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【 CASE REPORT 】

Pyogenic Spondylitis Caused by *Staphylococcus schleiferi* in a Patient with Crohn's Disease

Koji Fujimoto, Shuhei Hosomi, Rieko Nakata, Naoko Sugita, Yu Nishida, Shusei Fukunaga, Yuji Nadatani, Koji Otani, Fumio Tanaka, Noriko Kamata, Yasuaki Nagami, Koichi Taira, Toshio Watanabe and Yasuhiro Fujiwara

Abstract:
Staphylococcus schleiferi has rarely been reported to cause pyogenic spondylitis. A 42-year-old man had been treated for Crohn's disease with immunosuppressive agents and home parenteral nutrition via a central vein (CV) port. The patient was admitted to our hospital, presenting with neck pain and a fever. A neurological examination showed slight weakness in his left-hand muscles, and he was diagnosed with pyogenic spondylitis of C6 and C7 vertebral bodies due to catheter-related blood stream infection caused by *S. schleiferi*. An early diagnosis by magnetic resonance imaging, CV port removal and antibiotic therapy targeting *S. schleiferi* improved his symptoms.

Key words: pyogenic spondylitis, *Staphylococcus schleiferi*, Crohn's disease, home parenteral nutrition, immunosuppressive agents

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Introduction

Pyogenic spondylitis is an infrequent infection of the spine that arises via a hematogenous route and is most often reported in immunocompromised patients. A recent nationwide study (1) showed a greater increase in pyogenic spondylitis cases than in tuberculous spondylitis cases.

We encountered a patient with Crohn's disease, a chronic and progressive inflammatory disorder of the gastrointestinal tract. Patients often undergo multiple operations, eventually leading to the development of short bowel syndrome. Bowel rest, elemental diet and corticosteroids have been the main treatment; however, immunomodulatory therapies, such as anti-tumor necrosis factor antibodies (e.g. adalimumab), have become the main therapy in recent decades (2).

We herein report an immunocompromised Crohn's disease patient with catheter-related blood stream infection (CRBSI) leading to subsequent pyogenic spondylitis. Although many micro-organisms have been associated with pyogenic spondylitis, *Staphylococcus aureus* has been reported as the most common causative agent for pyogenic spondylitis (3). We found that *Staphylococcus schleiferi* was the cause of pyogenic spondylitis in our patient. *S. schleiferi* causes skin and ear infections in dogs and can be a zoonotic pathogen in humans (4, 5). Immunocompromised patients have a risk of zoonoses (6). A previous study linked *S. scheiferi* to pyogenic spondylitis as a zoonotic infection in an immunocompetent patient (7); however, to our knowledge, this is the first case report of pyogenic spondylitis caused by *S. schleiferi* in an immunocompromised patient with Crohn's disease.

Case Report

A 42-year-old man had been diagnosed with Crohn's disease 24 years ago. After several bowel resection surgeries, he developed short bowel syndrome and had been receiving home parenteral nutrition via a central vein (CV) port for nine years. He had been in clinical remission on adalimumab (80 mg every other week) and azathioprine (100 mg daily) for 8 years. He had a dog as a pet but no other risks

Department of Gastroenterology, Osaka City University Graduate School of Medicine, Japan
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Correspondence to Dr. Shuhei Hosomi, m1265271@med.osaka-cu.ac.jp

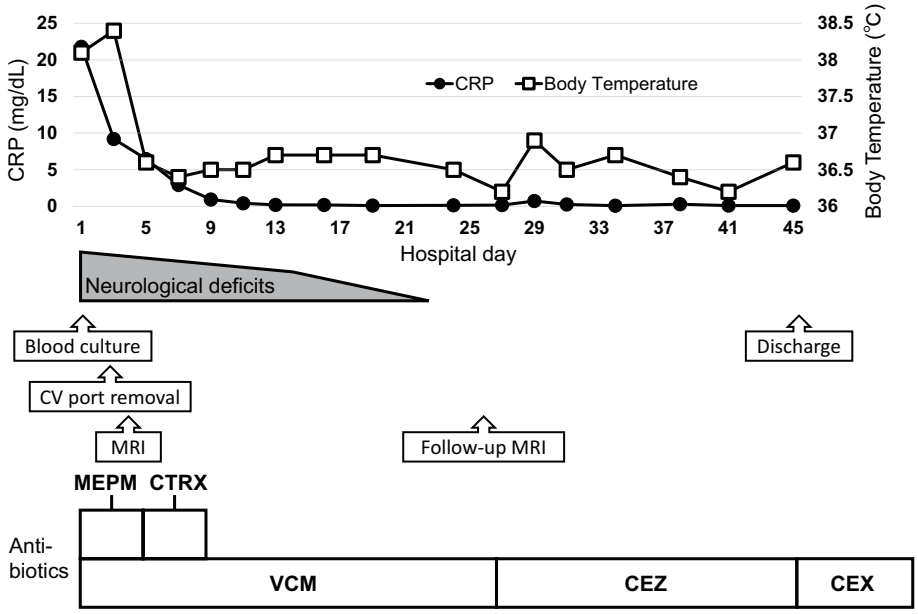

Figure 1. **Clinical course of the patient. CEX: cefalexin, CEZ: cefazolin, CRP: C-reactive protein, CTRX: ceftriaxone, CV: central vein, MEPM: meropenem, MRI: magnetic resonance imaging**

Table. **Results of Antimicrobial Susceptibility Testing of *Staphylococcus schleiferi* Isolates.**

Drug	Sensitivity	MIC
Oxacillin (MPIPC)	S	<=0.25
Ampicillin (PIPC)	R	>16
Cefazolin (CEZ)	S	<=4
Arbekacin (ABK)	NA	<=1
Gentamicin (GM)	S	<=1
Erythromycin (EM)	S	<=0.5
Minocycline (MINO)	S	<=1
Levofloxacin (LVFX)	S	<=0.5
Clyndamycin (CLDM)	S	<=0.5
Vancomycin (VCM)	S	<=1
Teicoplanin (TEIC)	S	<=2
Imipenem (IPM)	S	<=1
Daptomycin (DAP)	S	<=0.5
Sulfamethoxazole-Trimethoprim (ST)	S	<=0.5
Linezolid (LZD)	S	<=1

MIC: minimum inhibitory concentration, S: susceptible, R: resistant, NA: not available

of infection with *Staphylococci*, such as a history of dental procedures or skin diseases.

The patient was admitted to our hospital with symptoms of neck pain and a high fever lasting a week. On admission, his body temperature was recorded as 38.1°C. He showed slight weakness in his left-hand muscles. Manual muscle testing (MMT) revealed 4/5 of the left abductor pollicis brevis muscle and the left abductor digiti minimi muscle. A blood analysis showed an increase in the white blood cell count (WBC, 10,800/μL) and C-reactive protein (CRP, 21.8 mg/dL). Although computed tomography of his brain, chest and abdomen, showed no signs of infection, we started intravenous antibiotic treatment with meropenem and vancomycin empirically on suspicion of bacterial blood stream infection (Fig. 1).

On day 3 of admission, coagulase-negative and Gram-positive cocci were detected from two sets of blood culture obtained on the admission day. As the patient was diagnosed with CRBSI, the CV port was removed. *S. schleiferi* was detected in the blood culture and the tip of the CV port. The results of antimicrobial susceptibility testing are shown in Table.

Magnetic resonance imaging (MRI) performed on day 4 of admission based on the complaints of persistent headache and weakness in the hand revealed abnormal enhancement of C6 and C7 vertebras and anterior epidural abscess with spinal cord compression on fat-suppressed, gadolinium-enhanced, T1-weighted images (Fig. 2a). Based on these findings, the patient was diagnosed with hematogenous pyogenic spondylitis due to CRBSI. Immunosuppressive therapies (adalimumab and azathioprine) were discontinued. A follow-up blood culture obtained on day 6 of admission was found to be negative for *S. schleiferi*. The patient was administered vancomycin intravenously for approximately four weeks and was then switched to cefazolin due to cytopenia (Fig. 1).

Due to the presence of nuchal rigidity, the possibility of meningitis coexisting with spondylitis was considered, so meropenem administration was continued, followed by ceftriaxone in combination with vancomycin as a treatment for pyogenic meningitis. On day 9 of admission, ceftriaxone was discontinued, as the cerebrospinal fluid culture tested negative for *S. schleiferi* and no nuchal rigidity was observed (Fig. 1).

The WBC count and CRP levels were found to be normal. About three weeks after admission, there was a significant improvement in the neck pain and neurological deficits.

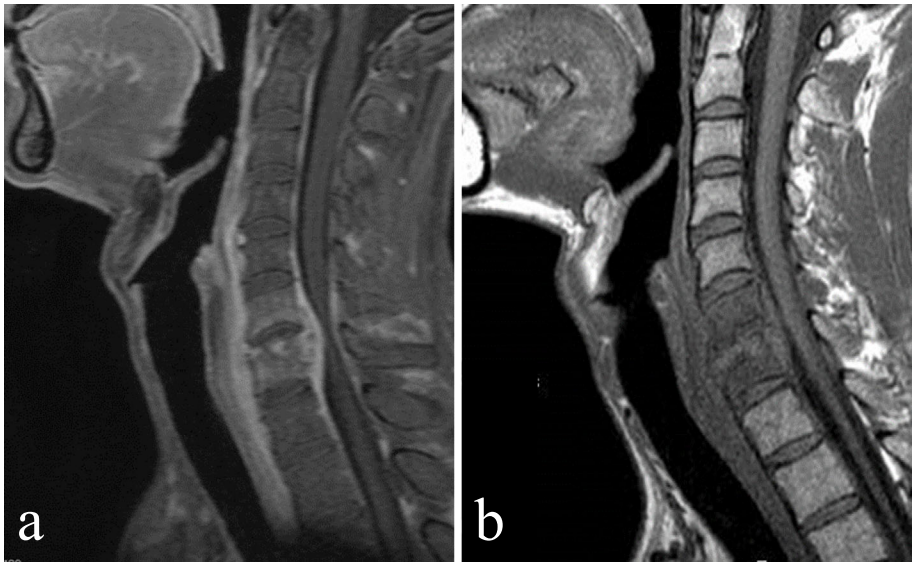

Figure 2. **a) Magnetic resonance imaging (MRI) on admission revealed the abnormal enhancement of C6 and C7 vertebral bodies and anterior epidural abscess with spinal cord compression. b) Follow-up MRI revealed improvement of the anterior epidural abscess and spinal cord compression.**

Follow-up MRI on day 26 of admission revealed improvement in the anterior epidural abscess and spinal cord compression (Fig. 2b). Approximately six weeks after admission, a CV port catheter was implanted, and immunosuppressive therapy (adalimumab and azathioprine) for managing Crohn's disease was restarted. The patient maintained clinical remission of Crohn's disease for six weeks after discontinuation of immunosuppressive drugs. The patient was discharged on day 46 of admission and continued to take cefalexin orally for two weeks after the discharge. No recurrence of pyogenic spondylitis has been observed for more than two years.

Discussion

Pyogenic spondylitis is a bacterial infection of the spine that commonly arises via the hematogenous route. Common symptoms of pyogenic spondylitis include neck or back pain, a fever, restricted movement, and neurological deficits. The early diagnosis of pyogenic spondylitis is important for ensuring a good treatment outcome (3), although the diagnosis may be difficult in cases where none of the typical symptoms are present.

We performed MRI, which is the most effective tool for making a diagnosis (3), in the early days of admission, as the patient had symptoms and potential risk factors for acquiring pyogenic spondylitis. Risk factors for pyogenic spondylitis have been reported to be diabetes mellitus, long-term steroid use, immunocompromised hosts, chronic renal failure and sepsis (3). In the present case, immunosuppressive therapy (adalimumab and azathioprine) for Crohn's disease was thought to be a factor in the development of pyogenic spondylitis. In fact, there are some case reports of pyogenic spondylitis in patients treated with immunosuppressive agents, such as azathioprine (8) or infliximab (9). Parenteral nutrition via a CV catheter may also pose a risk for acquiring pyogenic spondylitis, as described in a recent study showing CRBSI to be one of the most frequent complications in patients with Crohn's disease on home parenteral nutrition (10).

Although pyogenic spondylitis can be caused by *Streptococci*, *Enterococci*, *Escherichia coli* and *Pseudomonas* species, *Staphylococcus aureus* is reportedly the most common microorganism known to cause the infection (3). In the present case, *S. schleiferi* caused CRBSI, subsequently leading to pyogenic spondylitis. Although *S. schleiferi* is known to cause skin and ear infection in dogs, *S. schleiferi* subsp. *schleiferi*, which was first reported in 1988 (4) and is tube coagulase- and urease-negative, has been reported to cause wound infection (11), urinary tract infection (12), endocarditis (13), meningitis (14) and pacemaker infection (15) in humans. As reported by a study, *S. schleiferi* subsp. *schleiferi* is frequently associated with wound infections in immunocompromised patients with malignancies (16). In contrast, *S. schleiferi* subsp. *coagulans*, which was first reported in 1990 (17), is tube coagulase- and urease-positive and rarely causes infection in humans. There is only one case report of pyogenic spondylitis caused by *S. schleiferi* subsp. *coagulans*, which was considered to have been transmitted from a dog with a chronic ear infection to the patient, who was a 60-year-old immunocompetent woman (7). Although we did not describe the subspecies in the case report, we suspect that the subspecies in our patient was *S. schleiferi* subsp. *schleiferi*, as the microorganism isolated was found to be coagulase-negative.

In the present case, we continued intravenous antibiotic treatment with vancomycin until the patient revealed drug-induced cytopenia. Although we did not mention this in the case report, we performed several blood cultures, even after the blood culture on day 6 of admission was found to be

negative, as the patient would have needed have a surgery if the infection worsened. At the time of admission, we concluded that vancomycin treatment should be continued until all blood cultures were found to be negative. However, de-escalation of antibiotics should be performed earlier in cases where the pathogen of sepsis is identified (18).

The present patient had a dog as a pet. Although he did not remember whether or not his dog had an infection, we consider *S. schleiferi* to have been transmitted from his dog because the patient was immunocompromised, and there could have been many opportunities for micro-organisms existing on the dog's skin to be transmitted to the patient via a CV port when the patient conducted home parenteral nutrition. Immunocompromised patients are not the only patients at risk of zoonoses, but such zoonoses can become more severe in this population than in others (19). Furthermore, there are many other zoonoses and routes of transmission. Physicians should teach immunocompromised patients about zoonoses and how to prevent them, such as ensuring that they wash their hands after touching animals or avoid direct contact with animal feces (19).

Antibiotic treatment is the first choice of treatment for pyogenic spondylitis (3). The optimal duration of antibiotic treatment has not been established. The recommended duration, as reported by several studies, is four to eight weeks. Some cases also require surgery when patients have severe spinal cord compression or resistance to antibiotic treatment (3). In the present case, we considered surgery at the time of the diagnosis but continued with the conservative treatment based on the mild neurological deficit presented by the patient and the alleviation of symptoms after discontinuation of immunosuppressive therapy.

In conclusion, this report describes CRBSI development in a Crohn's disease patient receiving immunosuppressive therapy that led to subsequent hematogenous pyogenic spondylitis caused by *S. schleiferi*. Our report indicates the importance of the early diagnosis of pyogenic spondylitis for ensuring a positive treatment outcome by performing blood cultures and MRI at an early stage in patients with risk factors for developing pyogenic spondylitis and presenting with associated symptoms, such as a high fever and neck/back pain.

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

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