CASE REPORT

Purulent Meningitis Caused by Actinomyces Successfully Treated with Rifampicin: A Case Report

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Abstract

A 64-year-old woman presented with fever and headache. Lumbar puncture revealed cerebrospinal fluid (CSF) that contained 67,386/mm³ of WBC; CSF culture revealed Actinomyces species. She was diagnosed with purulent meningitis caused by actinomyces, and treated with intravenous ampicillin 12 g/day. The administration of ampicillin was effective, but not sufficient to control the inflammation in CSF. CSF inflammation persisted and a gradual increase in granulation tissue was found in the subdural space on lumbar MRI. After administration of rifampicin 450 mg/day, the CSF was normalized and the enhancement of granulation tissue decreased. The patient completely recovered 5 months after the therapy was initiated. We suggest that rifampicin may be an option for the treatment of meningitis caused by actinomyces.

Key words: actinomycosis, purulent meningitis, abducens nerve palsy, rifampicin, granuloma, MRI

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Introduction

Actinomycosis is characterized by chronic suppurative and granulomatous lesions on the face, cervix, thorax, and abdomen caused by Actinomyces species, which are Gram negative anaerobic bacteria. Recently, actinomycosis has become a rare disease because of improvements in hygiene and the widespread use of antibiotic therapy, but even healthy immunocompetent hosts can develop this disease. Actinomyces can rarely cause central nervous system (CNS) infection (1). Many of the reported CNS infections caused by Actinomyces were brain abscesses; however, reports of Actinomyces-associated meningitis remain limited (2, 3). We report a case of purulent meningitis caused by Actinomyces species that presented with abducens nerve palsy and the formation of granulation tissue in the lumbar subdural space, and was successfully treated with rifampicin.

Case Report

A 64-year-old previously healthy woman was admitted to our hospital with complaints of fever, headache, and diplopia. She developed fever and bioccipital headache one month before hospitalization and noted diplopia for 2 weeks before hospitalization. Her body temperature was 39°C, and physical examination did not indicate any abnormalities in her chest or abdomen. Her oral cavity revealed untreated dental caries. She presented with a Glasgow Coma Scale of E4V4M6. Neurologic exam revealed right abducens nerve paralysis (Fig. 1-A), but there was no evidence of other cranial nerve abnormalities. She did not show paralysis, ataxia in her limbs, abnormality of tendon reflexes, or sensory disturbance. She had stiffness of her neck and a positive Ker-nig’s sign. Blood tests revealed an elevated white blood cell count (WBC) of 18,440/μL with a differential count of 92% neutrophils. The C-reactive protein (CRP) was high at 10.4 mg/dL. Blood culture was negative. Lumbar puncture was performed and an opening pressure was unmeasurable be-
cause of the high viscosity of her cerebrospinal fluid (CSF).
The CSF appeared cloudy and white (Fig. 1-B) and demonstrated a WBC of 67,386/mm³ (mononuclear cells: polymorphonuclear cells 2:98), 803 mg/dL of total protein, and 18 mg/dL of glucose (simultaneous serum glucose level was 155 mg/dL). Gram stain of the CSF showed few gram-positive bacilli. Repeated CSF culture revealed Actinomyces species on two separate occasions. Polymerase chain reaction testing for tuberculosis in CSF was negative. She was diagnosed as having purulent meningitis caused by Actinomyces. A systemic survey was performed to determine the origin of infection. Neither sinusitis nor otitis was found. A full-body CT and gallium scintigram did not indicate an obvious focus of infection. The original focus of actinomycosis remained unclear, but she had some untreated cavities which may have been the origin of infection.

Brain MRI did not show any abnormality on T2-weighted or FLAIR images. Although abnormal enhancement with gadolinium was not observed in the leptomeninges, the right abducens nerve was enhanced with gadolinium (Fig. 1-C). The thoracic-lumbar MRI presented gadolinium enhancement of the surface of the lower spinal cord and nerve roots, but no abscess was observed (Fig. 2).

Therapy was initiated with intravenous ampicillin 12 g/day and dexamethasone 24 mg/day according to the guidelines for the treatment of bacterial meningitis in Societas Neurologica Japonica, because the gram stain of the CSF showed some gram-positive bacillus concerning for Listeria. The results of CSF culture revealed Actinomyces species sensitive to penicillins, and thus treatment with intravenous ampicillin was continued. Her clinical symptoms such as consciousness disturbance and fever improved a week after initiation of medication. The number of cells in the CSF gradually decreased, and CSF examination 2 weeks after initiation of medication showed 1,267/mm³ of WBC (mononuclear cells: polymorphonuclear cells 5:95), 163 mg/dL of total protein, and 33 mg/dL of glucose. Three weeks from the start of medication, the CRP in serum normalized and the number of cells in CSF decreased to 300/mm³. However, inflammation in the CSF persisted in spite of intravenous ampicillin of 12 g/day for 8 weeks (Fig. 3). Because the CSF inflammation was prolonged, we performed further investigation to determine the focus of infection. Although the patient did not complain of back pain or sensory disturbance, a gadolinium-enhancing mass lesion was found in the caudal side of the subdural space on lumbar MRI (Fig. 4-A, B). Repeated CSF culture turned negative for any bacteria including Actinomyces. We presumed that the treatment with
Figure 2. Sagittal thoracic-lumbar MRI (A-C) and axial lumbar MRI at the level of third lumbar vertebra (D-F). A, D: T1-weighted image (1.5T, TR=595 ms, TE=10 ms) B, E: T1-weighted images with Gd-DTPA enhancement (1.5T, TR=595 ms, TE=10 ms). C, F: T2-weighted images (1.5T, TR=3,000 ms, TE=120 ms). The surface of the lower spinal cord and cauda equina were enhanced with gadolinium. Abscess was not found.

Figure 3. Clinical course.
ampicillin was not sufficient to control the inflammation in CSF. The treatment regimen was changed from intravenous ampicillin to oral administration of rifampicin 450 mg/day. Subsequently, the number of cells in the CSF and the enhancement of granulation tissue in the subdural space decreased in the lumbar MRI after 4 months (Fig. 4-C). The abducens nerve palsy gradually improved after the initiation of the treatment, and completely recovered after five months. The gadolinium enhancement of the right abducens nerve on MRI disappeared. The patient completely recovered; she has no persistent focal neurologic defects, and has remained disease free for more than 10 months (Fig. 3).

Discussion

Actinomycosis is a chronic, suppurative infection characterized by abscess formation and granulomatous lesions caused by a species of the genus Actinomyces. A. israelii is the most common cause of actinomycosis infection in humans (1). Actinomyces habitually reside in the oral cavity, digestive tract and vagina, and sometimes form abscess on the face, neck, chest or abdomen. Actinomyces can cause CNS infection from contiguous extension of a neighboring focus such as paranasal sinusitis (4), or from hematogenous seeding from a distant infected site such as dental abscess (5). Smego reviewed actinomycosis cases in the literature in 1987 and reported that the types of CNS lesions included brain abscess (67%), meningitis (13%), actinomycosis (7%), subdural empyema (6%), and epidural abscess (6%) (1). After this report, additional cases of brain abscess were reported with good treatment responses (4, 6, 7). Meanwhile, reports of actinomyces-associated meningitis remain limited (2, 3). Although antimicrobial agents such as penicillin are generally effective for actinomycosis, the treatment course of the meningitis may be associated with complications such as cerebral infarction (2) and subarachnoid hemorrhage (3) as a result of secondary angiitis.

We reported a case of actinomycotic meningitis successfully treated with rifampicin that presented with abducens nerve palsy and the formation of lumbosacral granuloma. Meningitis with the disturbance of ocular movement has been reported in mycotic meningitis (8), tuberculous meningitis (9), carcinomatous meningitis (10), and pachymeningitis (11). The causes of oculomotor nerve palsy in these meningitides were neuritis, angiitis, invasion of carcinoma, and direct expansion of inflammation, respectively. We consid-
erated that the abducens nerve palsy of the present case was caused by neuritis which was associated with the inflammation in the CSF because the gadolinium enhancement of the right abducens nerve, consistent with right abducens nerve palsy, was shown without a mass lesion or enhancement of the peripheral meninges and peripheral blood vessels. The improvement of the abducens nerve palsy following the steroid therapy with antibiotics was satisfactory.

One of the features in this case was the formation of a lumbar sacral granuloma. The administration of ampicillin was effective, and clinical symptoms and laboratory findings were improved, with a lowered serum CRP and decreased cell number in CSF. However, a progressively growing mass lesion was found in the lumbar region associated with the prolonged inflammation in CSF. Because the mass lesion was enhanced throughout with gadolinium, it was felt to be most consistent with granulation tissue, as opposed to an abscess or subdural empyema which usually present with circumferential contrast enhancement (12). We could not rule out the possibility that the lumbar sacral granuloma was caused by a different, second pathogen that was resistant to ampicillin. However, repeated CSF culture did not detect another pathogen. A known characteristic of actinomycosis is the ready formation of granulation tissue in response to infection. Thus, we considered that the inflammation caused by Actinomyces could lead to formation of the lumbar sacral granuloma.

The administration of ampicillin was effective, but not sufficient to control the inflammation in CSF of the present case. Actinomyces species are susceptible to antimicrobial agents including Penicillin G, ampicillin, chloramphenicol, minocycline, and tetracycline. Penicillin antibiotics are used most frequently in the treatment of actinomycosis of the CNS (1). Meanwhile, rifampicin, which is generally used for the treatment of tuberculosis, is known to also have antibacterial effects against anaerobic bacteria. Lerner reported that rifampicin and erythromycin are the most active drugs against Actinomyces in vitro (13). In addition, rifampicin has good penetration into CSF while penicillins do not penetrate well into the CSF. Rifampicin was more effective in the present case, and improved the inflammation in the CSF and decreased the gadolinium-enhancement of granulation tissue. We described a case of actinomycotic meningitis which was only partially improved by ampicillin but recovered completely after switching to rifampicin. We suggest that rifampicin may be an option for the treatment of meningitis caused by Actinomyces species.

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

References