

## Case Report

**Yersinia Enterocolitica Endocarditis**

CHARILAOS A. PAPAIOANNOU, NIKOLAOS VARVARIGOS, GEORGE KARATSOLIS,  
NIKOLAOS PAPAIOANNOU, ANTONIOS DRAGANIGOS, CHRISTOS KATSANTOURIS,  
ALEXADROS KAPPAS, THEONI AVRAMOPOULOU

Department of Cardiology, "NIMTS", Hospital, Athens, Greece

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Endocarditis is a rare manifestation of *Yersinia enterocolitica* infection. We present the case of a 45-year-old man with prosthetic valve endocarditis due to *Yersinia enterocolitica* infection. The patient was successfully treated with ceftriaxone plus tobramycin, as proved by the negative cultures of the prosthetic valve that was removed at the end of therapy. Including this case report, only 12 cases of *Yersinia enterocolitica* endocarditis have been published to date and two describe prosthetic cardiac valve endocarditis. The clinical characteristics of the disease do not distinguish sepsis from endocarditis limited to the cardiac valves. Diagnosis, however, has been improved by the progress in echocardiography. Prognosis is poor but can be improved if appropriate antimicrobial agents are administered, i.e. combination of a third-generation cephalosporin plus an aminoglycoside. Fluroquinolones may also constitute a viable therapeutic alternative.

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## Address:

Charilaos A.  
Papaioannou

39 Macedonias St.,  
152 35, Vrilissia,  
Athens, Greece  
Tel.: (+30) 210-7288 654

**Y** *ersinia enterocolitica* is an enteric pathogen associated with a wide spectrum of clinical and immunological manifestations. *Yersinia enterocolitica* bacteremia and septicemia are most often reported in patients with a predisposing underlying disease, such as iron-overloaded state (haemochromatosis, acute iron poisoning), immunosuppressive therapy, diabetes mellitus, alcoholism, cirrhosis or malnutrition<sup>1</sup>.

*Yersinia enterocolitica* bacteremia is associated with a high mortality of 25 to 50%<sup>2</sup>. Bacteremia of this organism results in liver, splenic and renal complications, pulmonary abscesses, infection of vascular prostheses and intravenous catheters, meningitis and bone infections<sup>1,2</sup>, while endocarditis remains a rare complication<sup>2</sup>. Eleven endocarditis cases<sup>2-11</sup> have been reported and only one involves a cardiac prosthetic valve<sup>9</sup>.

**Case report**

A 45-year-old man was admitted to our hospital because of high fever accom-

panied by rigors, headache, nausea and vomiting. The patient had a medical history of rheumatic heart disease and five years ago, his mitral valve was replaced by a Starr-Edwards prosthetic valve and aortic valve insufficiency was corrected by valvuloplasty. Three months earlier the patient had been operated on for appendicitis.

On clinical examination his temperature was 39.5°C, blood pressure 120/70 mmHg, and his pulse rate was 90 beats/min. No sign of heart failure was found and the prosthetic valve was considered to be functioning normally, without abnormal findings upon auscultation. The blood tests revealed the following values: hematocrit at 45%, leucocytes 10500/mm<sup>3</sup> with 80% neutrophils, platelets 150000/mm<sup>3</sup>, ESR 45 mm/h and urinalysis was normal. Bilirubin was 1,9 mg/dl, SGOT 45 mg/dl, SGPT 50 mg/dl and  $\gamma$ -GT 55 mg/dl. Both the chest x-ray and electrocardiogram were normal. Ultrasound examination of the upper abdomen revealed multiple gallbladder stones. Three blood cultures were taken and therapy with cefamandole plus tobramycin initiated to

treat possible cholangitis. During the following 48 hours the patient developed jaundice, with bilirubin increase to 3,3 mg/dl,  $\gamma$ -GT to 101 mg/dl and leucocytes to 14000/mm<sup>3</sup>.

A transthoracic echocardiogram showed a normally functioning prosthetic valve with no detectable vegetation. On the fifth day of hospitalization the patient was still febrile, the leucocytes reached 17000/mm<sup>3</sup> and *Yersinia enterocolitica*, biotype IV, serotype 0:9, resistant to ceftriaxone, cefotaxime, ceftazidime, aztreonam, imipenem, ciprofloxacin, aminoglycosides, cotrimoxazole, tetracycline and chloramphenicol was spotted in initial blood cultures.

As fever and increased leucocytes persisted while all blood cultures obtained during treatment were negative, antimicrobial therapy was changed on the seventh day to imipenem (0.5 g, 3 times daily, IV). On day 10 a new transthoracic echocardiogram was performed, which was found to be normal, while on day 17 a computed tomography of the abdomen revealed findings compatible with a splenic infarct. On day 20 a transoesophageal echocardiogram revealed a large mobile vegetation (1.6 × 0.6 cm) on the mitral ring. Because the patient still had a high fever (37.5-38°C) with persistent leucocytosis, ceftriaxone (2 g, once daily) plus gentamicin (80 mg, twice daily) was administered. His fever subsided rapidly and leucocytes returned to normal values. Stool cultures were negative for *Yersinia*.

At the end of the therapy the patient's prosthetic valve was removed because of the large size and the mobility of the vegetation. Fibrinous material on all three metallic components was revealed. All cultures of this material were negative. No histological analysis was performed. The patient continued his medical treatment for an additional two weeks. Six months later, the patient was in excellent clinical condition. In the meantime he has undergone a prescheduled cholecystectomy, without any complications, while gallbladder stone cultures were negative.

## Discussion

*Yersinia enterocolitica* infection in human was first described in 1939<sup>1</sup>. To our knowledge this is the eighth case of *Yersinia enterocolitica* endocarditis reported in detail in the literature and the second involving a prosthetic valve<sup>9</sup>. Additionally, four other cases incompletely described have been reported<sup>2,10,11</sup>.

All cases reviewed in detail are presented in Table 1. They were all acute episodes that affected the mitral

valve (5 patients), the aortic valve (1 patient) or both valves (2 patients). Three patients had a history of rheumatic heart disease. It is interesting that underlying conditions were observed in only three patients (cases 1,4,5 of Table 1). The clinical presentation and the subsequent finding of *Yersinia* bacteremia in all cases of *Yersinia enterocolitica* endocarditis reviewed do not distinguish septicemia from endocarditis. Only in two patients (cases 1,7 of Table 1) did focal neurological symptoms strengthen the suspicion of endocarditis, while vascular and immunological signs were not observed.

The other case of prosthetic valve endocarditis concerned a 56-year-old male patient with a prosthetic mitral valve, hospitalized because of high fever, vomiting and watery diarrhea. The patient's condition was complicated with left hemiparesis due to a brain infarct. As in our case, transthoracic cardiac ultrasound did not reveal any vegetation. The patient was treated successfully with combined antibiotic medication (ceftriaxone plus gentamicin) and was not operated upon since he was hemodynamically stable.

It is well known that documented transmission of *Yersinia enterocolitica* to humans occurs primarily by the ingestion of contaminated food, water and milk or by transfusion of blood products<sup>1</sup>. However, a fecal-oral or oral-oral route from dogs, cats and swine to humans has also been reported. In our patient it could be speculated that the appendectomy performed three months earlier was complicated by portal vein bacteremia, leading to colonization of the preexisting gallbladder stones. The prosthetic mitral valve may have been infected during a subsequent episode of cholangitis.

Specific antibodies were positive in three cases and negative in the remaining 5 cases, although they do not confirm the presence of active disease, since they may persist for several years after infection<sup>1</sup>. On the other hand, serodiagnosis of yersiniosis has several disadvantages, since cross-antigen reactions occur among *Yersinia enterocolitica* and *Brucella abortus*, *Morganella morganii*, *Salmonella spp.* and *Rickettsia spp.*<sup>1</sup>. *Yersinia spp.* serotyping revealed serotypes 0:3, 0:8 and 0:9, which have been termed virulent serotypes and represent the most frequent causes of sporadic human disease worldwide<sup>1</sup>. Biotype IV predominated in 5 cases. A transthoracic echocardiogram was of little help in assisting the diagnosis of endocarditis while it is unfortunate that we noted in this review of the eight cases of *Yersinia*

**Table 1.** Clinical characteristics and laboratory findings in 8 cases of Yersinia enterocolitica endocarditis.

Case Number	Reference	Age (years)- Gender*	Clinical presentation	Transthoracic cardiac ultrasound	Positive/ total blood cultures	Therapy
1	3	68 M	Fever, right hemiparesis, brain, liver and spleen infarcts.	No data	Unknown	Gentamycin
2	4	72 M	Fever, chills.	Mitral valve vegetations	7/7	Ampicilline + gentamicin.
3	5	73 M	Fever, myalgia, vomiting, septic skin infarcts.	Aortic valve vegetations.	2/2	Tobramycine.
4	6	58 M	Fever, jaundice, liver failure.	No vegetations.	3/3	Ampicilline, followed by cefuroxime + gentamicin + metronidazole.
5	7	72 M	Fever, diarrhea, spleen, liver and bone infarcts.	Mitral and aortic valve vegetations.	6/6	Cefoxitine.
6	8	74 F	Fever, weakness.	No vegetations.	4/4	Ceftizoxime.
7	9	56 M	Fever, diarrhea, left hemiparesis, brain infarct.	No vegetations.	5/6	Ceftriaxone + gentamicin.
8	Present case	45 M	Fever, nausea, vomiting, spleen infarct.	No vegetations.	3/3	Cefamandole + tobramycine, then imipenem and finally ceftriaxone + gentamicin.

F=Female, M=Male.

*enterocolitica* endocarditis reported, that transesophageal echocardiography was not performed on any patient except ours. Diagnosis in the other seven patients was made before transesophageal echocardiography was performed routinely and the transthoracic cardiac ultrasound revealed vegetations in only three of them.

The 1982 WHO recommendation for anti microbial chemotherapy of *Yersinia enterocolitica* infections included tetracycline, chloramphenicol, gentamicin and trimethoprim-sulfamethoxazole<sup>12</sup>. Currently, third generation cephalosporins, aztreonam, imipenem and fluoroquinolones are considered alternatives for treating *Yersinia enterocolitica* infections<sup>13</sup>. Contrary to previous reports in which mortality associated with *Yersinia enterocolitica* was

very high (25-50%), mortality following treatment with the newer antimicrobial agents has decreased to 7.5%<sup>10</sup>.

Among the eight patients with *Yersinia enterocolitica* endocarditis reviewed here, three died of septicemia and autopsies carried out on all patients confirmed the presence of cardiac valve vegetations. It is worth noting that in the five successfully treated patients, including ours, a third-generation cephalosporin alone or in combination with gentamicin was administered. In our case the failure of imipenem to control fever and leucocytosis after two weeks of therapy is interpreted as tolerance of the certain strain, or/and poor intravegetation pharmacokinetics of imipenem. The coexistence of a possible spleen infarct may offer another explanation

for the poor therapeutic response to imipenem. However, the reported failure of third-generation cephalosporins and imipenem to treat *Yersinia enterocolitica* infections indicates a need for controlled clinical trials<sup>14,15</sup>.

From the current review, it is evident that *Yersinia enterocolitica* is able to cause severe acute endocarditis in normal, abnormal and prosthetic valves, mostly in elderly people, with or without predisposing underlying conditions. In the face of the increasing number of cases of *Yersinia enterocolitica* septicemia, it seems that the possibility of underlying endocarditis should be investigated. Recent evidence that enteropathogenic *Yersinia* mediates specific binding to cellular fibronectin and to collagen through the membrane protein Yad A strengthens this possibility, particularly in prosthetic valves<sup>16,17</sup>. Although the combination of a third-generation plus an aminoglycoside is justified, the therapeutic failures reported<sup>15</sup> prompt the use of the newer fluoroquinolones, alone or in combination with a newer  $\beta$ -lactam agent.

The surgical treatment of our patient is considered a relative indication, since large (>10 mm) and very mobile vegetations, even without important hemodynamic disturbances, are associated with a high incidence of systemic emboli<sup>18</sup>.

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