An Uncommon Cause of Recurrent Strokes

Tropheryma whippelii Endocarditis

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Background—Cardiac involvement in Whipple’s disease is not an uncommon phenomenon in autopsies, but its clinical occurrence is often overshadowed by gastrointestinal symptoms. We report a very atypical manifestation of this disorder.

Summary of Report—An extraordinary presentation of an extremely long-lasting, culture-negative endocarditis caused by Tropheryma whippelii is described, the clinical consequence of which has become apparent in recurrent strokes.

Conclusions—Cardiac involvement of Whipple’s disease should always be considered in culture and serologically negative endocarditis. The polymerase chain reaction technique may be a useful tool to confirm a presumed diagnosis of T whippelii endocarditis and consequently to apply an effective treatment regimen. (Stroke. 2000;31:2002-2003.)

Key Words: actinobacteria group • endocarditis • stroke • Whipple’s disease

Whipple’s disease is a rare systemic bacterial infection that was first described in 1907 and is characterized by fever, diarrhea, polyarthritits, and weight loss. Although cardiac involvement in Whipple’s disease is a well-known finding in autopsies, its occurrence often does not result in significant clinical manifestations. Because clinical diagnosis of cardiac involvement is rare and difficult, we describe an atypical presentation of Whipple’s disease with chronic active mitral valve endocarditis over 3 years.

A 51-year-old woman was admitted to the hospital in 1995 with a transient ischemic attack with temporary left-sided hemiplegia. History revealed intercurrent arthralgias in multiple changing joints. Clinical examination showed a snapping first heart sound and a diastolic murmur. Laboratory tests yielded no specific information. An ultrasonic duplex scanning of the extracranial arteries was normal, and paroxysmal atrial fibrillation was excluded in a 24-hour ECG. Transthoracic echocardiography showed a mild to moderate mitral stenosis in combination with a mild mitral regurgitation and an enlargement of the left atrium. On the basis of these findings, a cardiac thromboembolic origin of this minor stroke was suggested, and anticoagulation was initiated.

Three months later, the patient presented with a left-sided amaurosis fugax and a dysdiadochokinesia of the left hand, even though treatment with phenprocoumon showed an international normalized ratio of 2.5. Brain CT scans revealed multiple hypodense areas in the left thalamus area, in the right capsula interna, and in the right gyrus temporalis superior. At that time, the mitral stenosis was moderate at 2-dimensional echocardiography, with a planimetric orifice area of 1.2 cm² and a thickened anterior leaflet. In the transesophageal echocardiogram, no intracardiac thrombus formation was detected. As a main finding, mobile polypoid, echo-dense masses of 1 cm dimension were attached to the anterior mitral leaflet. Those vegetations were interpreted either as endocarditis or as thrombotic depositions in an antiphospholipid antibody syndrome. Therefore, repeated laboratory tests, including erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, and antinuclear and antcardiolipin antibodies, as well as 9 blood cultures, were performed. In the course of a few days, all laboratory findings and all blood cultures were negative, as were serology tests for Coxiella burnetii. Because there was still no evidence of bacterial endocarditis, anticoagulation was continued.

Figure 1. Transesophageal echocardiogram shows a diffusely thickened mitral valve (MV) with unusually large, pedunculated vegetations due to T whippelii. The bulk of the vegetation is on the atrial side of the mitral leaflets, but it also extends to involve the ventricular aspect of the valve. Repeated examinations over 3 years showed an increase in size of these vegetations. LA indicates left atrium; LV, left ventricle.
The patient did well for the next 3 years, until she was brought to the emergency room because of transient confusion and slight weakness of the left arm, as well as left-sided facial weakness. At hospital admission, physical examination was normal except for a slight left-sided central facial paresis. The ECG was inconspicuous, and the chest radiograph showed a mild cardiomegaly. For the first time, the erythrocyte sedimentation rate and C-reactive protein level were slightly elevated. Tests for rheumatoid factor, antinuclear and antiphospholipid antibodies, and 6 blood cultures were again negative. In the transesophageal echocardiogram, the earlier known echo-dense masses were distinctly enlarged. They presented now as 2.5-cm gross pedunculated vegetations on both leaflets (Figure 1). Taking into account the history and the echocardiographic findings, the patient was sent for mitral valve replacement. The histological examination of the native mitral valve showed a chronic inflammatory infiltrate with numerous macrophages containing typical periodic acid–Schiff–positive granules (Figure 2). Therefore, an infection with *Tropheryma whippelii* was suspected and finally confirmed by positive polymerase chain reaction (PCR) from the mitral valve. A small-bowel biopsy and an examination of the cerebral spinal fluid, obtained after valve replacement, were negative by microscopy and PCR. The patient was treated with trimethoprim-sulfamethoxazole. She showed an immediate resolution of the arthralgias and, during a follow-up of almost 1 year, a stable cardiac condition and no further neurological symptoms.

Cardiac involvement in Whipple’s disease is not an uncommon phenomenon, but in most patients, cardiac manifestation is overshadowed by gastrointestinal symptoms of the disorder. Up to 30% of patients with Whipple’s disease have been reported to present with heart murmurs, usually aortic insufficiency or mitral stenosis, and in postmortem studies an even higher incidence of endocarditis is observed. The significance of *T whippelii* endocarditis may be underestimated, probably owing to its development in the later course of the disease.

Our case of documented, extremely long-lasting endocarditis highlights the problem of diagnosing Whipple’s disease in patients who present with unusual manifestation. Neither the initial presentation of our patient nor the subsequent course was typical of Whipple’s disease, because of the domination by cerebral system disturbances. Cardiac involvement in Whipple’s disease should always be considered in culture and serologically negative endocarditis. Therefore, the PCR technique may be a useful tool to confirm a presumed diagnosis of *T whippelii* endocarditis and consequently to apply an effective treatment regimen.

References


![Figure 2. A, Thickened sclerotic mitral valve with fluoride vegetations on the surface (hematoxylin-eosin; low-power view, original magnification ×1.25). B, Periodic acid–Schiff–positive inclusions in necrotic macrophages (periodic acid–Schiff stain, original magnification ×100). C, Rod-shaped bacteria in macrophages and dispersed in fibrinous exudate (Warthin-Starry silver impregnation, original magnification ×630).](http://stroke.ahajournals.org/coverfigs/03/Naegeli_Tropheryma_whippelii_Endocarditis_With_Recurrent_Strokes_21402982.jpg)
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