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CASE REPORT

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Pyogenic vertebral osteomyelitis caused by *Prevotella intermedia*

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Abstract We describe a case of vertebral osteomyelitis caused by *Prevotella intermedia*, which is an extremely unusual cause of vertebral osteomyelitis. The organism was isolated from vertebral biopsies and the patient was treated successfully with intravenous ampicillin-sulbactam and clindamycin. Diagnosis and management of this condition are described, and the importance of anaerobic bacteria in the pathogenesis of vertebral osteomyelitis is discussed.

Key words Vertebral osteomyelitis · Anaerobic bacteria · *Prevotella intermedia* · Open surgical biopsy

Introduction

Prevotella intermedia is an anaerobic, non-spore-forming, gram-negative rod that contributes to the normal flora in the oral cavity, gastrointestinal tract, and vagina of humans. This organism rarely causes clinically significant infections and is frequently considered a contaminant even when isolated from a normally sterile site. We report a biopsy-proven case of vertebral osteomyelitis caused by *P. intermedia*, only few cases of which have previously been reported.

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Case report

A 60-year-old man was admitted to Saga Medical School Hospital for further evaluation of persistent spiking fever and back pain, with a paravertebral soft-tissue attenuation mass at the level of Th 7–8. He had initially developed thoracic back pain 4 months earlier, and had been treated with nonsteroidal anti-inflammatory drugs by his family physician. However, his symptoms did not improve, and he was transferred to another hospital 1 month later. There, a lung mass with bone destruction was identified on chest computed tomography (CT), and he was admitted to the hospital. One month later, a second chest CT showed rapid growth of the mass. He was then considered as having lung cancer with bone invasion, based on the CT findings alone, and was inadvertently started on cancer chemotherapy with intravenous cisplatin, together with thoracic irradiation, given for about 1 month. Despite these treatments, his back pain worsened, high fever appeared and inflammatory reactions in laboratory studies were elevated. An empiric trial of antibiotics was begun, but had no effect. So he was transferred to our hospital for further evaluation.

Physical examination on admission revealed that the patient's body temperature was 38.1°C; pulse rate, 96/min; blood pressure, 118/60 mmHg; and respiration rate, 16/min. There was tenderness over the sixth to eighth thoracic vertebrae. He complained of spontaneous pain and paresthesia in the Th 6–9 area. Deep tendon reflexes in his lower limbs were slightly increased, but results of other neurological examinations were normal.

The patient's leukocyte count was 8000/μl (80% neutrophils, 14% lymphocytes, 5% band cells with toxic granules); hemoglobin level was 7.7 g/dl, and the platelet count was 21.6×10^4/μl. The erythrocyte sedimentation rate (ESR) was 134 mm/h, and the level of C-reactive protein (CRP) was 17 mg/dl. Serum alkaline phosphatase derived from bone was also markedly elevated. The serum levels of tumor markers, including carcinoembryonic antigen, were normal. The tuberculin skin test (purified protein derivative) was negative.

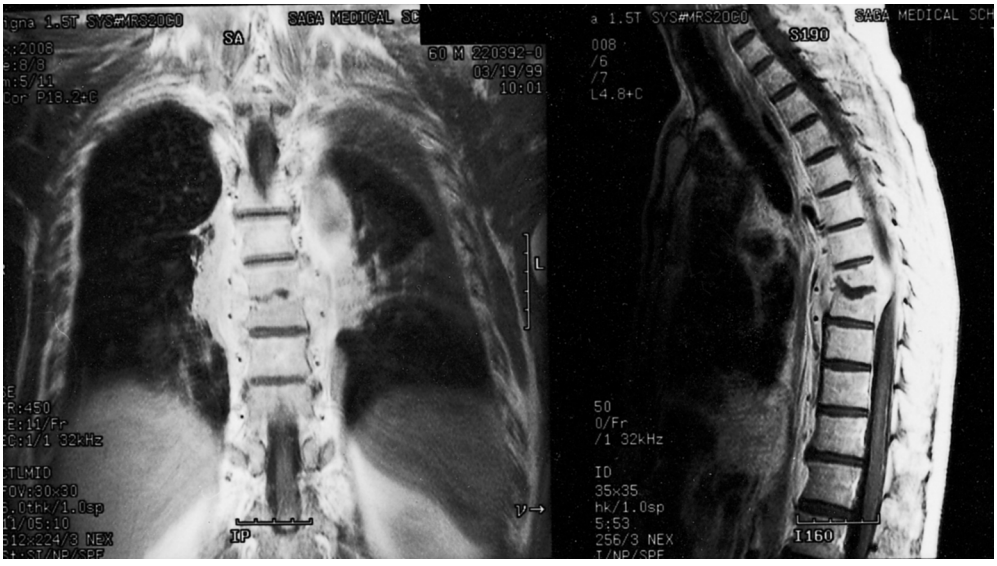

Fig. 1. Coronal and sagittal postcontrast T-1-weighted magnetic resonance images of the thoracic spine

A chest CT obtained elsewhere 3 months earlier had revealed an irregular soft-tissue attenuation mass surrounding and anterior to the 7–8 th thoracic vertebrae that was contiguous to the vertebrae, with bone destruction. On admission, a follow-up CT showed the rapid growth of the mass and progress of bone destruction. Magnetic resonance imaging (MRI) at the level of Th 7–8 revealed a paravertebral mass of 10 cm in diameter, and total loss of the disk space, with gross irregularities in the face joints. The mass had protruded into the spinal epidural space, slightly compressing the spinal cord (Fig. 1). These radiographic findings, the ineffectiveness of the previous treatments, and the increased inflammatory reactions, collectively, strongly suggested vertebral osteomyelitis.

Staphylococcus aureus is the most frequent etiologic agent of osteomyelitis, and therapy with intravenous cefazolin (1 g every 6 h) and minocycline (100 mg every 12 h) was started empirically. Despite these treatments, the patient still remained febrile, his back pain gradually increased, and a follow-up MRI revealed enlargement of the mass. Multiple samples of blood were obtained for culture, but no organism was isolated. So an open biopsy was performed.

Th7–8 diskectomy and curettage of the end plates, with anterior iliac crest graft implantation, were performed via a thoracic approach. The lesion was markedly swollen and was surrounded by dark red, hard fibrous tissue. When incised, the vertebrae were fragile and the Th7/8 disk space was not identified because of lytic change. There was no well-delineated abscess or release of purulent or foul-smelling material. Histopathology of the vertebrae showed chronic osteomyelitis with focal acute inflammation. The hard fibrous tissue consisted of a dense fibrous lesion with marked hyalinization (Fig. 2). There were no signs of malignant disease or granuloma. On the seventh postoperative day, the culture of the biopsied sample yielded *P. intermedia*. Fungal and mycobacterial stains and cultures were negative.

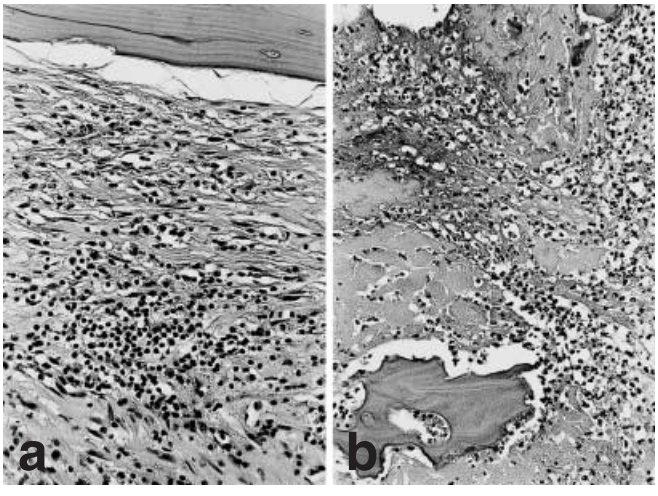

Fig. 2a,b. Histopathology of the vertebrae. **a** Chronic osteomyelitis. Bone marrow space reveals severe infiltration of lymphocytes and fibrosis. **b** Acute osteomyelitis. Numerous neutrophils and fibrinous exudates are noted, with bone destruction. **a** and **b** H&E, ×200

After the antimicrobial susceptibilities were reported, therapy was switched to the intravenous administration of ampicillin-sulbactam (1.5 g every 6 h) and clindamycin (600 mg every 12 h). During these therapies, the patient's fever subsided and his back pain gradually resolved. After 4 weeks, the antimicrobial therapy was changed to oral tosufloxacin (450 mg/day) for 2 months. CRP at the end of the patient's treatment was negative. Four months after admission, he was discharged from the hospital. He has remained well for 1 year, with no further progression of bone destruction.

Discussion

Vertebral osteomyelitis is usually a form of hematogenous osteomyelitis that occurs in elderly patients.[1,2] Although this disease is reportedly uncommon, the incidence is increasing and accounts for about 2% to 4% of all cases of pyogenic osteomyelitis.[2] In the immunocompetent host, *Staphylococcus aureus* remains the leading organism.[3–5] However, gram-negative and low-virulence, atypical organisms have been frequently isolated.[5] Culture-proven anaerobic vertebral osteomyelitis is rare, and a previous review of pyogenic vertebral osteomyelitis revealed that only 3% to 4% of bacterial isolates were anaerobes,[4,5] namely, such species as *Bacteroides*, *Peptostreptococcus*, and *Propionibacterium*.[3–6] In a recent review of the literature, anaerobic vertebral osteomyelitis may have reportedly occurred more frequently than has been considered.[6,7] With the increasing awareness of the role of anaerobes in human infections, in addition to the widely utilized, improvements in anaerobic culture techniques, we may see an increase in the incidence of anaerobic vertebral osteomyelitis.

In our patient, vertebral osteomyelitis was definitively caused by *P. intermedia*. This organism is an anaerobic, cocco-bacillary gram-negative rod previously designated as *Bacteroides* species, and it has been reclassified under the new genus, *Prevotella*, since 1990.[8] This organism normally inhabits the mucosal surfaces of the human body, such as the oral cavity, gastrointestinal tract, and vagina. Among the common infections caused by this bacteria are periodontal diseases, postaspiration pleuropulmonary infection, genital tract infections in women, and intra-abdominal abscesses, even though, when isolated in clinical specimens, this organism is usually regarded as a normal commensal rather than as pathogenic.

In our review of the English-language literature, we were able to find only one reported case of vertebral osteomyelitis caused by *P. intermedia*,[7] and five cases caused by *Bacteroides melaninogenicus* (now reclassified as *Prevotella* species).[3] One of the reasons for the rarity could be the reclassification of this organism and the lack of awareness of its pathogenicity. Another review revealed that *Prevotella* species were especially prevalent in osteomyelitis of the facial bones, and in episodes following human bites.[7]

In our patient, the route of infection was unclear. There was no clinical evidence of contiguous infection, such as pneumonia, pleuritis, or an infected wound, or infection at other sites, such as periodontal disease or genitourinary infection. The patient also had no predisposing factor for the development of pyogenic vertebral osteomyelitis at the site of the infection (prior fracture, surgical manipulation of the spine) and no impairment of the immune system, such as that caused by diabetes mellitus, alcoholism, or therapy with immunosuppressive drugs at the initial onset, although subsequent irradiation and chemotherapy may have promoted the disease progression. It was reported that approximately 37% of cases of vertebral osteomyelitis had no obvious or likely source of infection.[4]

The present case also demonstrates the difficulty of distinguishing vertebral osteomyelitis from spinal tumors. In this case, the patient was mistakenly treated for lung cancer with bone metastases, with diagnosis having been based on the clinical features alone. Carragee[5] reported, in his review, that 11 (10%) of the 111 patients who had pyogenic vertebral osteomyelitis had had previous irradiation for a malignant tumor of the spine but did not have evidence of an active neoplasm. Metastatic malignancy is one of the most important differential diagnoses to rule out, and careful evaluation is needed. MRI is reported to be particularly useful in the diagnosis of vertebral osteomyelitis.[9]

In addition, this case demonstrates the importance of fine-needle aspiration or open surgical biopsy of the intervertebral disk space to substantiate the diagnosis and provide culture materials, if empiric antimicrobial therapy targeting gram-positive bacteria is ineffective. Specimens obtained at biopsy from infected bones should be routinely submitted for anaerobic cultures as well. When an anaerobic isolate is recognized as a pathogen, treatment with appropriate antimicrobial agents should be initiated in a timely fashion. With prompt diagnosis and proper management, the prognosis should generally be good.

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References

1. Waldvogel FA, Medoff G, Swarts MN. Osteomyelitis: a review of clinical features, therapeutic considerations, and usual aspects. N Engl J Med 1970;282:198–206.
2. Torda AJ, Gottlieb T, Bradbury R. Pyogenic vertebral osteomyelitis: analysis of 20 cases and review. Clin Infect Dis 1995;20:320–8.
3. Lewis RP, Sutter VL, Finegold SM. Bone infections involving anaerobic bacteria. Medicine (Baltimore) 1978;57:279–305.
4. Sapico FL, Montgomerie JZ. Pyogenic vertebral osteomyelitis: report of nine cases and review of the literature. Rev Infect Dis 1979;1:754–76.
5. Carragee EJ. Pyogenic vertebral osteomyelitis. J Bone Joint Surg Am 1997;79:874–80.
6. Hall BB, Fitzgerald RH, Rosenblatt JE. Anaerobic osteomyelitis. J Bone Joint Surg Am 1983;65:30–5.
7. Brook I, Frazier EH. Anaerobic osteomyelitis and arthritis in a military hospital: a 10-year experience. Am J Med 1993;94:21–8.
8. Shah HN, Collins MD. Prevotella, a new genus to include *Bacteroides melaninogenicus* and related species formerly classified in the genus Bacteroides. Int J Syst Bacteriol 1990;40:205–8.
9. Tehranzadeh J, Wang F, Mesgarzadeh M. Magnetic resonance imaging of osteomyelitis. Crit Rev Diagn Imaging 1992;33:495–534.