Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.1806-18
Intern Med 58: 813-816, 2019
http://internmed.jp

【 CASE REPORT 】

Infectious Aneurysm Caused by *Citrobacter koseri* in an Immunocompetent Patient

Takahiro Ando[1], Satoshi Noguchi[1], Takako Enokida[1], Azusa Yamato[1], Hidenori Kage[1], Yasuhiro Yamauchi[1], Aiko Okazaki[2], Yoshitaka Wakabayashi[2], Kyoji Moriya[2], Haruo Yamauchi[3], Minoru Ono[3] and Takahide Nagase[1]

Abstract:

Citrobacter species can cause severe infection in immunocompetent patients. A 78-year-old man visited our hospital because he had had a fever lasting one day each month for the past 3 months. Antibiotics were initiated for suspected bronchial pneumonia, but the C-reactive protein level remained high. Contrast-enhanced computed tomography revealed saccular brachiocephalic artery aneurysm. *Citrobacter koseri* was isolated from a blood culture, and he was diagnosed with infectious brachiocephalic artery aneurysm. He underwent endovascular aneurysm repair after one month of intravenous cefepime and metronidazole. We herein report for the first time an immunocompetent patient with infectious aneurysm caused by *C. koseri* periodontal infection.

Key words: *Citrobacter koseri*, infectious aneurysm, periodontal disease, bloodstream infection, endovascular aneurysm repair

(Intern Med 58: 813-816, 2019)
(DOI: 10.2169/internalmedicine.1806-18)

Introduction

Citrobacter species, which are ubiquitous Gram-negative bacilli, are considered to have low virulence and rarely cause infection in humans. While the organism usually infects immunocompromised patients, patients can contract *Citrobacter* without underlying disease (1, 2). The organism may infect the urinary tract, gastrointestinal tract, respiratory tract, and wounds and result in bacteremia.

Infectious aneurysms are rare and are reported to account for 0.7% to 3.4% of aneurysms (3, 4). Infected aneurysms can rupture and become life-threatening. Gram-negative rods have been reported to be associated with a higher rate of rupture and mortality than other bacteria (5).

We herein report an immunocompetent patient with infectious aneurysm caused by *Citrobacter koseri* periodontal infection who was treated with antibiotic therapy combined with endovascular aneurysm repair.

Case Report

A 78-year-old man visited our hospital because he had had a fever lasting one day each month for the past 3 months and was suspected of having aspiration bronchitis. Despite treatment with ampicillin-clavulanate (375 mg three times daily) for 7 days, his symptoms did not improve, and he was admitted to our hospital for a further investigation. He had periodontal disease, for which he was had been receiving ongoing treatment for four months before admission. He had no history of diabetes mellitus or hypertension. He had smoked 30 cigarettes daily for 55 years and had hypoxemia on exertion due to chronic obstructive pulmonary disease (COPD). He was taking loxoprofen (60 mg twice daily) for back pain and dental pain.

On admission, his vital signs were as follows: blood pressure of 122/68 mmHg, heart rate of 88/min, respiratory rate of 18/min, percutaneous oxygen saturation values of 96% at

[1]Department of Respiratory Medicine, The University of Tokyo, Japan, [2]Department of Infectious Diseases, The University of Tokyo, Japan and [3]Department of Cardiac Surgery, The University of Tokyo, Japan
Received: July 10, 2018; Accepted: August 28, 2018; Advance Publication by J-STAGE: November 19, 2018
Correspondence to Dr. Takahiro Ando, takaando@me.com

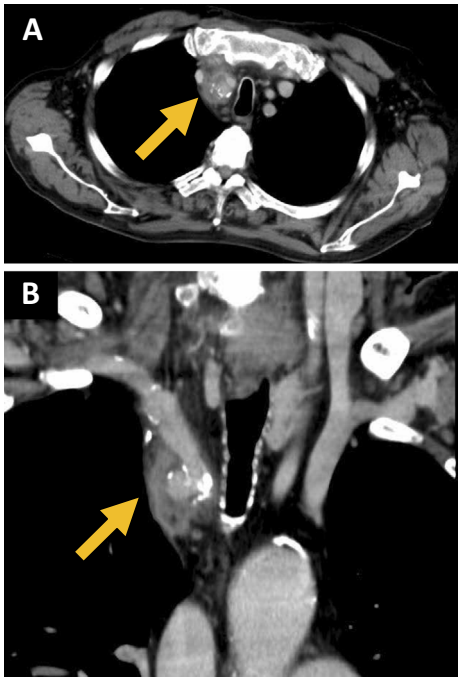

Figure 1. Contrast-enhanced CT on day 13 (A, B). A saccular brachiocephalic artery aneurysm and enhanced periarterial soft tissue are seen (arrows).

room air, and body temperature of 38.0℃. Crackles in the left lower lung on auscultation and clubbed fingers were observed. The rest of his examination findings were normal. His laboratory data indicated white blood cells 10,200/μL, neutrophils 74%, C-reactive protein 11.1 mg/dL, and procalcitonin 0.15 mg/dL. *Treponema pallidum* and human immunodeficiency virus screening test findings were negative. *C. koseri* was isolated from a sputum bacterial culture (M1 by Miller and Jones sputum classification), while an acid-fast bacterial culture and blood culture collected on the first hospital day were negative. *C. koseri* was not isolated from urine or stool cultures. Chest X-ray and chest computed tomography (CT) without contrast enhancement revealed slight infiltrates and bronchial wall thickening in the left lower lobe. Electrocardiography showed ST depression in leads II, III, and aVf. A respiratory function test showed a forced expiratory volume in 1 second ($FEV_{1.0}$) of 0.93 L and a percent predicted $FEV_{1.0}$ of 34.6%, which was equivalent to COPD stage III. Bronchial pneumonia was suspected, and piperacillin-tazobactam (4.5 g every 8 hours) was initiated.

Although his fever improved with antibiotics, his C-reactive protein levels remained elevated. Transthoracic echocardiography performed on day 7 of hospitalization revealed a slightly decreased ejection fraction but no valve abnormalities, including vegetation. Results of laboratory tests performed on day 11 were as follows: white blood cell count, 8,100/μL; neutrophils, 73%; and C-reactive protein, 7.0 mg/dL. On day 13, whole-body contrast-enhanced CT revealed saccular brachiocephalic artery aneurysms and enhanced periarterial soft tissue (Fig. 1). Calcifications in the brachiocephalic artery and aortic wall were also detected.

Table. Drug Susceptibility Test.

	MIC (μg/mL)	Susceptibility
Ampicillin	>16.0	Resistant
Piperacillin/tazobactam	≤ 8.0	Susceptible
Cefazolin	≤ 2.0	Resistant
Cefmetazole	≤ 2.0	Resistant
Ceftriaxone	≤ 1.0	Susceptible
Ceftazidime	≤ 2.0	Susceptible
Cefepime	≤ 2.0	Susceptible
Meropenem	≤ 1.0	Susceptible
Aztreonam	≤ 2.0	Susceptible
Gentamicin	≤ 1.0	Susceptible
Amikacin	≤ 8.0	Susceptible
Levofloxacin	≤ 1.0	Susceptible

MIC: minimum inhibitory concentration

Infectious brachiocephalic artery aneurysm was suspected, and meropenem (1 g every 8 hours) and teicoplanin (900 mg for a day, followed by 450 mg every 24 hours) were started after 2 sets of blood cultures were collected. On day 14, Gram-negative rods grew in one of the blood culture specimens, and the organism was identified as *C. koseri* with the same susceptibility pattern as in the previous sputum culture (Table). Based on these findings, we diagnosed the patient with infectious brachiocephalic artery aneurysm caused by *C. koseri*.

The predicted operative mortality according to logistic EuroSCORE was 32.5%, and the risk of aneurysm excision with arterial reconstruction was considered too high to perform surgery. A dental examination revealed chronic suppurative apical periodontitis of a right posterior tooth, and the tooth was extracted on day 15. Head CT angiography and magnetic resonance angiography revealed no cerebral aneurysms. Colonoscopy revealed no remarkable findings in the colon or rectum that could cause bacterial translocation. We therefore considered periodontal disease to be the cause of bacteremia and, subsequently, the infectious brachiocephalic artery aneurysm.

We changed the antibiotics to cefepime (1 g every 8 hours) and metronidazole (500 mg every 12 hours) on day 26. His C-reactive protein level gradually decreased and returned to normal on day 34. A re-examination of transthoracic echocardiography on day 35 revealed no vegetation, and two sets of blood cultures collected on day 42 were found to be negative. He underwent endovascular stent graft placement at the infected brachiocephalic artery aneurysm and carotid subclavian artery bypass surgery on day 46 (Fig. 2). After the surgery, he was treated with cefepime and metronidazole for three additional weeks and discharged on day 63. At discharge, he was switched to oral levofloxacin (500 mg once daily), which he has continued indefinitely. He has since remained stable without recurrence of infection at 12 months.

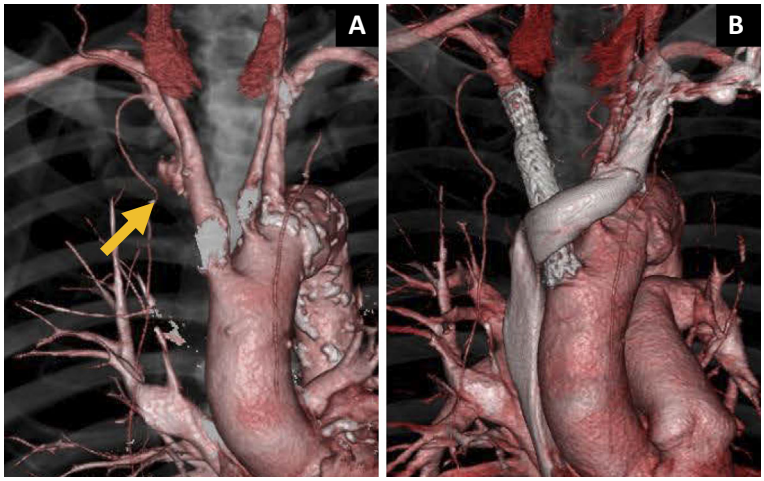

Figure 2. **CT angiography before (A) and after surgery (B). The saccular brachiocephalic artery aneurysm (arrow) was repaired with an endovascular stent graft.**

Discussion

C. koseri are aerobic Gram-negative bacilli found in water and soil and as normal flora of the human intestine. The virulence of *Citrobacter* species is considered to be low, but these bacteria can cause severe infection. While infection mainly occurs in immunocompromised patients, 1 report showed that 12% of patients did not have any underlying disease (1, 2). Common infection sites of *Citrobacter* species include the urinary tract, gastrointestinal tract, respiratory tract, and wounds (1, 2). Given that our patient was immunocompetent, *C. koseri* likely entered the bloodstream through his periodontal disease. While *Citrobacter* species have been reported as a rare cause of endocarditis or arteritis (6-8), to our knowledge, this is the first documented case of infectious aneurysm caused by *C. koseri* periodontal infection.

Infectious arterial aneurysm develops as a complication of endocarditis by infection of a preexisting intimal injury, such as atherosclerotic plaque, or by primary aortic wall infection and injury. Although the frequency of infectious aneurysm caused by bacterial endocarditis is decreasing, bacterial seeding of arteries with intimal injury is a common etiology (9). While *Staphylococcus aureus* and *Salmonella* species are considered the most common pathogens, Gram-negative organisms are also associated with infection (5, 10, 11). In the present case, *C. koseri* was isolated from saliva-like sputum that contained oral bacteria. Previous reports have demonstrated that enterobacteria, such as *Citrobacter* species, can be found in the oral cavity and cause periodontal disease (12, 13). Our patient underwent dental treatment for his periodontal disease before admission, which may have caused the bacteremia (14). In addition, he was an elderly person with a history of heavy smoking and had calcification in the aorta and brachiocephalic artery. The aneurysm may have developed after *C. koseri* entered the bloodstream because the intima was vulnerable in the brachiocephalic artery.

No definitive treatment for infectious aneurysm has been established because no randomized control studies have been conducted. The current standard treatment is antibiotic therapy combined with surgical debridement and revascularization (4, 15). Endovascular aneurysm repair has been reported as a less-invasive and effective treatment for infected aneurysm (16, 17). A life-table analysis in 48 patients with thoracic or abdominal aortic aneurysm showed that the 2-year survival rate was 82.2±5.8% (14). In addition, the 12-month survival rate of the persistently infected group was 39.0±17.0%, and that of the healed group was 94.0±4.0% (16). Preoperative control by the administration of antibiotics for a sufficient duration is important for obtaining a good outcome. In our case, surgical therapy of the brachiocephalic artery aneurysm was considered very risky because his cardiopulmonary function was low. Therefore, he was treated with endovascular aneurysm repair with preoperative antibiotics for 46 days.

The optimum duration of antibiotic therapy is uncertain, but a minimum of six weeks of therapy has been widely accepted (9). In previous studies, the period of antibiotic treatments ranged from 6 weeks to lifelong (3, 4, 9). Cina et al. reported no marked difference in the survival or recurrence rate between lifelong therapy and therapy for 6 weeks to 12 months (4). However, the lifelong use of antibiotics can lead to an increased risk of bacterial resistance or side effects, depending on the type of antibiotics. Our patient tolerated levofloxacin and has been stable without recurrence for 12 months of antibiotics therapy. Close follow-up is considered important, as recurrence after discontinuation of antibiotic therapy has been reported (4).

In conclusion, we herein report the first case of infectious aneurysm caused by *C. koseri* in an immunocompetent patient. He was successfully treated with antibiotic therapy combined with endovascular aneurysm repair.

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

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