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## 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.<sup>1</sup> 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

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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 funduscopy. 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/mm<sup>3</sup> with a differential count of 66% neutrophils, 11% bands and 20% lymphocytes, platelet count 398.000/mm<sup>3</sup>, 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.

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## Discussion

*Bacteroides fragilis* is an anaerobic Gram-negative rod and constitutes 1% to 2% of the normal colonic bacterial microflora in humans.<sup>2</sup> 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.<sup>3</sup> Because of their fastidious nature, they are difficult to isolate from infectious sites and are often overlooked.<sup>4</sup>

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.<sup>5-11</sup> 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<sup>3</sup> described 11 cases of endocarditis due to *B. fragilis* and the clinical features are showed 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.<sup>12</sup> 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.<sup>1</sup> 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.<sup>13</sup>

Valvular destruction, aortic-ring abscess, congestive heart failure, cardiogenic shock dysrhythmias and thromboembolic events<sup>1,3</sup> 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<sup>14</sup> and decreased when adequate therapy was started early.<sup>15</sup> 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 neoplasia, 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.<sup>12</sup> This enzyme can accelerate the intravascular clotting and may contribute with thrombus formation. In mice, *Bacteroides* can trigger coagulation probably secondary to a cell-wal component.<sup>16</sup> Surface

Table 1 - Characteristics of endocarditis due to *Bacteroides fragilis* since 1980

Author	n	Sex/age	Prior heart or valvular disease	Valve affected	Predisposing conditions	Probable source of infection	Duration of symptoms	Diagnosis	Complications	Therapy	Outcome
Tabaqchali et al. <sup>5</sup>	1	M/14	NR	Aortic prosthesis	None	NR	NR	Blood culture	Congestive heart failure	Cep + Met Surgery	Cured
Esteban et al. <sup>6</sup>	1	M/54	Ischemic heart disease	None	Colitis	Gastrointestinal tract	2 weeks	Blood culture	Myocardial abscess, septic shock, cerebral embolism	Amp + Gt Chl/Cfx	Died
Jackson and Dopp <sup>7</sup>	1	M/78	Aortic valve sclerosis	Aortic valve	Diverticulum of the colon and esophagus (Zenker's)	Gastrointestinal tract	6 weeks	Blood culture	None	Pip Imp + Met Amx/Clv	Cured
Lortholary et al. <sup>8</sup>	1	F/78	Aortic stenosis	Aortic prosthesis	Ovarian carcinoma, small bowel occlusion	Gastrointestinal tract	1-2 weeks	Blood and prosthetic valve culture	Cardiogenic shock	Ctx + Sb + Orn + Amc	Died
Bishrarat et al. <sup>9</sup>	2	F/74	Aortic stenosis	Aortic prosthesis	Colonic neoplasia	Gastrointestinal tract	2 weeks	Blood culture	None	Met	Cured
		F/50	Rheumatic heart disease (aortic stenosis + mitral regurgitation)	Aortic valve	Endometrial neoplasia	Genital tract	1-2 weeks	Blood culture	Myocardial abscess, congestive heart failure	Met	Died
Le Goff et al. <sup>10</sup>	1	M/73	Ischemic heart disease	Aortic valve	Diverticulosis, diabetes	Gastrointestinal tract	3 weeks	Blood culture	Thrombosis of the portal vein	Pip + Met	Cured
Bachion et al. <sup>11</sup>	1	M/46	Bicuspid aortic valve	Aortic/mitral valve	Dental abscess	Gastrointestinal tract	NR	Blood culture	Perivalvar abscess	Imp + Gt surgery	Cured
PR	1	M/64	None	Aortic valve	Diverticulosis	Gastrointestinal tract	8 weeks	Blood culture	Thrombosis of the portal and superior mesenteric vein	Met	Cured

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; Orn, ornidazole; Oxc, oxacillin; Pen, penicillin; PR, present report; Sb, sulbactam; NR, not known or not reported.

**Table 2 - Clinical characteristics of patients with endocarditis due to *Bacteroides* spp.**

	Felner and Dowell, 1970 <sup>3</sup> (n = 11)	Present review (after 1980)* (n = 9)
Mean age	50 years (range 6-75 yr)	59 years (range 14-78 yr)
Male : female ratio	8:3	6:3
Duration of symptoms (median)	NR	3 weeks
Previous heart disease	7 (64%)	7 (78%)
Tract gastrointestinal (probable source of infection)	6 (55%)	7 (78%)
Complications		
Heart failure or cardiogenic shock	4 (36%)	3 (33%)
Valvular destruction or abscess	NR	3 (33%)
Thromboembolic events	6 (55%)	3 (33%)
Deaths	6 (43%)	3** (33%)

\*Including present case; \*\*two patients had advanced neoplasia; NR, not reported.

components enhance fibrin clotting with macrophages activation and start the clotting cascade.<sup>17,18</sup> 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 anti-cardiolipin antibodies<sup>19</sup> and other prothrombotic disorders (antiphospholipid syndrome, neoplasms).<sup>20</sup> 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.<sup>21</sup> 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.<sup>22</sup> The etiology of underlying hypercoagulable disorder should be studied<sup>19</sup> 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  $\beta$ -lactams with a  $\beta$ -lactamase inhibitor (clavulanate, sulbactam and tazobactam) and some quinolones (moxifloxacin) have a good activity against *B. fragilis*<sup>22</sup> 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 as imipenem, amoxicillin-clavulanate and piperacillin-tazobactam, could be adequate alternatives with relatively low toxicity in the treatment of endocarditis due to 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*.<sup>23</sup>

## 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

- Nord CE. Anaerobic bacteria in septicemia and endocarditis. *Scand J Infect Dis.* 1982;11:95-104.
- Drasar BS, Duerden BI. Anaerobes in the normal flora of man. In: BI Duerden, BS Drasar, Anaerobes in Human Disease, Wiley-Liss, New York, p. 162-179.

3. Felner JM, Dowell VR Jr. Anaerobic bacterial endocarditis. *N Engl J Med.* 1970;283:1188-92.
4. Brook I. Endocarditis due to anaerobic bacteria. *Cardiology.* 2002; 98: 1-5.
5. Tabaqchali S, Wills AR, Riordan T, Banin SO, Rees GM. Anaerobic endocarditis: is it missed? *Lancet.* 1981;i:148-149.
6. Esteban A, Wilson WR, Ruiz-Santana S, Fernandez-Segoviano P, Martinez Cabruja R. Endocarditis caused by *B. fragilis*. *Chest.* 1983;84:104-6.
7. Jackson RT, Dopp AC. *Bacteroides fragilis* endocarditis. *South Med J.* 1988;81:781-782.
8. Lortholary O, Buu-Hoi, Podglajen I, et al. Endocarditis caused by multiply resistant *Bacteroides fragilis*: case report and review. *Clin Microbiol Infect.* 1995;1:44-47.
9. Bishrarat N, Goldstein L, Raz R, Elias M. Gram-negative anaerobic endocarditis: two cases reports and review of the literature. *Eur J Clin Microbiol Infect Dis.* 2001;20:651-654.
10. Le Goff B, Agard C, Hamidore M, Boutoille D, Bonnel C, Grollean J. Endocarditis due to *Bacteroides fragilis* revealed by portal thrombosis: a case report. *La revue de medicine interne.* 2004;25:470-77.
11. Bachion F, Cukon S, Rizzoli G, et al. Infective endocarditis in bicuspid aortic valve: atrioventricular block as sign of perivalvular abscess. *Cardiovasc Pathol.* 2007;16:252-255.
12. Gesner B, Jenkin C. Production of heparinase by *Bacteroides*. *J Bacteriol.* 1965;81:595-600.
13. Wexler HM. *Bacteroides*: the good, the bad, and the nitty-gritty. *Clin Microbiol Rev.* 2007;20 (4):593-621.
14. Cabell CH, Pond KK, Peterson GE, et al. The risk of stroke and death in patients with aortic and mitral valve endocarditis. *Am Heart J.* 2001;142(1):75-80.
15. Fabri J Jr, Issa VS, Pomerantzeff PM, Grinberg M, Barretto AC, Mansur AJ. Time- elated distribution, risk factors and prognostic influence of embolism in patients with left-sided infective endocarditis. *Int J Cardiol.* 2006;110(3):334-9. Epub 2005 Oct 6.
16. Bjornson H, Hill E, Altemeier W. Role of L-forms *Bacteroides* species and *Sphaerophorus* in acute and recurrent thromboembolic disease. *Bacterial Proceedings.* 1970;141:87-88.
17. Rosenthal GA, Levy G, Rotstein OD. Induction of macrophage procoagulant activity by *Bacteroides fragilis*. *Infect Immun.* 1989;57:338-43.
18. Choi Y-H, Roehrl MH, Kasper DL, Wang JY. A unique structural pattern shared by T-cell-activating and abscess-regulating zwitterionic polysaccharides. *Biochemistry.* 2002;41:15144-51.
19. Liappis AP, Roberts AD, Schwartz AM, Simon GL. Thrombosis and infection: a case of transient anti-cardiolipin antibody associated with pylephlebitis. *Am J Med Sci.* 2003;325:365-8.
20. Ni Y, Wang N, Peng M, Chou Y, Chang F. *Bacteroides fragilis* bacteremia associated with portal vein and superior mesentery vein thrombosis secondary to antithrombin III and Protein C deficiency: a case report. *J. Microbiol Immunol Infect.* 2002;35:255-58.
21. Condat B, Pessione F, Helene DM, Hillaire S, Valla D. Recent portal or mesenteric thrombosis: increased recognition and frequent recanalization on anticoagulant therapy. *Hepatology.* 2000;32:466-70.
22. Kanellopoulou T, Alexopoulou A, Theodossiades G, Koskinas J, Archimandritis AJ. Pylephlebitis: an overview of non-cirrhotic cases and factors related to outcome. *Scand J Infect Dis.* 2010;42:804-11.
23. Chow A, Patten V, Guze L. Susceptibility of anaerobic bacteria to metronidazole. *J Infect Dis.* 1975;131:182-185.