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CASE REPORT

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A fatal case of pyogenic spondylitis rapidly progressing to epidural abscess caused by a novel ST-type methicillin-susceptible *Staphylococcus aureus* ST9378

Takeru Inoue[1,*], Tomoe Setoguchi[1], Michiaki Akashi[2], Nobuyuki Shimono[3], Yasuhisa Iwao[4], Shoko Kutsuno[4], Junzo Hisatsune[4]

[1] Department of Infectious Disease, Karatsu Red Cross Hospital, Saga, Japan;
[2] Department of Pathology, Karatsu Red Cross Hospital, Saga, Japan;
[3] Center for the Study of Global Infection, Kyushu University Hospital, Fukuoka, Japan;
[4] Antimicrobial Resistance Research Center, National Institute of Infectious Diseases, Tokyo, Japan.

Abstract: Pyogenic spondylitis can be life-threatening; however, its diagnosis remains challenging because of the initial presentation of nonspecific symptoms. Given the vulnerability of the infected site, patients are highly at risk for severe complications, such as epidural abscesses or bacterial meningitis, which can considerably worsen the prognosis. Herein, we report a case of lumbar pyogenic spondylitis initially identified through methicillin-susceptible *Staphylococcus aureus* bacteremia, which subsequently progressed to an epidural abscess. The abscess rapidly ascended to the cervical region, causing bacterial meningitis and ultimately, a fatal outcome. The strain (JARB-OU3818) was positive for the virulence factor genes of the enterotoxin gene cluster (*seg*, *sei*, *sem*, *sen*, and *seo*) but negative for the Panton-Valentine leucocidin (PVL) and toxic shock syndrome toxin-1 (TSST-1) coding genes. Additionally, JARB-OU3818 was ST9378 belonging to the clonal complex 45 lineage. Clinicians should recognize that pyogenic spondylitis may follow an aggressively progressive clinical course, as demonstrated by this case.

***Keywords*:** pyogenic spondylitis, epidural abscess, *Staphylococcus aureus*

Introduction

Pyogenic spondylitis is an infection associated with a relatively high mortality rate of 5%–13% among inpatients (*1-5*). The onset-to-diagnosis period for hematogenous pyogenic spondylitis varies from several days to several weeks (*6*). Cases caused by gram-negative bacilli are generally acute, whereas those caused by gram-positive cocci are often chronic (*7*). Hematogenous cases typically begin with nonspecific symptoms (*7*), such as fever and joint pain, delaying the diagnosis and appropriate treatment.

Various bacteria can act as causative pathogens in pyogenic spondylitis, with *Staphylococcus aureus* being notably common, especially in hematogenous cases (*6*). *S. aureus* can also cause abscess formation; in pyogenic spondylitis, complications such as epidural abscesses, psoas muscle abscesses, and sometimes, bacterial meningitis may develop. Of note, when pyogenic spondylitis develops into bacterial meningitis, the mortality rate significantly increases (*8*).

Herein, we report a case of lumbar pyogenic spondylitis caused by methicillin-sensitive *S. aureus*, progressing rapidly with complications such as epidural abscess and meningitis and ultimately, a fatal outcome, in a 77-year-old man. Multilocus sequence typing (MLST) analysis of the strain revealed a novel sequence type. Informed consent to publish this paper was obtained from his family. This case report was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Case Report

A 77-year-old man with diabetes history visited our emergency department complaining of worsening pain in his right lower leg over 10 days. He twisted his foot while working as a plasterer 12 days prior, leading to persistent right thigh pain. After 6 days, given the lack of improvement, he visited an orthopedic clinic, where an X-ray revealed no bone abnormalities; thus, he was merely prescribed with a nonsteroidal anti-inflammatory drug (NSAID). However, the pain worsened, prompting a visit to our emergency department 2 days before

admission. Initial blood tests revealed elevated inflammatory markers, including a white blood cell count of 11,800/mm^3 and a C-reactive protein (CRP) level of 25.6 mg/dL. Chest and abdominal computed tomography (CT) scans showed no apparent fever source and no evident bone lysis or fractures. Blood cultures were taken, and the patient returned home. On admission day, blood cultures turned out to be positive for gram-positive cocci (in 2 of 2 sets); hence, he was hospitalized for further treatment. Upon admission, physical examination showed no signs of conjunctival hemorrhage, abnormal heart, or lung sounds, but he had spontaneous pain extending from the lumbar region to the right thigh, with marked percussion tenderness around the sacral area. Laboratory results showed elevated inflammatory markers (CRP: 32.38 mg/dL), renal impairment (blood urea nitrogen, 49.7 mg/dL; serum creatinine 1.74 mg/dL), and hyperglycemia (HbA1c, 7.7%).

Following the detection of gram-positive cocci in blood cultures, empirical vancomycin therapy was initiated. On day 1, the organism was identified as methicillin-susceptible *S. aureus*; thus, the drug was switched to cefazolin. Magnetic resonance imaging (MRI) of the lumbar spine performed on day 2 revealed high-intensity T2- and diffusion-weighted imaging signs from thoracic (Th)6 to lumbar (L)5, indicating an epidural abscess, as well as vertebral osteomyelitis at L5 (Figure 1A). Nonetheless, neurological findings remained unremarkable. Therefore, conservative management without surgical drainage was chosen. However, on day 4, he developed upper limb tremors. Subsequent MRI of the head and neck revealed that the epidural abscess extended from Th5 to cervical (C)1 (Figure 1B). Therefore, the orthopedic surgeons deemed surgical intervention inappropriate. Lumbar puncture revealed cerebrospinal fluid (CSF) findings (cell count, 1,173/μL; glucose level, 21 mg/dL [versus blood glucose level of 231 mg/dL]) suggestive of bacterial meningitis. Hence, ceftriaxone was initiated, leading to gradual improvement in inflammatory markers (CRP, 15.31 mg/dL; CSF cell count, 483/μL by day 11). Unfortunately, the patient developed consciousness disturbance (Japan coma scale, III-100) on day 13 and passed away on day 14.

Pathological autopsy revealed an enlarged right iliopsoas muscle with a bloody purulent discharge upon incision (Figure 2A). An abscess adhered to the dorsal meninges at the foramen magnum, with numerous granular white spots on the arachnoid internal surface (Figure 2B, 2C). Histologically, the iliopsoas abscess had inflammatory cell infiltration and hemosiderin deposition. Extensive inflammatory cell infiltration was also observed along the dura mater, extending from the lumbar spine to the cervical spine and brainstem, including the medulla, pons, and cerebellum surfaces. Of all the various sites examined by culture, only the right iliopsoas region exhibited *S. aureus* growth. This strain was named JARB-OU3818. Table 1 lists the susceptibility test results for this strain. Meanwhile, the heart valves and other organs had no abscess formation.

We investigated the genotype of JARB-OU3818 by whole-genome analysis, following previously described methods (*9*). The sequence type (ST) of JARB-OU3818 was defined using mlst v2.22.1 (*https://github.com/tseemann/mlst*), which extracts seven housekeeping genes (*arcC*, *aroE*, *glpF*, *gmk*, *pta*, *tpi*, and *yqiL*) from the whole-genome sequence of this strain and matches them against characterized ST number in the *S. aureus*

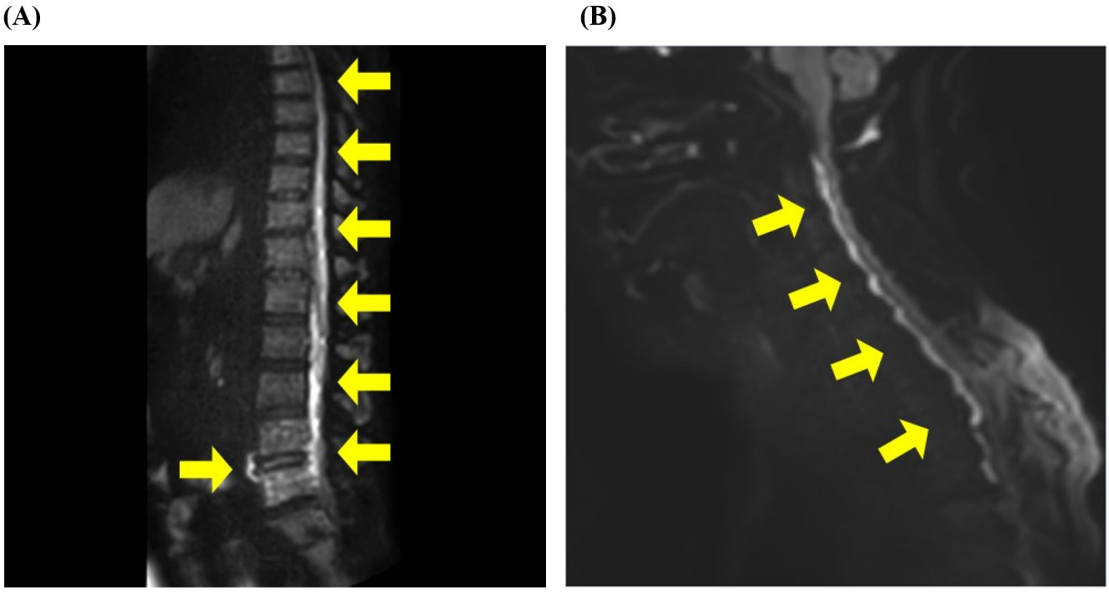

Figure 1. (A) DWI image of lumbar spine. High signal in L5 vertebral body suggested osteomyelitis, and high density area in Th6 to L5 suggested epidural abscess. **(B) DWI image of cervical spine.** High density area in C1 to Th5 suggested epidural abscess.

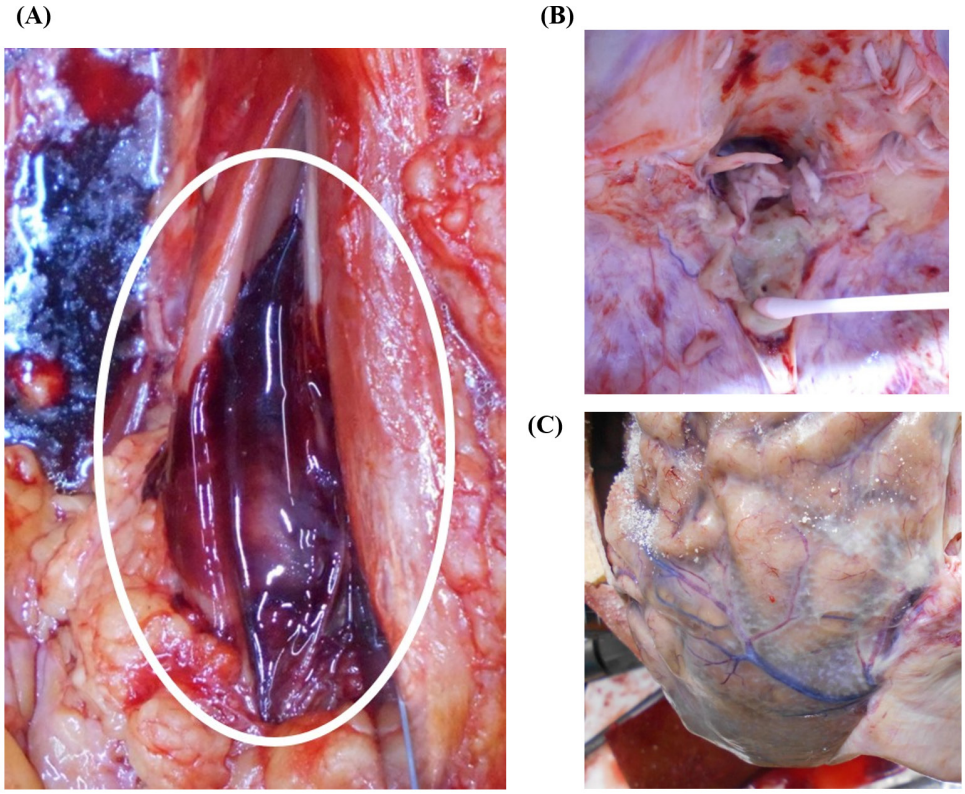

Figure 2. (A) Incision finding in right iliopsoas muscle. Bloody purulent fluid was discharged. **(B) Foramen magnum finding.** An abscess adhered to the dorsal meninges. **(C) Head finding**. Numerous granular white spots were found on the arachnoid surface.

PubMLST database (*https://pubmlst.org.organisms/staphylococcus-aureus/*). As a result of the search, no ST numbers were found in the PubMLST database that matched the allele numbers of the seven genes (*arcC*, 10; *aroE*, 14; *glpF*, 8; *gmk*, 6; *pta*, 1102; *tpi*, 3; and *yqiL*, 2) of JARB-OU3818. Therefore, these seven allele numbers of JARB-OU3818 were registered as a new ST9378. The raw read sequence data have been deposited in the DDBJ Sequence Read Archive under the accession number DRR628060. We found that JARB-OU3818 had no *mecA*, the methicillin resistance gene, and any other antimicrobial resistance genes. However, it contained virulence-factor-related genes such as the coagulase type VIIb gene and the enterotoxin gene cluster (*egc*; *seg*, *sei*, *sem*, *sen*, and *seo*), while Panton–Valentine leukocidin (*PVL*) and toxic shock syndrome toxin 1 (*TSST-1*) genes were not detected. JARB-OU3818 was classified as a new ST9378 type by MLST analysis and as clonal complex 45 by eBURST analysis.

Table 1. Susceptibility test results of JARB-OU3818

Antibiotics	MIC (μg/mL)	Interpretation
penicillin G	0.06	S
oxacillin	≤ 0.25	S
sulbactam/ampicillin	≤ 2	S
cefazolin	≤ 4	S
cefmetazole	≤ 4	S
imipenem	≤ 1	S
arbekacin	≤ 1	S
gentamicin	≤ 0.5	S
erythromycin	≤ 0.25	S
clindamycin	≤ 0.25	S
minocycline	≤ 0.5	S
vancomycin	1	S
teicoplanin	≤ 0.5	S
linezolid	2	S
levofloxacin	≤ 0.12	S
fosfomycin	≤ 8	S

MIC, minimum inhibitory concentration; S, susceptible.

Discussion

Pyogenic spondylitis remains to be highly fatal, with recent in-hospital mortality rates ranging between 5% and 13% (*1-5*). Its diagnosis is often delayed because of the nonspecificity of its initial symptoms, such as fever and back pain. In some cases, the absence of fever makes an early diagnosis even more challenging (*6,10*). For instance, our patient presented with a normal body temperature (36.7°C) at admission, partly attributed to prior NSAID (loxoprofen) use for back pain. Nonetheless, we should always consider pyogenic spondylitis as a differential diagnosis, even in the absence of fever. Early-stage diagnostic imaging can also be inconclusive. For example, X-rays may not reveal significant changes until 3–6 weeks after symptom

onset (*10*). The sensitivities of CT and MRI scans are reportedly superior (65–75% and 82–100%, respectively) (*11*). However, their limitations often lead to delayed diagnosis, especially in emergency settings where MRI scans are not always immediately available. Our patient initially visited the emergency department 2 days before admission; despite the unremarkable findings on CT, a blood culture taken the same day returned positive, leading to the diagnosis.

Moreover, blood cultures are crucial for pyogenic spondylitis diagnosis, with reported positivity rates within 38%–78% (*12,13*). By identifying the causative organism, physicians can prescribe the appropriate antibiotics. Blood culture is also easier to perform than other invasive sample collection procedures, such as bone sample collection or CT-guided biopsies. Therefore, we should actively collect blood cultures when pyogenic spondylitis is suspected, even if the initial symptoms are nonspecific.

Although nonoperative treatment is effective in 90% of cases (*14*), surgical intervention is sometimes necessary in patients with spinal instability, neurological symptom deterioration, extensive bone destruction, epidural abscess formation, conservative treatment failure, or intractable back pain (*15-17*). In our patient's case, surgical drainage was considered because of the presence of an epidural abscess. However, considering the wide spread of the abscess, the orthopedic team ruled out surgical intervention as a viable option.

Treatment with ceftriaxone seemed to be effective, given the improved results of the blood test and CSF findings. However, the patient's condition deteriorated rapidly on day 12, resulting in a fatal outcome. We conducted an autopsy to determine the extent of the lesion. Numerous inflammatory cells infiltrated the brainstem (cerebellum, pons, and medulla oblongata) without bacterial presence. This inflammation seemed to cause tissue destruction and subsequent failure of critical life-sustaining functions.

Specific bacterial toxins, such as PVL and TSST-1, play a role in bone infections, particularly PVL (*18*). The MSSA JARB-OU3818 strain isolated in this case was positive for *egc* (*seg*, *sei*, *sem*, *sen*, and *seo*), which is typically associated with gastrointestinal symptoms, but this gene cluster was deemed less relevant to this case's pathology.

Conclusion

This report presents a case of pyogenic spondylitis accompanied with severe complications, including extensive epidural abscesses and bacterial meningitis, which progressed rapidly and ultimately resulted in a fatal outcome. This case underscores the importance of recognizing that pyogenic spondylitis can follow such an aggressive clinical course.

Given the rapid progression, we investigated the pathogenic characteristics of the causative strain. Although JARB-OU3818 was negative for known cytotoxic virulence genes, such as *PVL* and *TSST-1*, it was identified as a novel ST9378. Therefore, the strain might harbor as-yet-unidentified virulence genes, highlighting the need for further research.

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Conflict of Interest: The authors have no conflicts of interest to disclose.

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**Address correspondence to*:
Takeru Inoue, Department of infectious disease, Karatsu Red Cross Hospital, Watada 2430, Karatsu City, Saga, Japan.
E-mail: takeru.inoue1006@gmail.com