INTERNAL MEDICINE

□ CASE REPORT □

Mycotic Aneurysm Caused by *Bacteroides fragilis* in an Elderly Immunosuppressed Patient

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Abstract

An 82-year-old Japanese man, who presented with a fever and abdominal pain, was admitted to our hospital. According to enhanced computed tomography images, the probable diagnosis was abdominal aortic mycotic aneurysm. Eight sets of blood cultures obtained from the patient were negative. Despite administering treatment with vancomycin and ceftriaxone, the aneurysm progressively enlarged. He underwent open debridement surgery and *in situ* replacement because of an aneurysmal rupture. *Bacteroides fragilis* was isolated from the tissue culture of the aortic wall. Metronidazole was administered and discontinued without any infection relapse. When faced with similar cases, rare pathogens should thus be considered as possible causes of mycotic aneurysms.

Key words: *Bacteroides fragilis*, mycotic aneurysm, infected abdominal aneurysm, immunosuppressed patient, metronidazole

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Introduction

Mycotic aneurysm could be a fatal infectious disease if not appropriately managed. Previous reports indicate that most of the causative pathogens are Gram-positive cocci, such as *Staphylococcus aureus* or *Streptococcus pneumoniae*, and aerobic Gram-negative bacteria, such as *Salmonella* spp. (1).

An 82-year-old man was diagnosed with rheumatic arthritis and underwent long-term treatment with methotrexate (during the past 2 years). He then developed a mycotic aneurysm which had been caused by an anaerobic bacterial infection with *Bacteroides* (*B.*) *fragilis*. As this finding is extremely rare in terms of mycotic aneurysms, we herein describe the assessment, clinical course, and management of this case.

Case Report

An 82-year-old Japanese man was admitted to our hospital because of a 3-day history of chills and abdominal and back pain. He was diagnosed with rheumatoid arthritis, for which he had been prescribed methotrexate 4 mg/week 2 years earlier. Additionally, he had a history of hypertension and angina pectoris. He had no history of tuberculosis, syphilis, or previous abdominal surgery. He denied having any digestive symptoms such as nausea, diarrhea, or melena. There was no evidence that he had a colonic diverticulum.

On admission, he was alert, his vital signs were blood pressure of 144/84 mmHg, heart rate of 115 beats/min, body temperature of 38.3°C, respiration rate of 16 breaths/min, and SpO_2 of 96% with ambient air. His physical examination revealed pain and tenderness on his right lower abdominal quadrant, but no pulsatile masses.

Laboratory findings showed an elevated white blood cell count of 16,400/μL (neutrophils, 92%; lymphocytes, 2.1%)

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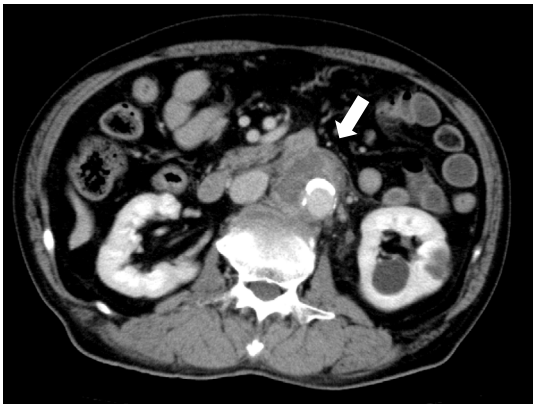

Figure. Abdominal aortic aneurysm on enhanced computed tomography taken on admission day.

and C-reactive protein of 22.39 mg/dL. His serological tests for syphilis were negative. Enhanced computed tomography displayed an abdominal aortic aneurysm (Figure).

According to a clinical suspicion of a mycotic aneurysm, three sets of blood cultures were obtained on admission, followed by a series of blood cultures taken on 3 consecutive days. Ceftriaxone 2 g intravenously (IV) every 12 h and vancomycin 1 g IV every 24 h were immediately administered for coverage of Gram-positive cocci and Gram-negative bacilli, such as *Salmonella* spp. We consulted a cardiovascular surgeon who recommended medical therapy as the primary therapy, but with continuous monitoring. The six sets of blood cultures obtained from the patient were negative. Then, vancomycin was discontinued because it was less likely that the infection was caused by Gram-positive bacteria.

On the seventh hospitalization day, he developed a high-grade (40°C) fever. Abdominal ultrasound revealed acalculous cholecystitis. At that time, two additional sets of blood cultures were obtained, and ceftriaxone was replaced with cefepime 2 g IV every 12 h.

On the ninth hospitalization day, the abdominal aneurysm became enlarged and finally ruptured; therefore, urgent open debridement and *in situ* replacement were performed. There was no evidence indicating either intestinal or colonic comorbidity or any abnormal laparoscopic findings. No serious complications occurred during the surgery. The Gram stain of the necrotic tissue of the aortic wall revealed Gram-negative bacteria suspected to be an anaerobe; thus, piperacillin/tazobactam 4.5 g IV every 6 h and metronidazole 500 mg PO (per os) three times daily were administered according to the general antimicrobiogram findings. On the 11th hospitalization day, piperacillin/tazobactam was replaced by sulbactam/ampicillin 1.5 g IV every 6 h because *B. fragilis* was isolated from the tissue culture. The bacterial profile indicated that the strain was sensitive to sulbactam/ampicillin and metronidazole, but resistant to clindamycin. While sulbactam/ampicillin was discontinued on the 22nd hospitalization day because of a skin eruption, metronidazole was maintained as suppressive therapy. The patient was discharged after 32 days of hospitalization without any complications. Metronidazole was discontinued after 6 months of treatment because the patient complained of dizziness. The dizziness disappeared and the patient was free of infection relapse for 3 years after the cessation of metronidazole. He ultimately died from an unrelated case of pneumonia.

Discussion

We experienced a case of mycotic aneurysm caused by an obligate anaerobic bacterium, *B. fragilis*, which was successfully treated with surgical intervention and long-term antimicrobial treatment.

Physicians should be alert when using empiric therapy against common pathogens. We selected vancomycin and ceftriaxone to provide coverage for the most common pathogens involved in mycotic aneurysms, such as staphylococci (60%) and *Salmonella* (20-25%) (1). Although the eight sets of blood cultures obtained during hospitalization were negative, *B. fragilis* was isolated from the tissue culture of the necrotic aortic wall that was obtained during surgery. This causative pathogen was not covered by the empirical therapy initially administered; however, it is practically impossible to provide antimicrobial coverage for all the microorganisms that could potentially cause some disease in a given patient. Nevertheless, if the clinical course is not progressing as expected after the beginning of antimicrobial therapy, physicians should consider that the causative pathogen may be a rare or unusual one. While antimicrobial coverage for anaerobes was not initially achieved by empirical therapy (e.g., carbapenems), no data are available regarding the effect of medical therapy alone (2). Therefore, whether the patient's clinical course was altered by the management provided remains equivocal.

Additionally, the duration of antimicrobial treatment was debated. Some experts mention that adverse drug reactions to metronidazole therapy are rare, but include central nervous system toxicity (3). A review article reported that metronidazole treatment over 6 months led to encephalopathy; however, this adverse event was resolved after the discontinuation of metronidazole (4). In the present case, we decided to continue the treatment for as long as possible until the onset of any adverse events.

It is extremely rare for an anaerobic microorganism to cause a mycotic aneurysm, and it is also difficult for such microorganisms to be cultured successfully from blood samples. To the best of our knowledge, only 22 cases of mycotic aneurysm caused by the *B. fragilis* group have been previously reported in both English and Japanese literature (2, 5-16). Of these, only nine reports confirmed bacteremia secondary to *B. fragilis* infection (Table). Likewise, in our case, we failed to isolate *B. fragilis* from a number of blood cultures. In addition, six patients presented conditions associated with an immunosuppressive state such as diabetes mellitus, liver cirrhosis, active malignancy, or the use of immunosuppressive agents, similar to our patient. Moreover,

Table. Features of 23 Patients with Mycotic Aneurysm Caused by *Bacteroides Fragilis* Group.

Number	culture result	author	bacteremia	immuno-suppression	relation with GI tract	known aneurysm	surgical procedure	complication	antibiotics	prognosis
1	*Bacteroides* spp.	Sheehan	-	-	NA	NA	-	+	ampicillin + cloxacillin	died
2	*B. fragilis*	Reddy	+	+	NA	-	+	+	MNZ	survived
3	*B. fragilis*	Suddelson	+	-	-	+	+	-	MNZ	survived
4	*Bacteroides* spp.	Taylor	+	NA	-	+	+	NA	iv+poATB	survived
5	*B. fragilis*	Jewkes	NA	-	+	+	+	-	gentamicin+MNZ	survived
6	*B. fragilis*	Reddy	NA	NA	-	NA	+	-	ivATB	survived
7	*B. fragilis*		NA	NA	-	-	+	+	ivATB	survived
8	*B. fragilis*	Sessa	NA	NA	NA	NA	+	+	ATB	died
9	*B. fragilis*		NA	NA	NA	NA	+	+	ATB	survived
10	*B. fragilis, Peptostreptococcus prevotii*	Brook	NA	-	+	-	+	+	NA	died
11	*B. fragilis*	O'Donnell	+	+	NA	NA	+	+	piperacillin /tazobactam +gentamicin	died
12	*B. fragilis*	Doita	-	-	-	NA	+	-	NA	survived
13	*B. thetaiotaomicron*	Hsu	NA	NA	NA	NA	+	+	NA	died
14	*B. fragilis*	Matsuyama	-	+	+	NA	+	-	imipenem/cilastatin	survived
15	*B. fragilis*	Beland	+	-	+	NA	+	-	MNZ+cefepime	survived
16	*B. fragilis*	Lee	+	+	+	NA	+	+	cefotaxime +teicoplanin	died
17	*B.thetaiotaomicron*	Maeda	-	NA	NA	NA	+	+	NA	died
18	*B.thetaiotaomicron Acinetobacter lwofii*	Kim	+	+	NA	NA	+	-	MNZ+ ciprofloxacin	survived
19	*B. fragilis*	Ohuchi	NA	-	+	NA	+	+	cefmetazole	died
20	*B. fragilis*	Unno	+	-	NA	-	+	+	NA	died
21	*B. fragilis*	Hanada	+	-	+	+	+	-	meropenem	survived
22	*B. fragilis*	Aizawa	+	-	NA	NA	+	-	cefmetazole +clindamycin	survived
23	*B. fragilis*	Fukuchi	-	+	-	NA	+	-	MNZ	survived

NA: not available, ATB: antibiotics, MNZ: metronidazole

six patients had comorbidity with either the gastrointestinal tract or genital infectious diseases.

We then hypothesized that this patient's unusual infection was probably related to the immunosuppressive status or some colonic comorbidity (17). However, there was no available evidence to confirm such a hypothesis. Furthermore, as we generally recommend to our patients, we advised the patient to undergo colonoscopy, which he refused. If there had been a colonic malignancy, it is likely that he would have died from this disease. Thus, we might be able to rule out the possibility of colonic comorbidity, particularly colon cancer.

Previous research reported up to the late 1980s has referred to the relationship between mycotic aneurysms and endocarditis or a previously known atherosclerotic aneurysm; however, the tendency has become less common in recent studies. Further research is needed to elucidate this disease.

In similar cases, when the results of multiple blood cultures are negative, but the patient has progressive clinical manifestations of infection, we recommend that clinicians consider rare pathogens, such as facultative anaerobes, as causative agents.

The authors state that they have no Conflict of Interest (COI).

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