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Case report

Yersinia enterocolitica endocarditis on aortic bioprosthesis: A case report

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ABSTRACT

Yersinia enterocolitica is a Gram-negative bacillus and an unusual cause of endocarditis. We report the first case of a 74-year-old woman who developed a *Yersinia enterocolitica* endocarditis on an aortic bioprosthesis. Case of a 74-year-old woman with chronic hepatitis C who developed a *Yersinia enterocolitica* endocarditis on an aortic bioprosthesis in the weeks following an infective diarrhea with bacteremia. The patient was cured without surgery using ceftriaxone followed by oral fluoroquinolone according to the antimicrobial sensitivity testing (AST) results. *Y. enterocolitica* is a very rare cause of endocarditis and iron overload and chronic hepatitis C have been reported as predisposing conditions. The pathogenicity and virulence of the various serotypes of *Y. enterocolitica* are discussed.

Introduction

Yersinia spp are non-spore forming Gram negative bacilli that typically cause fever, enterocolitis, acute diarrhea, abdominal pain, mesenteric lymphadenitis. In rare cases, extraintestinal infections due to hematogenous spread may occur. Y. enterocolitica is an important foodborne human enteropathogen that causes sporadic outbreaks [1]. The main source of infection is known to be pork product [1]. Other modes of transmission such human-to-human transmission and waterborne transmission have been exceptionally described [2]. Most of time *Y. enterocolitica* bacteremia affect patients with iron overload, iterative transfused, alcoholic, cirrhotic or immunocompromised patients [3,4]. The involvement of a cardiac valve in Yersinia spp bacteremia is rare. Only 12 cases of infective endocarditis (IE) due to Yersinia spp have been described so far. In IE due to *Yersinia spp*, a prosthetic cardiac valve was involved in only 2 (17 %) patients with a mechanic mitral prosthesis infection [5,6]. An additional case has been described on a cardiac implantable electronic device [7]. Because of the rarity of this disease, the optimal treatment of *Yersinia spp* IE has not been established.

In this paper, we describe a case of an IE caused by Yersinia enterocolitica which involved an aortic bioprosthesis.

Case

A 74-year-old woman was admitted to our hospital because of subacute diarrhea starting 2 weeks prior to hospital admission. The patient describes eating pork meat before the onset of symptoms. Six months earlier a bioprosthetic aortic valve (Sorin Perceval M) was implanted because of aortic valve stenosis.

At the emergency room, physical examination revealed a high-grade fever (temperature 39.4 °C), a blood pressure of 101/46 mm Hg, a heart rate of 106/min and a previously known arrhythmia (atrial fibrillation). No murmur on cardiac auscultation, no clinical findings of heart failure on examination. Abdominal and neurological examinations were normal.

Laboratory blood tests, drawn at admission, showed C-reactive-protein 139 mg/L, white blood cell count 25 G/L with a neutrophil count of 22.5 G/L and an hemoglobin level of 10.8 g/dL. There was no thrombocytopenia. Liver blood tests were normal except transaminases under twice the upper limit of the normal value. Prothrombin time and activated cephalin test were in the normal range. The blood iron and ferritin levels were normal.

Two blood culture sets and one stool sample collected on the day of admission grew *Y. enterocolitica* bioserotype 4/O:3. Antimicrobial sensitivity testing (AST) showed that the bacteria was sensitive to ceftriaxone, ceftazidime, cefepime, nalidixic acid, ciprofloxacin, levofloxacin, gentamycin, amikacin, imipenem, meropenem, trimethoprim-sulfamethoxazole combination, but was resistant to amoxicillin-clavulanic acid.

An antibiotic treatment using ceftriaxone 2 g per day intravenously allowed the alleviation of diarrhea and apyrexia within 2 days. Blood culture follow-up showed a clearance of *Y. enterocolitica* at 24 h of

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ceftriaxone initiation.

A transesophageal echocardiography (TEE) revealed a 11 mm oscillating vegetation on a thickened antero-aortic cusp. There was no aortic leak nor abscess.

The thoraco-abdomino-pelvic CT-scan examination did not find any abnormality. There was no sign of stroke or abscess on brain MRI.

The TEE was repeated at 1 week and showed the disappearance of the vegetation. After collegial discussion, no surgical care was indicated thanks to a favorable evolution under medical treatment only. The patient remains asymptomatic during the entire hospitalization.

Due to the lack of knowledge about the best therapeutic options, ceftriaxone (2 g once daily) was initially planned for a total duration of 12 weeks in the absence of surgical treatment. Because of difficulties in venous access after 6 weeks of treatment, this one was complete with oral levofloxacin 500 mg every 24 H. The TTE evaluation at 12 months of follow up showed a normal valvular function.

During hospitalization, a chronic hepatitis C was diagnosed with an RNA level of 630.957 UI/mL Severe fibrosis (F3) was found on the pulsed elastography. An antiviral treatment was started after the end of endocarditis treatment.

In this patient, a chronic blood monocytosis had been found on several white blood cell counts for at least 3 years. No explanation was found. The patient refused any additional exploration.

Discussion

Y. enterocolitica is associated with a wide spectrum of clinical and immunological manifestations including digestive diseases, mesenteric lymphadenitis, terminal ileitis [4]. Bacteremia is rare and often notified in immunocompromised, cirrhotic, or iron overloaded patients. *Y. enterocolitica* 4/O:3 is a low virulence pathogen in the absence of free iron because it lacks yersiniabactin, the iron binding siderophore [3]. In case of infection in a host with iron overload, the virulence of *Y. enterocolitica* is increased and infection can range from a simple digestive symptomatic state to bacteremia [8].

Y. enterocolitica bioserotypes 4/O:3, 2/O:9 and, to a lesser extent, 2/O:5,27, 1B/O:8 cause disease in human. The bioserotype 4/ O:3 is the most frequently identified in endocarditis reported cases (5/12 42 %) [4,6]. This bioserotype is also the most represented in human infections in Europe whereas strains classified as bioserotype 1B/O:8 is more common in North America [9]. This frequency of human infection caused by certain *Yersinia* subgroups might be related to exposure to specific animal sources: pigs and pork meet.

Indeed, some characteristic allows the easier colonization on animal sources such as invasive protein (invA) which is highly express at 37 °C in *Y. enterocolitica* serotype O:3 whereas 25 °C in other serotypes [9]. Furthermore, the strains of the bioserotype 4/O:3 induce very low level of interleukin 8 which is not available for neutrophils recruitment [9]. This immune evasion mechanism promotes pig's intestine long term colonization.

Experiments in animals have demonstrated that specific rheologic conditions modify the endocardic endothelium and leads to non-bacterial thrombotic endocarditis. Then, when present in the blood flow some bacteria may take advantage of these endothelial alterations. For example, bacteria blood carried through a narrowed valvular orifice may attach to the endothelium at the low-pressure sink immediately beyond an orifice, or at the site of altered endothelium secondary to a jet stream strike. It has been shown that bacterial adhesins are able to bind extracellular matrix components of the altered endothelium, which in turn transforms the non bacterial thrombus in a bacterial endocarditis [9]. *Y. enterocolitica* endocardium adhesion is promoted by 3 adhesins: YadA, Invasin and Ail. YadA is a plasmid-encoded non fimbrial adhesin with a collagen-binding activity which allows extra-cellular adhesion, subvertion of host immune system and auto-agglutination helping to resist to phagocytosis. This adhesin seems to be one of the more important factors of bacterial adherence to the endocardium [10]. Invasin is a chromosomally encoded protein binds to bêta-1 integrin domains which promotes rearrangement of the host cell cytoskeleton and leads to internalization of the bacteria [10]. This adhesion is mainly involved in promoting the internalization by enterocytes and M cells in Peyer's patches. Ail surface associated protein is also associated with cell invasion with less important role than the others [10].

During bacterial infection, iron is essential for the bacteria to accomplish several biological processes. In low iron availibility, the production of siderophore is essential for bacterial growth. Most of *Yersinia spp* secrete a siderophore termed yersiniabactin encoded by *irp*2 (iron regulated protein 2) but this gene is absent in *Y. enterocolitica* O: 3 which explains its low virulence in a poor iron environment. In case of iron overload, as in the case we reported, the bacteria is able to invade deeper tissues and to cause bacteremia [11].

In this case, the patient presented chronic C hepatitis infection with severe fibrosis score. Hepatitis C chronic infection decreases hepcidin level and promotes iron overload [12] which may play a role in *Y. enterocolitica* serotype O:3 invasion.

Concerning antibiotic treatment, *Y. enterocolitica* is most of time susceptible to aminoglycosides, cotrimoxazole, tetracycline, fluoroquinolones and third generation cephalosporins but is resistant to penicillin, ampicillin and first-generation cephalosporin. The intrinsic resistance is a consequence of chromosomally beta-lactamase genes: *blaA* and *blaB*. These two genes are produced by the O: 3 and O: 9 serogroups [13].

In most of the published studies endocarditis due to *Y. enterocolitica* was treated with a bêta-lactam and aminoglycoside combination (83 %). A fluoroquinolone was used in 42 % of all cases [5]. Median duration was 6 weeks in reported cases [5].

Several cases of *Y. enterocolitica* endocarditis have been described; however, very few cases occurred in patients with prosthetic valves. Giamarellou et al. and Papaioannou C.A and al have described 2 cases of *Y. enterocolitica* in mechanical prosthetic valves [6,7]. In both cases, the treatment was based upon a third-generation cephalosporin and aminoglycoside combination for 6 weeks and underwent surgical management because of a clinical worsening and severe valvular lesions.

Our case is the first to describe a *Y. enterocolitica* endocarditis developing on a biological prosthetic valve [5,6] and with a favorable evolution under exclusive medical treatment.

We reported the first *Y. enterocolitica* endocarditis on an aortic bioprosthesis. The evolution was favorable under antibiotic treatment only, including 6 weeks of IV treatment and 6 weeks of oral therapy.

Well-known risks factors are associated with *Y. enterocolitica* bacteremia and an infective endocarditis in such patients should not be neglected especially in patients with predisposing heart disease.

CRediT authorship contribution statement

Marin Delaunay: Conceptualization, Writing – original draft. **François Laterza:** Writing – review & editing. **Renaud Verdon:** Supervision.

Author statement

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Ethical approval

Not applicable

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflict of Interest Statement

None.

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