

Cardiac complications in Whipple's disease

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Whipple's disease or intestinal lipodystrophy is an infection induced by *Tropheryma whipplei*. It is rare with an estimated incidence of 0.4 per million. Symptoms are arthropathy, weight loss, and diarrhoea, but other organs notably the central nervous system may be affected. We demonstrate a case of cardiac complications in Whipple's disease. The patient presented with endocardial infiltrations on TEE examinations and heart failure and improved after antibiotic treatment.

Case

A 54-year-old woman presented with weight loss of about 20 kg and intermittent fever. She was diagnosed for dermatomyositis 10 years ago and treated with steroids. Since arthropathy worsened, the therapy was escalated with MTX, Azathioprin, and Chloroquin without clinical improvements of her symptoms.

Transthoracic echocardiography demonstrated myocardial hypertrophy in the absence of arterial hypertension, impaired systolic function, and sclerosis of the aortic valve and mitral anulus (see Supplementary material online, Clip 1). Systolic and diastolic myocardial velocities by tissue-Doppler imaging were dramatically reduced (Figure 1). Transesophageal echocardiography (TEE) examinations, performed to exclude endocarditis, revealed endocardial and intramyocardial echogenic 'infiltrations', especially in the free wall of the right atrium (see Supplementary material online, Clip 2, Figure 2). Small-bowel biopsy characterized by inclusions in the lamina propria staining with periodic-acid Schiff (PAS), which represent the causative bacteria of Whipple's disease. The patient refused further cardiac investigations, including heart catheterization or myocardial biopsy to confirm a myocardial infection with *Tropheryma whipplei*.

Prospective studies on the choice or duration of antibiotic treatment are ongoing. Our patient was treated with a 2-week course of intravenous meropenem followed by oral trimethoprim-sulfamethoxazole treatment (160/800 mg orally twice daily) given for 1 year. In addition, the patient received standard therapy for heart failure including beta-blockers and angiotensin converting enzyme (ACE) inhibitors.

Although the ultimate proof a biopsy was not feasible, an echocardiographic follow-up after 6 months of antibiotic treatment demonstrated a normalization of left ventricular function. Therefore, the reaction on antibiotic therapy supports our view and suggests a cardiac complication of Whipple's disease in this case.

Discussion

Whipple's disease is rare, and no valid estimate of the incidence is available. Whipple's disease occurs mainly in middle-aged individuals (mean age at diagnosis about 50 years) and in about eight times more men than women. A genetic susceptibility is suggested by the finding that ~26% of patients (three to four times more than expected) are positive for HLA B27.^{1–2}

Macrophages from infected patients show decreased intracellular degradation and a decrease in phagocytosis. Thus, a subtle defect of cellular immunity seems to involve activation and interaction of macrophages and T cells and allow invasion of the bacillus from the gastrointestinal mucosa to peripheral organs.³

Whipple's disease has traditionally been regarded as a gastrointestinal disease with weight loss, abdominal pain, and diarrhoea, but in many cases, the disease begins insidiously with arthropathy. Clinical presentation can vary to a great extent owing to differential organ involvement, and no major organ is excluded from infections by *T. whipplei*. A central nervous system manifestation can first become apparent as a memory disorder, personality change, or dementia in many patients.⁴

Cardiac involvement is common and has been reported to be an important clinical sign. It might present as cardiac murmurs, insufficiency of the aortic or mitral valve necessitating replacement, or with the clinical picture of

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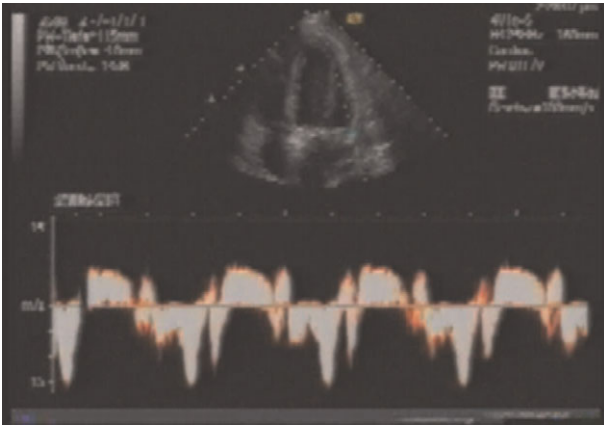


Figure 1 Tissue-Doppler imaging of lateral annulus demonstrate significantly reduced systolic ($s = 8$ cm/s) and diastolic velocities ($e = 4$ cm/s) indicating severe systolic and diastolic heart failure.

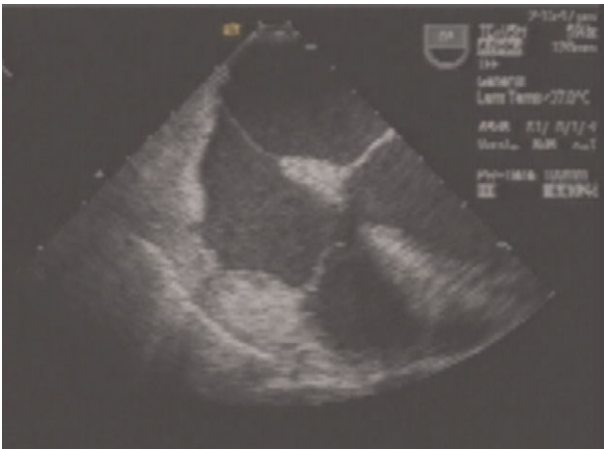


Figure 2 TEE show endocardial 'infiltrations'.

blood-culture-negative endocarditis; many of these cases are diagnosed by histological analysis of the cardiac valves.⁵⁻⁷ For detailed information see review by Marth and Raout.⁸ In contrast to previous reports, we did not observe valvular insufficiency or endocarditis, but systolic and diastolic heart failure and endocardial infiltrations suggest cardiac involvement of Whipple's disease.

Differential diagnosis of these intracardiac abnormalities would include congestive heart failure, ischaemic cardiomyopathy, hypertrophy due to hypertension or aortic stenosis, viral myocarditis, nutritive or toxic cardiomyopathy, or Fabry disease. However, the reaction on antibiotic therapy supports our view of a cardiac complication of Whipple's disease in this case.

When the disease is suspected, duodenal-biopsy specimens should be obtained. Histological analysis reveals granular foamy macrophages stained purple with PAS. Duodenal samples are infiltrated by macrophages.

Untreated Whipple's disease can be fatal. However, antibiotic therapy leads to rapid improvement in clinical status. In the past, various antibiotic regimens were used up to 12 months on an empirical basis, but no prospective studies are available on the choice or duration of antibiotic treatment. If the patients have a good clinical response, they can simply be followed up with duodenal biopsies 6 and 12 months after diagnosis. Antibiotic treatment can generally then be stopped if no PAS-positive material is identified.

Supplementary material

Supplementary material associated with this article can be found in the online version.

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