

Short Communication

Infectious Spondylitis in a Patient with Chronic Kidney Disease: Identification of *Campylobacter fetus* Subsp. *testudinum* by 16S Ribosomal RNA Sequencing

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SUMMARY: We report the first case of spondylitis with bacteremia caused by *Campylobacter fetus* subsp. *testudinum* identified by 16S ribosomal ribonucleic acid (rRNA) gene sequencing. An 81-year-old man presented with fever and general weakness. His medical history included end-stage renal disease, hypertension, and type 2 diabetes. Despite empirical antibiotic treatment, his fever and back pain persisted. Magnetic resonance imaging with gadolinium enhancement showed a low-signal-intensity lesion in T1-weighted imaging and a high-signal-intensity lesion in T2-weighted imaging at the L3 vertebral body. *C. fetus* grew on 1 pair of blood cultures. *C. fetus* subsp. *testudinum* was identified via 16S rRNA sequencing of the cultivated organisms. The patient recovered uneventfully after 6 weeks of optimal antibiotic treatment, selected using susceptibility tests. *C. fetus* spondylitis is a very rare disease. In this unique case involving end-stage renal disease, the underlying pathogen was identified by 16S rRNA sequencing.

Campylobacter fetus causes opportunistic infection in immunocompromised humans and spontaneous abortion in cattle and sheep (1). In humans, infection occurs through the intake of contaminated food (milk or meat) and contact with infected animals (2). *C. fetus* infection can result in a spectrum of clinical diseases, such as infective endocarditis, meningitis, enteritis, and bacteremia (3), but spondylodiscitis also occurs as a very rare condition. Here, we present a case of spondylitis with bacteremia caused by *C. fetus* subsp. *testudinum* identified as the underlying pathogen by 16S ribosomal ribonucleic acid (rRNA) gene sequencing.

An 81-year-old man was admitted to the emergency department at our hospital complaining of general weakness and intermittent fever with chills that persisted over 6 days. He had a history of hypertension, type 2 diabetes mellitus (diagnosed approximately 10 years earlier and for which he received gliclazide 30 mg once daily), and stage 5 chronic kidney disease without maintenance dialysis. He did not have an occupation and denied any contact with cattle or sheep. His blood pressure was 140/60 mmHg, heart rate was 100 beats/min, respiratory rate was 22/min, and body temperature was 37.5°C. Initial laboratory tests revealed a white blood cell count of 8,300 cells/mm³, C-reactive protein level of 22.5 mg/dL, hemoglobin A1c level of 7.0%, blood urea nitrogen level of 68.7 mg/dL, creatinine level of 5.4 mg/dL, and estimated glomerular filtration rate of 9.15 mL/min/1.73 m². Two hours after admission, his body temperature rose to 37.9°C;

7 hours later, it reached 38.3°C and was accompanied by chills. He complained of mid-back tenderness on physical examination and had diarrhea on the second day of admission. We suspected that the patient might have infectious enterocolitis and therefore began ceftriaxone (2 g intravenously, once daily) as empirical treatment. The diarrhea ceased soon thereafter, but his fever and back pain persisted, and the laboratory parameters did not improve for approximately 4 days. We stepped up the antibiotics therapy to teicoplanin plus azithromycin to provide coverage for *Staphylococcus aureus*, which is the most common pathogen underlying infectious spondylitis and is an atypical pathogenic cause of systemic febrile illness. We performed abdomino-pelvic computed tomography (CT) and lumbar spine magnetic resonance imaging (MRI) to clarify the focus of the infection. On lumbar spine MRI with gadolinium enhancement, the T1-weighted image showed low signal intensity at the lower portion of the L3 vertebra. Further, the T2-weighted image showed high signal intensity for the same lesion (Fig. 1). Abdomino-pelvic CT showed no significant abnormal findings. *C. fetus* grew on 1 pair of blood cultures from both arms, which had been taken on the day of admission. We analyzed 16S rRNA gene sequencing to confirm the isolation of *C. fetus*. The genomic DNA was extracted, and polymerase chain reaction for 16S rRNA was performed. The 16S rRNA gene was amplified with universal primers (forward, 5'-AGTTTGATCCTGGC TCAG-3'; reverse, 5'-GTATTGCCGGGCTGCTG-3') using the Biometra T3000 Thermocycler (Analytik Jena, Gottingen, Germany). It was sequenced using the Applied Biosystems 3130lx Genetic Analyzer (Applied Biosystems, Foster City, CA, USA). *C. fetus* subsp. *testudinum* strain pet-3 (GenBank accession number: CP009226.1) was verified with 99% similarity, which was confirmed by a nucleotide basic local alignment search tool analysis (GenBank nucleotide BLAST). In vitro susceptibility testing for selected antibiotics

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(erythromycin and ciprofloxacin) was performed using the E-test method. The cultured strain showed susceptibility to erythromycin and resistance to ciprofloxacin. Based on the results of the antibiotics susceptibility test, only azithromycin was continued. Thereafter, the patient's fever and the intensity of his back pain decreased, and the laboratory parameters also improved (Fig. 2). Defervescence was achieved 7 days after the start of azithromycin, and blood culture conversion was observed beginning the day after azithromycin was started. Azithromycin was maintained for a total of 6 weeks, and the patient recovered uneventfully.

S. aureus is the most common pathogen that causes infectious spondylitis, whereas *C. fetus* rarely causes this disease (4–8). *C. fetus* spondylitis and bacteremia usually occur in immunocompromised or elderly patients (9). Our patient was elderly and had diabetes and advanced chronic kidney disease. It is well known that old age, diabetes, and kidney disease induce immunodeficiency that can contribute to morbidity and mortality. Because *C. fetus* is an uncommon pathogen in infectious spondylitis, we performed 16S rRNA gene sequencing, which allowed us to accurately determine the causative organism. As a result, we were able to treat the patient successfully. In addition, the complete genome sequence of *C. fetus* subsp. *testudinum* strain pet-3 was reported very recently (10). This is the first case in which *C. fetus* subsp. *testudinum* strain pet-3 has been identified as a pathogen in infectious spondylitis. Erythromycin and fluoroquinolones are usually recommended for the treatment of *Campylobacter* infection. In previous reports, a combination of doxycycline and erythromycin (6,8), amoxicillin only (5), or multiple combinations (7) have been used. The treatment duration also varied across previous reports. Roblot et al. suggested that antibiotic treatments for infectious spondylitis could be safely shortened to 6 weeks without increasing the risk of relapse (11). A vertebral biopsy was precluded because the lesion of the lower posterior endplate of the L3 vertebra was technically difficult to approach and because the patient's general condition was quite poor. However, the results of 3 blood cultures were positive for *C. fetus* during a clinically compatible illness that featured typical back pain and MRI findings. Further, no other suspicious infection focus was discovered.

In summary, we reported a case of infectious spondylitis caused by *C. fetus* in an elderly patient with advanced chronic kidney disease. The diagnosis was based

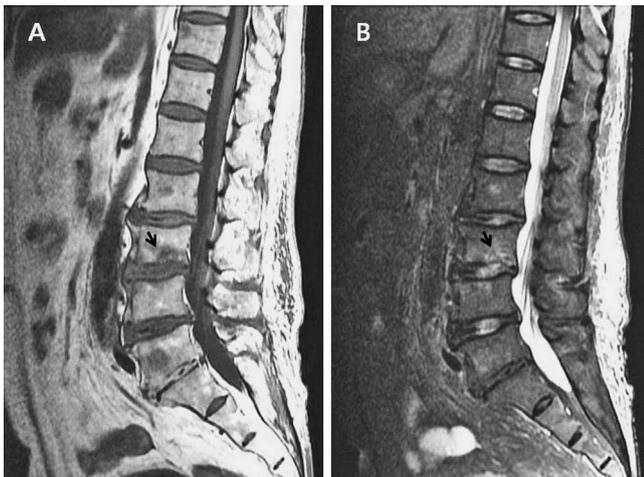


Fig. 1. Magnetic resonance imaging with gadolinium enhancement. On a T1-weighted image (A), low signal intensity (black arrow) was observed in areas of the L3 vertebra body. On a T2-weighted image (B), high signal intensity (black arrow) was observed on the L3 vertebra body.

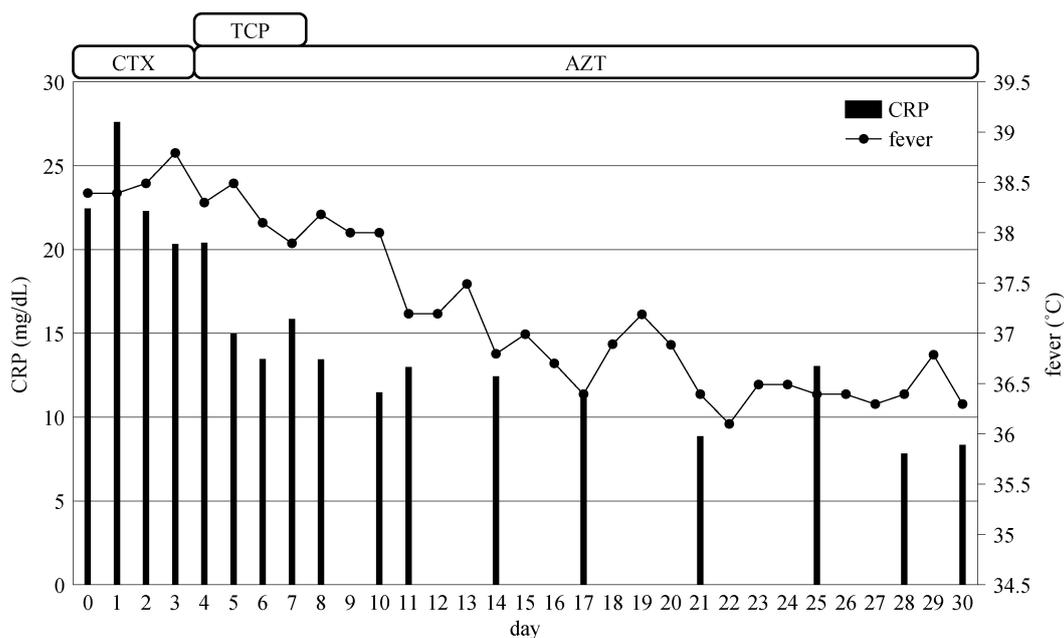


Fig. 2. The course of treatment during hospitalization. The solid line (right vertical axis) represents the peak daily body temperature in degrees Centigrade. The solid bar (left vertical axis) represents CRP. CRP, c-reactive protein; CTX, ceftriaxone; TCP, teicoplanin; AZT, azithromycin.

on bacterial identification confirmed by analyzing the 16S rRNA sequence and lumbar spine MRI. To our best knowledge, this was a unique case of *C. fetus* spondylitis in a patient with advanced chronic kidney disease and identification of *C. fetus* subsp. *testudinum* strain pet-3.

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Conflict of interest None to declare.

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