAL ENDOCARDITIS?

Our patient received an EPIC bioprosthetic valve, which was chosen on the basis of on patient and family preference. The patient was reluctant to take warfarin, and there was concern for the risk of hemorrhagic conversion with anticoagulation. Selection of a replacement valve is based on consideration of life expectancy, patient preference, compliance with anticoagulant agents, lifestyle, risk of bleeding, and risk of recurrent surgery (2). The patient's age alone should not be the determining factor. Structural valve dysfunction over time, leading to regurgitation or stenosis, is the major disadvantage of bioprosthetic valves and the major reason for repeat intervention.

3. WHAT IS THE TIMING OF SURGERY FOR INFECTIVE ENDOCARDITIS IN THE SETTING OF STROKE?

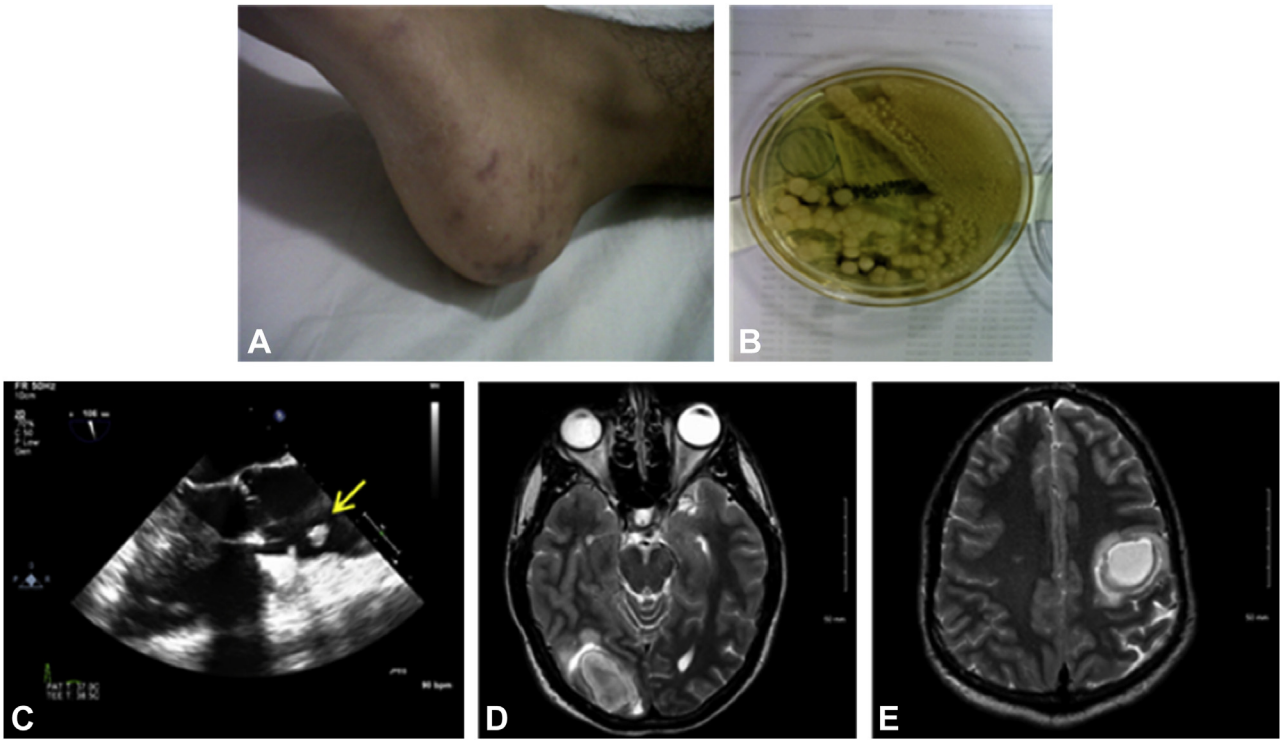
The management of complications of infective endocarditis or neurological sequelae is controversial. Cerebrovascular complications secondary to embolization from endocardial vegetations have a 20% to 40% incidence and are associated with an increased risk of post-operative morbidity and mortality (1,3). Guidelines from the American Heart Association and the European Society of Cardiology recommend delaying surgery for at least 4 weeks following intracranial hemorrhage (1,3,4). Results of a previous retrospective study demonstrated higher mortality when valve replacement was performed within 7 days of intracranial hemorrhage (5). Our patient's brain lesions were embolic with hemorrhagic transformation, which raised concern regarding the use of high-dose heparin during the surgical procedure. Following extensive discussions with the patient, family members, and the multidisciplinary care team, the decision was made that the benefit of surgery outweighed the risks. The patient tolerated the surgery without complications, and MRI performed following surgery showed no evidence of hemorrhage or enlargement of prior lesions.

Intraoperatively, a vegetation measuring 10 mm was discovered on the anterior wall of the aorta, and a perforation was noted on 1 leaflet of the EPIC valve. The valve was replaced, and the anterior wall was patched with bovine pericardium. A wet mount of the vegetation showed numerous hyphae, and the final pathology examination that showed positive results for *Trichosporon asahii* yielded the diagnosis of fungal endocarditis (**Figure 1B**).

4. WHAT IS THE ORIGIN OF FUNGAL ENDOCARDITIS?

The etiologic agents most frequently isolated are *Candida* and *Aspergillus* (6). The genus *Trichosporon* currently contains 37 recognized species, of which 8 are associated with infection or allergy: *T. asahii, T. asteroides, T. cutaneum, T. inkin, T. mucoides, T. ovoides, T. domesticum,* and *T. montevideense* (6,7).

FIGURE 1 Manifestations of *Trichosporon asahii* Endocarditis



(A) Janeway lesions. **(B)** *Trichosporon asahii* spores. **(C)** Aortic valve vegetation **(arrow).** Magnetic resonance imaging of the brain without contrast enhancement showing cerebral emboli **(D)** in the right occipital lobe and **(E)** in the left parietal lobe, with hemorrhagic transformation.

5. WHAT ARE THE RISK FACTORS FOR FUNGAL ENDOCARDITIS?

Fungal endocarditis is a rare clinical entity that has been associated with prior drug use, indwelling catheters, prosthetic valves, or immunocompromised states (1,6).

Trichosporon infection can lead to disseminated fungal infection in immunocompromised individuals, particularly in patients with malignant disease (8). Fungal infection with *T. asahii* carries a grave prognosis with a high mortality rate (1,8). Invasive *Trichosporon* infections have been associated with prior antibiotic therapy, a history of central catheter use, malignant disease, and hospitalization in intensive care units (8). The route by which *T. asahii* invades the human body remains unknown, however (8,9). One prior study of *Trichosporon* infections determined that blood, urine, and surgical wounds were the most common sites of infection, and *T. asahii* was the most frequently isolated species (8). This study also identified neutropenia, central venous catheters, malignant disease, surgical wounds, and male sex as risk factors for infection. We believe that the surgical wound was the likely source of infection in our patient. Few reports have described *T. asahii* infection of heart valves. Our review of publications yielded 1 report of *T. asahii* endocarditis of the mitral and aortic valve, and the patient was treated with fluconazole and valve replacement (9).

6. HOW IS FUNGAL ENDOCARDITIS MANAGED?

Infections with *Trichosporon* spp. are susceptible to treatment with amphotericin B, ketoconazole, and itraconazole. However, evidence suggests an emerging resistance to treatment because of the formation of biofilms (10). Our patient was successfully treated with amphotericin B, ketoconazole, and voriconazole. Current guidelines recommend treatment of fungal endocarditis with valve surgery in addition to parenteral antifungal therapy, followed by lifelong suppressive therapy with an azole agent (1).

Following valve replacement, our patient received intravenous treatment with amphotericin B and ketoconazole for 2 weeks. He was then transitioned to an 18-month course of oral voriconazole: 400 mg 3 times a day for 6 months, followed by 400 mg twice a day for 6 months, and 400 mg daily for 6 months. Our patient made a complete recovery without further complications. A repeat TTE showed normal function of the new prosthetic valve, without vegetations, and an intact anterior wall pericardial patch. Antifungal therapy was stopped on the basis of normalization of biological markers of inflammatory response and brain and cardiac imaging findings. On recent follow-up 5 years after surgery, and $3^1/_2$ years after stopping voriconazole, the patient remains stable without clinical or laboratory evidence of recurrent infection. Repeat blood cultures, C-reactive protein values, and erythrocyte sedimentation rate were unremarkable. His neurological condition improved in the first 2 weeks of treatment and completely normalized to the point that the patient graduated from college with a major in engineering.

The current case illustrates a distinctive presentation of fungal endocarditis from *T. asahii* infecting an immunocompetent man with a history of bioprosthetic AVR. Our patient presented 1 year following his initial valve replacement and was treated for a sternal wound infection, which is a recognized risk factor for fungal endocarditis (8). The patient's first signs of disease were skin lesions localized to the palms of the hands and soles of the feet. Although the skin manifestations were very suggestive of endocarditis, the presence of negative blood culture results made the diagnosis of endovascular infection particularly challenging. The duration of treatment is also poorly understood. This case highlights the importance of consideration of fungal endocarditis in patients with prosthetic valves.

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