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Atypical Osteomyelitis of the Skull Base and Craniovertebral Junction Caused by Actinomyces Infection

—Case Report—

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Abstract

A 44-year-old man presented with a very rare case of skull base osteomyelitis manifesting as persistent diplopia. He initially had the symptom with fever after dental extraction. Biopsy from the cervix and upper pharynx performed in a previous hospital had showed negative findings by histological and bacterial examinations. Magnetic resonance (MR) imaging disclosed enhanced lesions in the right cavernous sinus, clivus, and right cervical regions. Computed tomography revealed osteolysis, and fluorodeoxyglucose positron emission tomography (FDG-PET) showed areas of increased uptake. Bacteriological examination of the isolated clival lesion disclosed *Actinomyces israelii*, and he was treated with intravenous penicillin, 18 million units a day for 6 weeks. MR imaging revealed reduction of intensity in the enhanced areas, and FDG-PET showed disappearance of the increased uptake. After 6 months of oral antibiotics administration, MR imaging disclosed disappearance of the enhanced lesions, and the patient had no sign of neurological deficits. Skull base osteomyelitis resembles neoplasm or inflammatory disease of this region in neurological and radiographic findings. The biopsy specimen should be ideally obtained from an isolated region, and prepared to identify a wide range of organisms and to differentiate other diseases. The serum level of C-reactive protein and FDG-PET are useful to follow up the efficacy of antibiotic therapy.

Key words: osteomyelitis, skull base, clivus, craniovertebral junction, actinomyces

Introduction

Skull base osteomyelitis is a rare disease which is still very difficult to correctly identify in the early stage because the neurological presentation and the radiographic findings are quite similar to those of more common pathologies such as neoplasm or inflammatory disease.[9,10] Skull base osteomyelitis can be divided into typical and atypical types.[7,10] Typical osteomyelitis usually occurs in compromised patients with certain predisposing factors such as diabetes mellitus or immunocompromised state, and is initiated by otitis externa, and the origin of the infection and causative bacteria are relatively easy to identify. Atypical osteomyelitis is not associated with paranasal or ear infection, and the primary causative organism is difficult to identify. Since progression of the disease is relatively slow, and the presenting symptoms are initially subtle, the diagnosis is often made after considerable advance of the disease, which occasionally makes treatment difficult.[13]

Here we report a rare case of atypical skull base osteomyelitis caused by actinomyces infection involving the cavernous sinus, clivus, and craniocervical regions, and discuss the radiographic characteristics, diagnostic approach, and its treatment.

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Case Report

A 44-year-old man presented with persistent diplopia and was referred to our hospital. Eight months before, the patient developed alveolar pyorrhea and underwent dental extraction from the left maxilla. A few days later he had a high fever and noticed diplopia. He consulted a local physician, and after 10 days of oral antibiotics administration, his symptoms were transiently ameliorated. However, 2 months later, the symptoms recurred with swelling of the right cervical region, and he was referred to a local general hospital. Laboratory examination revealed marked leukocytosis and an elevated level of C-reactive protein (CRP) to 17.8 mg/dl. Radiographic examination showed mass lesions in the skull base and the right cervical regions, so he underwent biopsy in the right cervical lymph node and the mucosa of upper pharynx for suspected malignancy. Histological examination revealed inflammatory cells without malignancy and the bacterial culture was sterile. He was referred to our university hospital for further examination and treatment.

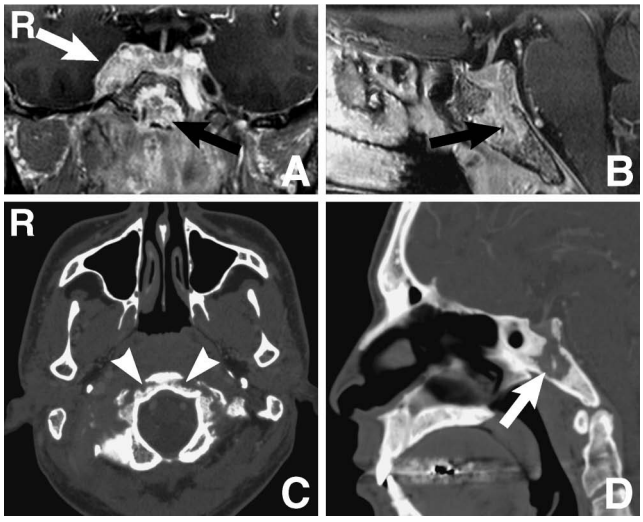

Fig. 1 A, B: T_1-weighted magnetic resonance images with gadolinium (A: coronal, B: sagittal) showing diffuse enhanced lesions in the right cavernous sinus (*white arrow*), clivus (*black arrows*), posterior pharyngeal space, and around the nuchal venous plexus continuing to the right cervical area. C, D: Computed tomography scans (C: axial, D: sagittal) revealing osteolytic lesions in the bilateral occipital condyles (*white arrowheads*) and. the clivus (*white arrow*).

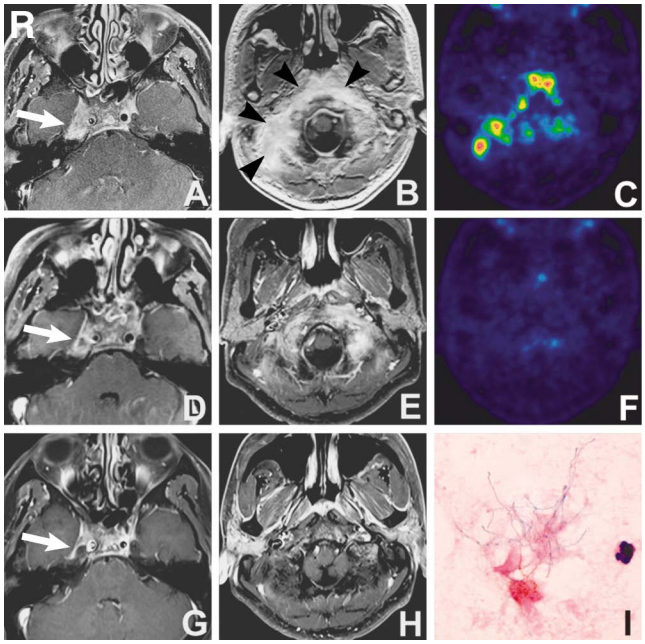

Fig. 2 A, B: Axial T_1-weighted magnetic resonance (MR) images with gadolinium before treatment showing diffuse enhanced lesions in the right cavernous sinus (*white arrow*) and around the nuchal venous plexus (*black arrowheads*). C: Fluorodeoxyglucose positron emission tomography (FDG-PET) scan demonstrating increased uptake in the same territories. D, E: T_1-weighted MR images with gadolinium obtained 6 weeks later revealing reduction of intensity in the enhanced areas (*white arrow*). F: FDG-PET scan showing the increased uptake had disappeared. G, H: T_1-weighted MR images with gadolinium obtained 6 months later showing disappearance of the enhanced lesions (*arrow*). I: Photomicrograph of the biopsy specimen showing actinomycosis. Gram stain, ×1000.

On admission, neurological examination showed mild right abducens nerve palsy. Laboratory data disclosed a slightly elevated level of CRP, 3.36 mg/dl, with normal counts of white blood cells. Magnetic resonance (MR) imaging disclosed a diffuse enhanced lesion in the right cavernous sinus, clivus, sphenoid sinus, posterior pharyngeal space, and around the nuchal venous plexus continuing to the right cervical area (Figs. 1A, B and 2A, B). Computed tomography disclosed osteolytic lesions in the clivus and bilateral occipital condyles, which were partially affected without cervical instability (Fig. 1C, D). Fluorodeoxyglucose positron emission tomography (FDG-PET) demonstrated increase uptake in the same territories (Fig. 2C).

Active infection or inflammatory disease was the most suspected diagnosis, followed by malignancy based on the neuroimaging findings. Since the neck wound of the previous biopsy had ruptured with continuous effusion, contaminating by other non-pathogenic bacteria was already possible. Therefore, to clarify the diagnosis, the patient underwent transnasal biopsy of the clival lesion with neuroendoscopy. Drilling of the anterior wall of the clivus resulted in discharge of yellow purulent matter. Sufficient tissue samples were obtained in sterile fashion from this area for both bacteriological and histological examinations. Bacteriological examination including polymerase chain reaction detection disclosed *Actinomyces israelii* (Fig. 2I), and histological examination showed inflammatory granulation tissues without sign of malignancy. The diagnosis was cranio-cervical actinomycosis.

The patient was treated with intravenous penicillin, 18 million units a day for 6 weeks. After the antibiotic therapy was started, the serum level of CRP gradually decreased and became normal (less than 0.3 mg/dl) 4 weeks later. MR imaging obtained 6 weeks later revealed reduction of intensity in the enhanced areas (Fig. 2D, E), and FDG-PET showed the increased uptake had disappeared (Fig. 2F). He was discharged, and followed the recommended treatment course or actinomycosis[6,11] with continued oral administration of the antibiotics for 6 months. MR imaging obtained 6 months later disclosed disappearance of the enhanced lesions (Fig. 2G, H), and the patient showed no sign of neurological deficits.

Discussion

Various organisms have been reported as causative pathogens of the skull base osteomyelitis, including *Pseudomonas aeruginosa*, mycobacterium, aspergillus, and candida in the typical disease,[4,5,7,10] and *Staphylococcus aureus*, coagulase-negative staphylococcus, and pseudomonas in the atypical disease.[7,10] Anaerobes are frequently the cause of bacterial infection in endogenous origin, but are very difficult to identify from infectious sites, and are often overlooked.[3] Therefore, to definitively diagnose

these lesions, the specimens should be obtained from isolated lesions in sterile fashion, and must be incubated anaerobically with appropriate medium. Actinomyces are gram-positive, anaerobic, filamentous bacteria, causing chronic infection in compromised patients in various systemic lesions.[11,15] The most frequent site is the craniofacial region, whereas involvement of the skull base is quite rare,[14] with only a few cases.[1,12] The delay until the biopsy was very long in the previous cases, and the definitive diagnosis was made after the disease was rather advanced.

From our patient's history, the onset of fever coincided with recurrence of abducent nerve palsy, so we initially considered the possibility of all types of infectious diseases before the radiographic and bacteriological examinations. To obtain the biopsy specimen, we chose the deep clival lesion because it is isolated from the external environment and the cervical lesions had been already contaminated by the previous biopsy. Consequently, we successfully detected the anaerobic bacterium, *Actinomyces israelii*, and started the appropriate antibiotics therapy with penicillin according to the results of the sensitivity test.

The active infectious lesions are observed as hot spots by FDG-PET and were very difficult to differentiate from malignancy.[2] However, once the diagnosis is confirmed with biopsy, PET can evaluate the gross activity of the disease, so is very useful to assess the efficacy of antibacterial therapy.[8] In our patient, after administration of penicillin 18 million units a day for 6 weeks, PET showed complete remission of increased uptake, reflecting the change in the serum level of CRP, and the enhanced lesions on MR imaging completely disappeared 6 months later.

Skull base osteomyelitis is a very rare disease that resembles other more common diseases in neurological and radiographic findings. If infectious disease is suspected from the patient's history, biopsy is essential. The specimen should be ideally obtained from an isolated region, and prepared for identification of a wide range of organisms and to differentiate other diseases. The serum level of CRP and FDG-PET are useful for follow up of the efficacy of antibiotic therapy.

References

1) Albright L, Toczek S, Brenner VJ, Ommaya AK: Osteomyelitis and epidural abscess caused by Arachnia propionica. Case report. *J Neurosurg* 40: 115–119, 1974
2) Bleeker-Rovers CP, Vos FJ, Wanten GJ, van der Meer JW, Corstens FH, Kullberg BJ, Oyen WJ: 18F-FDG PET in detecting metastatic infectious disease. *J Nucl Med* 46: 2014–2019, 2005
3) Brook I: Microbiology and management of joint and bone infection due to anaerobic bacteria. *J Orthop Sci* 13: 160–169, 2008
4) Chandler JR, Grobman L, Quencer R, Serafini A: Osteomyelitis of the base of the skull. *Laryngoscope* 96: 245–251, 1986
5) Farrior J: Osteomyelits of the skull base. *South Med J* 82: 719–722, 1989
6) Foster SV, Demmler GJ, Hawkins EP, Tellman JP: Pediatric cervicofacial actinomycosis. *South Med J* 86: 1147–1150, 1993
7) Grobman LR, Ganz W, Casiano R, Goldberg S: Atypical osteomyelitis of the skull base. *Laryngoscope* 99: 671–676, 1989
8) Hakim SG, Bruecker CW, Jacobsen HCh, Hermes D, Lauer I, Eckerle S, Froehlich A, Sieg P: The value of FDG-PET and bone scintigraphy with SPECT in the primary diagnosis and follow-up of patients with chronic osteomyelitis of the mandible. *Int J Oral Maxillofac Surg* 35: 809–816, 2006
9) Keane JR: Combined VIth and XIIth cranial nerve palsies: A clival syndrome. *Neurology* 54: 1540–1541, 2000
10) Malone DG, O'Boynick PL, Ziegler DK, Batnitzky S, Hubble JP, Holladay FP: Osteomyelitis of the skull base. *Neurosurgery* 30: 426–431, 1992
11) Oluwadamilola A, Numa G, Kenji M, Khadidjatou K, John P: Multiple brain abscess due to actinomyces species. Case report. *Clin Neurol Neurosurg* 110: 847–849, 2008
12) Per-Lee JH, Clairmont AA, Hoffman JC, McKinney AS, Schwarzmann SW: Actinomycosis masquerading as depression headache: case report—management review of sinus actinomycosis. *Laryngoscope* 84: 1149–1158, 1974
13) Robinson JL, Vaudry WL, Dobrovolsky WD: Actinomycosis presenting as osteomyelitis in the pediatric population. *Pediatr Infect Dis J* 24: 365–369, 2005
14) Sari M, Yazici M, Bağlam T, Inanli S, Eren F: Actinomycosis of the larynx. *Acta Otolaryngol* 127: 550–552, 2007
15) Smergo RA: Actinomycosis of the central nervous system. *Rev Infect Dis* 9: 855–865, 1987

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