Case Report

Bacteroides fragilis endocarditis: a case report and review of literature

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ABSTRACT

Endocarditis due to Bacteroides fragilis is a rare disorder. This article describes a case of Bacteroides fragilis endocarditis associated with portal and superior mesenteric venous thrombosis in a patient without preexisting valvular heart disease and review the cases of endocarditis due to this anaerobic bacterium in medical literature since 1980.

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Introduction

Bacteroides fragilis is an anaerobic Gram-negative bacillus and represents a common cause of endogenous infections in humans. It is a component of the normal flora in human terminal ileum, the colon and the vagina and is frequently associated with polymicrobial infections such as intra-abdominal, diabetic foot and obstetric-gynecologic tract. This microorganism is an uncommon cause of endocarditis and a few cases in the literature have been described. Its exact frequency is difficult to surmise due to the lack of adequate methods for their isolation and the identification requiring appropriate techniques of collection, transportation and cultures of specimens. Herein we report a case of Bacteroides fragilis endocarditis associated with portal and superior mesenteric venous thrombosis in a patient without preexisting valvular heart disease and review the cases of endocarditis due to this microorganism in the English-language medical literature since 1980.

Case presentation

A 64-year-old male was referred to the hospital with a two-month history of fever, chills, anorexia and general weakness. Past medical history was unremarkable except for a dental infection treated with amoxicillin fifteen days before the fever started and a colonoscopy which showed diverticulosis in a routine exam six months prior. During ambulatory care he had a normal transthoracic echocardiography and abdominal ultrasonography one week before his admission. Two sets of aerobic blood cultures were collected at that time and remained sterile. Upon hospital admission his
physical examination showed body temperature of 39.1°C, blood pressure of 120/70 mm Hg, pulse rate of 100 beats/min, painless hepatomegaly, normal heart sounds, no sign of petechiae or evidence of peripheral emboli and normal fundoscopy. Laboratory tests were collected including three sets of blood cultures and empirical treatment with intravenous aqueous crystalline penicillin 4 MU six times daily plus gentamicin 1.5 mg/kg three times daily was prompt initiated as a routine antibiotic regimen used at our institution for subacute endocarditis. Laboratory studies showed hemoglobin of 11 g/dL, white blood cell count of 10.300/mm³ with a differential count of 66% neutrophils, 11% bands and 20% lymphocytes, platelet count 398.000/mm³, aspartate and alanine aminotransferase were normal, urea nitrogen 26 mg/dL, and creatinine 1.2 mg/dL. Studies of coagulation factors, urinalysis and chest radiography were normal. Abdominal ultrasonography showed thrombosis of the portal vein without collateral blood flow or portal hypertension and computed tomography scan revealed portal and superior mesenteric vein thrombosis. On day two of his admission, anticoagulation was initiated with subcutaneous low-molecular-weight heparin (enoxaparin) at a dosage of 1 mg/kg twice daily. Colonoscopy confirmed diverticulosis with no signs of acute inflammatory process. Transesophageal echocardiogram was conducted and showed small vegetation (not sized) on the aortic valve without regurgitation. Four days after antibiotic therapy was initiated, the patient remained febrile and two new sets of blood cultures were drawn. On day five of the patient admission, two of the three initial sets and the last sample of anaerobic blood cultures yielded B. fragilis susceptible to metronidazole, amoxicillin/clavulanate, clindamycin, imipenem/cilastatin, piperacillin/tazobactam and resistant to penicillin. Identification of the B. fragilis strain was performed in the automatic ATB Expressions system (bioMérieux – France) using biochemical API 20 A® or Vitek ANC card (bioMérieux – France). Minimal inhibitory concentrations (MICs) were determined according to the reference agar dilution method described by the Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS).

Therefore, the antibiotic therapy was switched to monotherapy with intravenous metronidazole at a dosage of 500 mg three times daily according to susceptibility testing. Three days later, he became afebrile with improvement of overall condition. The patient was treated with intravenous metronidazole for four weeks without any adverse effects and was discharged home with oral anticoagulation (warfarin potassium) for six months, discontinued after abdominal ultrasonography revealed complete disappearance of the thrombus in the portal vein. His one-year follow-up showed no signs of recurrent infection.

Discussion

Bacteroides fragilis is an anaerobic Gram-negative rod and constitutes 1% to 2% of the normal colonic bacterial microflora in humans. However, these organisms can also be responsible for infections of endogenous origin including dental abscess, peritonitis, cholecystitis, appendicitis, aortoduodenal fistula, obstetric-gynecologic, diabetic foot and skin structure infections. Because of their fastidious nature, they are difficult to isolate from infectious sites and are often overlooked.

Endocarditis due to anaerobic bacteria is an uncommon event and endocarditis due to Bacteroides fragilis is rarely reported.

We performed a review of literature in MEDLINE (source PubMed) from 1980 to 2009 and found eight cases of endocarditis due to Bacteroides fragilis. We also reviewed the list of references of review articles and excluded the repeated cases related to previous studies. The characteristics of reported cases (including the present report) are shown in Table 1. Elderly patients (mean age, 59 years; range, 14-78 years) were mostly affected and the presence of prior heart or valvular disease in this population are common findings (78%). In 1970, Felner and Dowell described 11 cases of endocarditis due to B. fragilis and the clinical features are shown in Table 2.

The development of infective endocarditis depends on the ability of bacteria to adhere to the vascular endothelium and the capacity to invade valvular leaflets. In this context, two characteristics of Bacteroides fragilis are important: invasiveness and production of toxins. Invasiveness can lead to damage in the local tissue while toxins can be transported to other sites causing much more damage than the original lesion. Its pathogenicity has been attributed to several virulence factors including the lipopolysaccharide (LPS), the polysaccharide capsule and a variety of enzymes (protease, heparinase, collagenase, haemolysin) which protect it of the host immune system. The LPS is responsible for abscess formation and histolytic enzymes can mediate tissue destruction, common events found in infections caused by these bacteria.

Valvular destruction, aortic-ring abscess, congestive heart failure, cardiogenic shock dysrhythmias and thromboembolic events are the most important complications in endocarditis due to B. fragilis. Among the 9 available reported cases (Table 1), 3 patients (33%) had congestive heart failure or cardiogenic shock, 3 (33%) had valvular destruction/abscess and 3 (33%) had thromboembolic events.

Thromboembolism is common in patients with endocarditis due to aerobic bacteria occurring in 20-25% of cases and decreased when adequate therapy was started early. In this review, thromboembolic events occurred in 33% (3/9), not significantly more common than described in endocarditis caused by others agents.

Here, we described a case of endocarditis due to B. fragilis with an asymptomatic local thrombosis (portal and mesenteric vein), frequently associated with more than one risk factor not found in this patient, including neoplasmia, cirrhosis, gastrointestinal infection, myeloproliferative disorders, thrombophilia, pregnancy, or liver transplantation.

There is a possible pathogenic role of prothrombotic phenomena during an invasive B. fragilis infection probably associated with heparinase production by these microorganisms. This enzyme can accelerate the intravascular clotting and may contribute with thrombus formation. In mice, Bacteroides can trigger coagulation probably secondary to a cell-wall component.
<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>Sex/age</th>
<th>Prior heart or valvular disease</th>
<th>Valve affected</th>
<th>Predisposing conditions</th>
<th>Probable source of infection</th>
<th>Duration of symptoms</th>
<th>Diagnosis</th>
<th>Complications</th>
<th>Therapy</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tabaqchali et al.(^5)</td>
<td>1</td>
<td>M/14</td>
<td>NR</td>
<td>Aortic prosthesis</td>
<td>None</td>
<td>NR</td>
<td>NR</td>
<td>Blood culture</td>
<td>Congestive heart failure</td>
<td>Cep + Met</td>
<td>Surgery</td>
</tr>
<tr>
<td>Esteban et al.(^6)</td>
<td>1</td>
<td>M/54</td>
<td>Ischemic heart disease</td>
<td>None</td>
<td>Colitis</td>
<td>Gastrointestinal tract</td>
<td>2 weeks</td>
<td>Blood culture</td>
<td>Myocardial abscess, septic shock, cerebral embolism</td>
<td>Amp + Gt</td>
<td>Chl/Cfx</td>
</tr>
<tr>
<td>Jackson and Dopp(^7)</td>
<td>1</td>
<td>M/78</td>
<td>Aortic valve sclerosis</td>
<td>Aortic valve</td>
<td>Diverticulum of the colon and esophagus (Zenker’s)</td>
<td>Gastrointestinal tract</td>
<td>6 weeks</td>
<td>Blood culture</td>
<td>None</td>
<td>Pip Imp + Met Amx/Clv</td>
<td>Cured</td>
</tr>
<tr>
<td>Lortholary et al.(^8)</td>
<td>1</td>
<td>F/78</td>
<td>Aortic stenosis</td>
<td>Aortic prosthesis</td>
<td>Ovarian carcinoma, small bowel occlusion</td>
<td>Gastrointestinal tract</td>
<td>1-2 weeks</td>
<td>Blood and prosthetic valve culture</td>
<td>Cardiogenic shock</td>
<td>Ctx + Sb + Orn + Amc</td>
<td>Died</td>
</tr>
<tr>
<td>Bisharat et al.(^9)</td>
<td>2</td>
<td>F/74</td>
<td>Aortic stenosis</td>
<td>Aortic prosthesis</td>
<td>Colonic neoplasia</td>
<td>Gastrointestinal tract</td>
<td>2 weeks</td>
<td>Blood culture</td>
<td>None</td>
<td>Met</td>
<td>Cured</td>
</tr>
<tr>
<td>Le Goff et al.(^10)</td>
<td>1</td>
<td>M/73</td>
<td>Ischemic heart disease</td>
<td>Aortic valve</td>
<td>Diverticulosis, diabetes</td>
<td>Gastrointestinal tract</td>
<td>3 weeks</td>
<td>Blood culture</td>
<td>Thrombosis of the portal vein</td>
<td>Pip + Met</td>
<td>Cured</td>
</tr>
<tr>
<td>Bachion et al.(^11)</td>
<td>1</td>
<td>M/46</td>
<td>Bicuspid aortic valve</td>
<td>Aortic/mitral valve</td>
<td>Dental abscess</td>
<td>Gastrointestinal tract</td>
<td>NR</td>
<td>Blood culture</td>
<td>Perivalvar abscess</td>
<td>Imp + Gt surgery</td>
<td>Cured</td>
</tr>
<tr>
<td>PR</td>
<td>1</td>
<td>M/64</td>
<td>None</td>
<td>Aortic valve</td>
<td>Diversiculosis</td>
<td>Gastrointestinal tract</td>
<td>8 weeks</td>
<td>Blood culture</td>
<td>Thrombosis of the portal and superior mesenteric vein</td>
<td>Met</td>
<td>Cured</td>
</tr>
</tbody>
</table>

Amp, ampicillin; Amk, amikacin; Amx/Clv, amoxicillin/clavulanate; Cep, cefuroxime; Ctx, cefotaxime; Chl, chloramphenicol; Cfx, cefoxitin; Gt, gentamicin; Imp, imipenem; Met, metronidazole; NA, not applicable; Om, omidazole; Oxc, oxacillin; Pen, penicillin; PR, present report; Sb, sulbactam; NR, not known or not reported.
components enhance fibrin clotting with macrophages activation and start the clotting cascade.17,18 The other factors include the release of procoagulant factors (E-selectin and P-selectin) by endothelial cells collaborating with the thrombosis, the genetic thrombophilia (protein S and protein C deficiency, prothrombin gene mutation, factor V Leiden mutation), a transient development of antiphospholipid antibodies19 and other prothrombotic disorders (antiphospholipid syndrome, neoplasms). In summary, the pathogenic role of Bacteroides in thromboembolic events is unclear and more thorough studies are needed to clarify this controversial issue.

The signs and symptoms, physical examination and laboratory tests found in endocarditis due to B. fragilis are similar to those seen in endocarditis due to other bacteria. The real role of anticoagulation therapy in documented superior or inferior mesenteric vein thrombosis is controversial but may be considered in patients with normal clotting function.21 Early anticoagulation could reverse or prevent progression of thrombosis thus minimizing the risk of bowel ischemia and infarction and improved outcome with a high recanalization rate, lower portal hypertension and mortality.22 The etiology of underlying hypercoagulable disorder should be studied but in most cases, the infection is responsible for this acute disorder.

The treatment of infective endocarditis should be done with bactericidal antimicrobials agents. Appropriate antimicrobial therapy is associated with lower mortality and empiric antibiotic therapy should be started immediately after collection of cultures. Nitroimidazoles (metronidazole), carbapenems (imipenem, meropenem, ertapenem and doripenem), combinations of β-lactams with a β-lactamase inhibitor (clavulanate, sulbactam and tazobactam) and some quinolones (moxifloxacin) have a good activity against B. fragilis22 and can be used in the treatment of endocarditis caused by these bacteria.

Despite the small number of cases reported and the limited experiences in treating B. fragilis endocarditis, we suggested the administration of intravenous metronidazole for 4-6 weeks, based on other reported cases. Other antimicrobial agents with bactericidal activity against B. fragilis, such imipenem, amoxicillin-clavulanate and piperacillin-tazobactam, could be adequate alternatives with relatively low toxicity in the treatment of endocarditis due these bacteria.

In the last three decades, the mortality and thromboembolic events decreased, probably due to early diagnosis and introduction of metronidazole, a potent antimicrobial agent with good bactericidal activity against Bacteroides.23

Conclusion

In summary, endocarditis due to Bacteroides fragilis could be considered in elderly individuals with preexisting valvular or heart disease and unexplained fever for more than two weeks, anemia, malaise and a previous history of gastrointestinal tract manipulation or disorder. We emphasize that Bacteroides fragilis is a rare agent of endocarditis and these patients should be carefully evaluated for the complications associated with this anaerobic infection.

Conflict of interest

All authors declare to have no conflict of interest.

References