Bacteroides fragilis Bacteremia and Infected Aortic Aneurysm Presenting as Fever of Unknown Origin: DiagnosticDelay without Routine Anaerobic Blood Cultures

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We report the case of a 71-year-old male with Bacteroides fragilis bacteremia and infected aortic aneurysm that went undiagnosed, in part, because routine anaerobic blood cultures were not obtained. Bacteremia caused by anaerobes has been reported to be declining, and recommendations to discontinue routine anaerobic blood cultures have been implemented in some hospitals. To our knowledge, this is the first report of an anaerobic bacteremia and infection that had a delay in diagnosis due to this change in blood-culturing protocol. The potential impact of deleting anaerobic blood cultures from routine protocols is discussed.

Fever of unknown origin (FUO) is a clinical entity that requires an organized and thorough approach to determine a diagnosis. Multiple routine blood cultures for isolation of bacterial pathogens are recommended for patients with FUO, and failure in making a diagnosis of such infections has been linked to inadequate numbers of cultures and to performance of culture while the patient is receiving concurrent antibiotic therapy [1, 2]. Successful isolation of bacterial pathogens from blood is directly dependent upon the volume of blood obtained and the timing of collection of blood [3]. Traditional protocols for blood culture include 2 bottles per set: 1 aerobic blood culture bottle and 1 anaerobic blood culture bottle. Recently, however, there have been reports of a decreasing frequency of anaerobic bacteremias, and it has been recommended that anaerobic blood culture bottles be replaced with either another aerobic blood culture bottle or a medium for isolating fungi [4, 5]. We describe a patient who presented with FUO and was found to have anaerobic bacteremia and intravascular infection that were initially missed, because anaerobic blood cultures had been eliminated from the standard blood culture protocol where he was first assessed.

Case Report

A 71-year-old male with a medical history of coronary artery disease, hypertension, type II insulin-requiring diabetes mellitus, and bladder carcinoma was transferred to our institution because of a 5-week history of recurrent fevers. The patient had been healthy until he developed fevers (temperature to 40°C), sweats, and rigors 5 weeks previously. He was admitted to an outside hospital. Blood cultures were all negative, CT of the abdomen and pelvis was unremarkable, and urine culture yielded >10^5 cfu of Escherichia coli. The patient was treated with presumptive E. coli urinary tract infection with 7 days of intravenous cefazolin and was discharged afebrile without antibiotic therapy.

Within 5 days of returning home, his fevers and rigors recurred, and he was readmitted to the community hospital. Blood and urine cultures were negative. A transthoracic echocardiogram was unremarkable. A gallium scan showed increased uptake in the mid-thoracic area. The patient was treated with unspeciﬁed intravenous antibiotics, and his fever resolved; he was discharged. Because of his history, he underwent outpatient cystoscopy 1 week later, and was treated with a 5-day course of an unspeciﬁed oral antibiotic. Within 1 week of completing oral antibiotic therapy, fevers and rigors recurred, and he was readmitted to the community hospital.

Blood and urine specimens for culture were obtained, and treatment with intravenous ticarrellin/clavulanic acid and gentamicin was started 24 h after hospitalization. He continued to be febrile and was transferred to our institution 48 h after this third hospitalization. At admission to our hospital, he complained only of vague, mild, diffuse abdominal pain over the past month and a 20–30-lb weight loss over the course of the illness. He speciﬁcally denied nausea, vomiting, diarrhea, constipation, gastrointestinal bleeding, and genitourinary symptoms. His medications at the time of transfer included the above-mentioned antibiotics, docusate, insulin, and acetaminophen.

Initial physical examination revealed an oral temperature of 39°C, blood pressure of 110/50 mm Hg, pulse rate of 100, and respiratory rate of 20. He was ill-appearing, and rigors were found during physical examination. His skin was without rashes. Lung examination revealed crackles at the right base. Heart examination revealed tachycardia, without murmurs, rubs, or gallops. Normal
bowel sounds were heard, and the abdomen was soft and mildly tender to deep palpation in the midepigastric area; no masses, bruits, or hepatosplenomegaly was observed. Results of examination of his extremities were within normal limits, neurological examination was nonfocal, and rectal examination was negative for occult blood or masses.

Laboratory studies disclosed the following: hemoglobin level, 12.5 g/dL; platelet count, 300,000/mm³; and WBC count, 21,500/mm³ (80% granulocytes, 12% band forms, 4% lymphocytes, 3% monocytes, and 1% basophils). The erythrocyte sedimentation rate was 94 mm/h, the blood urea nitrogen level was 22 mg/dL, and the serum creatinine level was 1.0 mg/dL. A chest radiograph obtained at admission showed no infiltrates or effusions. Laboratory studies disclosed the following: hemoglobin level, 12.5 g/dL; platelet count, 300,000/mm³; and WBC count, 21,500/mm³ (80% granulocytes, 12% band forms, 4% lymphocytes, 3% monocytes, and 1% basophils). The erythrocyte sedimentation rate was 94 mm/h, the blood urea nitrogen level was 22 mg/dL, and the serum creatinine level was 1.0 mg/dL. A chest radiograph obtained at admission showed no infiltrates or effusions.

Blood and urine specimens for culture were obtained upon transfer, and empirical therapy with piperacillin/tazobactam and gentamicin was begun. CT of the abdomen and pelvis revealed a saccular abdominal aortic aneurysm. An arteriogram confirmed the presence of a bilobed saccular aneurysm of the abdominal aorta that originated just below the diaphragm and measured 8.0 x 4.5 x 5.0 cm. The aneurysm terminated before the celiac axis. There was no leak. Subsequent MRI suggested a mycotic aneurysm. A transesophageal echocardiogram showed no vegetations.

On the third hospital day, one of the anaerobic cultures of blood obtained at the time of admission was reported as positive for a gram-negative rod that was subsequently identified as *Bacteroides fragilis* and was β-lactamase-positive. Repeated blood cultures were negative. On the 11th hospital day, the patient underwent repair of his aneurysm and died in the operating room of bleeding and persistent ventricular arrhythmias. Gross findings at that time were consistent with an infected abdominal aortic aneurysm, but there was no evidence of an aortoenteric fistula. Examination of tissue specimens from the aortic wall, the thrombus within the aorta, and the periaortic fat pad revealed acute inflammation and necrosis. Analysis of the thrombus specimen showed extensive neutrophilic infiltrates, acute and chronic inflammation, and necrosis consistent with an infected aneurysm. Gram staining, fungal staining, and staining for acid-fast bacilli were all negative; *B. fragilis* grew only in broth cultures of all tissue specimens.

The outside hospital from which the patient had been referred did not routinely include anaerobic blood culture bottles as part of their blood culture procedures.

Discussion

Our patient presented with episodes of FUO that were suppressed with antibiotic therapy but recurred quickly once antibiotic therapy was withdrawn. Aerobic blood cultures performed 3× over the course of his 5-week febrile illness were negative. Further details regarding the outside hospital’s blood culture systems and protocols were not known. Without anaerobic blood cultures, the patient’s *B. fragilis* bacteremia and subsequent infected aortic aneurysm went undiagnosed. Microbiological identification was made quickly once blood specimens for anaerobic cultures were obtained at the time of transfer to our institution. Before his death, there was suspicion of an aortoenteric fistula; however, this condition was ruled out after he died. The source of his bacteroides bacteremia remains unknown.

In a recent study, 14% of anaerobic bacteremias identified were of unknown origin [6]. It is unclear whether earlier detection of anaerobic bacteremia and infection would have altered the ultimate outcome in our case. Historically, mortality rates among individuals with mycotic aneurysms are high [7]. In addition, *B. fragilis* bacteremia from any source has recently been shown to be associated with an excess or attributable mortality rate of close to 20% [8]. Although infected aortic aneurysms have been fairly well described in the medical and surgical literature, an aneurysm infected solely with *B. fragilis* is unusual. To our knowledge, there are only 2 other case reports of a similar process, 1 occurring after translumbar aortography and the other a result of secondary infection of an appendiceal abscess [9, 10].

Within the past 2 decades, the incidence of anaerobic bacteremias among hospitalized patients is thought to have been decreasing, and cases of fungemia have been reported more commonly [4]. Acknowledging this changing pattern, some experts have suggested that within the set of 2 blood culture bottles, the anaerobic blood culture bottle be replaced with either another aerobic blood culture bottle or a medium for isolating fungi [5]. Anaerobic blood cultures would then be used selectively, as the clinical situation warrants. Some laboratories have subscribed to this recommendation and have changed their routine blood culture sets accordingly.

Whether such a change in blood culture protocols is wise continues to be debated [11]; reasons for considering continued use of routine anaerobic cultures are numerous. First, in a recent article, Cockerill et al. [12] reported that in the last 4 years of the period 1984–1992, the incidence of bacteremias due to obligate anaerobes and facultatively anaerobic gram-positive bacteria actually increased. These investigators point to other researchers who have also noticed a reversal in the prior trend toward a decreasing frequency of anaerobic bacteremias and suggest that because of these findings they believe that anaerobic blood cultures are warranted at their institution. Second, the selective use of anaerobic blood cultures, such as for patients with FUO or when abdominal or pelvic sites of infection are suspected, may still miss a significant number of bacteremias [6, 11]. Salonen et al. [6] reported on 57 cases of clinically significant anaerobic bacteremias, and 18% of their patients had either unknown or extremely unusual foci of infection. Microbiological identification for these patients, like ours, would likely not have been made if anaerobic cultures had not been performed. Third, when anaerobic cultures are routinely performed, the yield of both obligate anaerobes and facultative anaerobes, including streptococci, is higher [11, 13].

We believe that our case illustrates the need for infectious diseases clinicians and other researchers to be aware of what
type of blood culture bottles are being routinely used by the laboratory as part of the standard blood culture protocol. Although this single case does not suggest that all standard blood culture protocols include an anaerobic blood culture bottle, it does serve as a reminder to practicing clinicians that anaerobic cultures continue to be important and should be specifically requested in situations where there is a high level of suspicion for anaerobes playing a role in the infectious process or FUO. Finally, our case is representative of the morbidity and mortality that may result when anaerobic bacteremias and infections occur.

References