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

Takahiro Ando¹, Satoshi Noguchi¹, Takako Enokida¹, Azusa Yamato¹, Hidenori Kage¹, Yasuhiro Yamauchi¹, Aiko Okazaki¹, Yoshitaka Wakabayashi¹, Kyoji Moriya², Haruo Yamauchi¹, Minoru Ono¹ and Takahide Nagase¹

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 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
a percent predicted FEV 1.0 of 34.6%, which was equivalent to COPD stage III. Bronchial pneumonia was suspected, and two sets of blood cultures collected on day 42 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 supplicative 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.

### Table. Drug Susceptibility Test.

| MIC (μg/mL) | Susceptibility |
|-------------|----------------|
| Ampicillin  | >16.0          | Resistant       |
| Piperacillin/tazobactam | ≤ 8.0 | Susceptible |
| Cefazolin   | ≤ 2.0          | Susceptible     |
| Cefmetazole | ≤ 2.0          | Resistant       |
| Ceftriaxone | ≤ 1.0          | Susceptible     |
| Cefazidime  | ≤ 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 supplicative 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 1.** Contrast-enhanced CT on day 13 (A, B). A saccular brachiocephalic artery aneurysm and enhanced periarterial soft tissue are seen (arrows).
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).
References

1. Drelichman V, Band JD. Bacteremias due to citrobacter diversus and citrobacter freundii. Incidence, risk factors, and clinical outcome. Arch Intern Med 145: 1808-1810, 1985.
2. Mohanty S, Singhal R, Sood S, Dhawan B, Kapil A, Das BK. Citrobacter infections in a tertiary care hospital in northern india. J Infect 54: 58-64, 2007.
3. Meerkin D, Yinnon AM, Munter RG, Shemesh O, Hiller N, Abraham AS. Salmonella mycotic aneurysm of the aortic arch: Case report and review. Clin Infect Dis 21: 523-528, 1995.
4. Cina CS, Arena GO, Fiture AO, Clase CM, Doobay B. Ruptured mycotic thoracoabdominal aortic aneurysms: A report of three cases and a systematic review. J Vasc Surg 33: 861-867, 2001.
5. Jarrett F, Darling RC, Mundth ED, Austen WG. Experience with infected aneurysms of the abdominal aorta. Arch Surg 110: 1281-1286, 1975.
6. Dzeing-Ella A, Szwebel TA, Loubinoux J, et al. Infective endocarditis due to citrobacter koseri in an immunocompetent adult. J Clin Microbiol 47: 4185-4186, 2009.
7. Tellez I, Chrysant GS, Omer I, Dismukes WE. Citrobacter diversus endocarditis. Am J Med Sci 320: 408-410, 2000.
8. Phade SV, deFreitas D, Powell CS, Stoner M. Evolution of bacterial arteritis into a mycotic aortic aneurysm. Vasc Endovascular Surg 41: 158-160, 2007.
9. Kim YW. Infected aneurysm: Current management. Ann Vasc Dis 3: 7-13, 2010.
10. Moneta GL, Taylor LM Jr, Yeager RA, et al. Surgical treatment of infected aortic aneurysm. Am J Surg 175: 396-399, 1998.
11. Dick I, Tiwari A, Menon J, Hamilton G. Abdominal aortic aneurysm secondary to infection with pseudomonas aeruginosa: A rare cause of mycotic aneurysm. Ann Vasc Surg 24: 692.e1-692.e4, 2010.
12. Gendron R, Grenier D, Maheu-Robert L. The oral cavity as a reservoir of bacterial pathogens for focal infections. Microbes Infect 2: 897-906, 2000.
13. Gonçalves MO, Coutinho-Filho WP, Pimenta FP, et al. Periodontal disease as reservoir for multi-resistant and hydrolytic enterobacterial species. Lett Appl Microbiol 44: 488-494, 2007.
14. Forner L, Larsen T, Kilian M, Holmstrup P. Incidence of bacteremia after chewing, tooth brushing and scaling in individuals with periodontal inflammation. J Clin Periodontol 33: 401-407, 2006.
15. Reddy DJ, Shepard AD, Evans JR, Wright DJ, Smith RF, Ernst CB. Management of infected aortoiliac aneurysms. Arch Surg 126: 873-879, 1991.
16. Kan CD, Lee HL, Yang YJ. Outcome after endovascular stent graft treatment for mycotic aortic aneurysm: A systematic review. J Vasc Surg 46: 906-912, 2007.
17. Sorelius K, Mani K, Bjorck M, et al. Endovascular treatment of mycotic aortic aneurysms: A european multicenter study. Circulation 130: 2136-2142, 2014.

The Internal Medicine is an Open Access journal distributed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License. To view the details of this license, please visit (https://creativecommons.org/licenses/by-nc-nd/4.0/).