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Case Reports

Valvular Endocarditis and Biventricular Heart Failure in the Setting of *Tropheryma whipplei* Disease

Defne Gunes Ergi, MD[1]; Hind J. Fadel, MD[2]; Hector I. Michelena, MD[3]; Grace Lin, MD[3]; Kevin L. Greason, MD[1]; Arman Arghami, MD, MPH[1]

[1]Department of Cardiovascular Surgery, Mayo Clinic, Rochester, Minnesota
[2]Department of Internal Medicine, Division of Infectious Diseases, Mayo Clinic, Rochester, Minnesota
[3]Department of Cardiology, Mayo Clinic, Rochester, Minnesota

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Abstract

Whipple disease is a rare systemic illness associated with weight loss, diarrhea, and arthralgia. Asymptomatic carriage is common, but the disease can be complicated by cardiac involvement and may result in culture-negative endocarditis. Cardiac manifestations of the disease can lead to death. This report presents the case of a 66-year-old man with Whipple disease and biventricular heart failure with cardiogenic shock. Medical therapy followed by successful replacement of the aortic and mitral valves resulted in substantial improvement.

Keywords: Endocarditis; heart failure; *Tropheryma*

Case Report

Presentation and Medical History

A 66-year-old man with a history of Whipple disease, heart failure with cardiomyopathy, cirrhosis, chronic kidney disease, and pulmonary hypertension (PHT) was referred to the clinic. On admission, he was severely malnourished and experiencing cardiogenic shock. Intestinal biopsy 2 months before admission had led to a diagnosis of Whipple disease, which was treated with 4 weeks of ceftriaxone followed by oral trimethoprim sulfamethoxazole.

Differential Diagnosis

The patient presented with anasarca, and the differential diagnosis included not only cardiac issues but also hypoalbuminemia caused by Whipple disease.

Management

Because of the patient's tenuous condition on arrival at the clinic, transesophageal echocardiography was not initially conducted. Transthoracic echocardiography revealed an ejection fraction of 46%, severely reduced right heart function, and severe aortic and mitral valve regurgitation. The left ventricular chamber size was enlarged, with a diastolic dimension of 57 mm and a systolic dimension of 44 mm. Right heart catheterization demonstrated a severely elevated right atrial pressure of 32 mm Hg, precapillary PHT with a mean pulmonary arterial pressure of 55 mm Hg, a pulmonary capillary wedge pressure of 27 mm Hg, and a pulmonary vascular resistance of 10 Wood units. Results of

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Corresponding author: Arman Arghami, MD, MPH, Department of Cardiovascular Surgery, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (arghami.arman@mayo.edu)

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Whipple polymerase chain reaction (PCR) in blood culture were negative. Right ventricular endomyocardial biopsy findings were negative for myocardial inflammation or involvement with Whipple disease. Enoxaparin sodium, intravenous furosemide, dobutamine, and bumetanide were started. Trimethoprim sulfamethoxazole was discontinued, and doxycycline was initiated at 100 mg every 12 hours and hydroxychloroquine at 200 mg every 8 hours; use of both agents had a planned duration of 6 months to 1 year.

Heart valve intervention was postponed until the patient's nutritional status improved and the infection was treated. He was discharged home with inotropic dobutamine therapy administered via a peripherally inserted central catheter at a rate of 2 μg/min. Although transcatheter edge-to-edge repair of the mitral valve was initially considered, the patient's condition improved following hemodynamic stabilization, and he underwent definitive surgical treatment.

Technique

Intraoperative echocardiography demonstrated postinflammatory changes, including thickening, retraction, and decreased mobility of the mitral valve (Fig. 1A) and calcification at the coaptation of the aortic valve (Fig. 1B). The patient was placed on cardiopulmonary bypass and was cooled to 32 °C; the heart was arrested using del Nido cardioplegia. Intraoperative inspection of the aortic valve revealed scarred and thickened cusps, with retraction of the tip of the left coronary cusp. The bases of all cusps were inflamed and severely scarred. Inspection of the mitral valve also revealed postinflammatory changes involving the entire valve, where endocarditis appeared as thickened, bowing tissue (Fig. 2). Given the concern for reinfection in the setting of Whipple disease, the mitral valve was replaced with a 31-mm Epic valve (St Jude Medical), followed by aortic valve replacement with a 23-mm Inspiris Resilia valve (Edwards Lifesciences).

Key Points

- Whipple disease is a systemic illness characterized by weight loss, diarrhea, and arthralgia.
- When complicated by culture-negative endocarditis, the clinical course can be fatal, and patients may be too ill for surgery.
- With meticulous multidisciplinary planning and optimal preoperative medication, clinical conditions can be improved, making surgery possible. Definitive surgical treatment is safe and has satisfactory outcomes.

Abbreviations and Acronyms

PCR	polymerase chain reaction
PHT	pulmonary hypertension

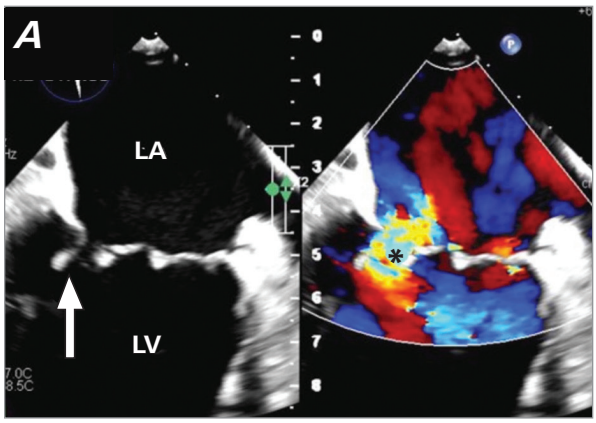

Fig. 1 A) Intraoperative prebypass transesophageal echocardiogram without (left) and with Doppler technique (right). Midesophageal still frame in early systole (left) shows the posteromedial aspect of the posterior leaflet of the mitral valve (arrow), with evidence of postinflammatory changes, including thickening, retraction, and decreased mobility. These changes generate a jet of moderate to severe mitral valve regurgitation (right; asterisk). **B**) Intraoperative prebypass transesophageal echocardiogram without (left) and with Doppler technique (right). Midesophageal still frame of the aortic valve (left) shows thickening/calcification at the coaptation (central arrow) and at the bases of the cusps (upper and lower arrows), resulting in moderate central aortic valve regurgitant jet (right; asterisk).

Supplemental motion images available for Figure 1A and Figure 1B.

Ao, aorta; LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract.

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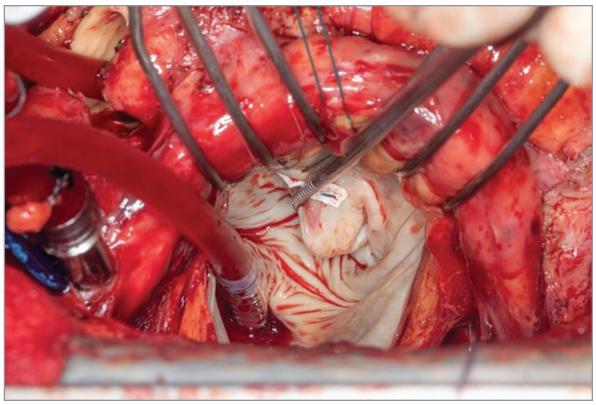

Fig. 2 Intraoperative photograph of the mitral valve, where *Tropheryma whipplei* endocarditis appears as a thickened bowing tissue.

Outcome

Postoperative echocardiography demonstrated satisfactory results without paravalvular leak and with a mean gradient of 13 mm Hg across the aortic valve and 5 mm Hg across the mitral valve. The ejection fraction improved to 50% (from 46% preoperatively). The postoperative course was uneventful, and the patient was discharged on postoperative day 7.

Histopathologic findings of the mitral valve indicated postinflammatory mitral valve disease. Although results of PCR testing on mitral valve tissue were positive for *Tropheryma whipplei,* no histiocytic infiltrate or strong periodic acid–Schiff stain positivity was observed. Histopathologic findings of the aortic valve demonstrated postinflammatory aortic valve disease. No histiocytic infiltrate or strong periodic acid–Schiff stain positivity was observed in the aortic valve.

Follow-Up

One-year extended therapy with doxycycline and hydroxychloroquine was planned. At the 3-month follow-up, the patient was asymptomatic and well, without signs of heart failure.

Discussion

Whipple disease is a systemic illness often characterized by weight loss, diarrhea, and arthralgia.[1] Asymptomatic carriage is common, but Whipple disease can be complicated by cardiac involvement and is an important cause of culture-negative endocarditis. Cardiac manifestations can be fatal, but only a few cases of proven Whipple endocarditis have been reported.[2,3] Findings on physical examination may provide insights into potential cardiac involvement, including signs such as dyspnea, edema, and jugular venous distention, which could indicate right heart congestion.

The prevalence of *T whipplei* in cases of culture-negative endocarditis appears high. Geissdörfer et al[4] reported that *T whipplei* was identified in 6.3% of cases in which infective endocarditis was diagnosed through cultivation or detection by molecular or histologic methods from cardiac valve tissue.

In this case, echocardiography on patient admission demonstrated severe PHT with severe right ventricular dysfunction, which raised the question of whether (1) precapillary PHT occurred in the setting of valvular insufficiency or (2) Whipple disease was associated with primary PHT. Research on the association between PHT and Whipple disease is limited to a few case reports.[5] Macrophage dysfunction in Whipple disease has been described as a result of impaired immunity.[6] Replication of *T whipplei* has been associated with macrophage apoptosis, which plays a role in dissemination. Increased production of transforming growth factor beta was observed among these patients, and alterations in transforming growth factor beta signaling pathways were described as a central factor in PHT.[6,7] In the patient in this case report, right ventricular dysfunction seemed to be out of proportion to the degree of PHT and suggested primary myocardial involvement. Because of the negative myocardial biopsy results, however, uncertainty remains as to whether the cardiomyopathy was directly related to Whipple disease involvement or was a hemodynamic consequence of endocarditis.

Management of culture-negative endocarditis, in which a specific pathogen is not identified, may differ from management of cases in which the pathogen is known. Typically, empirical antibiotics are initiated based on clinical suspicion. Pathogen identification, even through PCR alone, can guide a more targeted course of treatment. The advent of next-generation sequencing has revolutionized diagnosis by analyzing microbial cell-free DNA in plasma. The Karius Test (Karius, Inc) conducts next-generation sequencing by extracting microbial cell-free DNA from plasma, offering a rapid and noninvasive approach to identifying *T whipplei*.[8]

When *T whipplei* is identified, a multidisciplinary approach involving infectious disease specialists and gastroenterologists may be warranted because

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of the bacteria's association with Whipple disease. Some reports in the literature describe *T whipplei* endocarditis without gastrointestinal involvement.[9] In this case, Whipple disease was diagnosed by intestinal biopsy, with multiple organ involvement at the time of diagnosis.

The antibiotic regimen on patient admission in this case included doxycycline 100 mg every 12 hours and hydroxychloroquine 200 mg every 8 hours, with a plan to continue this regimen for 6 months to 1 year. Given a positive PCR finding of *T whipplei* in the mitral valve, it was decided to extend postsurgical treatment for another year. This approach ensured a smooth perioperative course, and this strategy could be implemented in similar cases.

Conclusion

When cardiac signs are accompanied by symptoms such as arthralgia, weight loss, and other systemic symptoms, it is important to consider the possibility of a cardiac manifestation from a systemic illness. Intestinal biopsy often confirms the diagnosis of suspected Whipple disease. Definitive surgical treatment is safe, and its long-term results are satisfactory when combined with optimal antimicrobial therapy.

Article Information

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