

[CASE REPORT]

Clival Osteomyelitis with Cavernous Sinus Thrombosis Due to *Fusobacterium nucleatum* and *Campylobacter rectus* Induced by Tooth Extraction

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Abstract:

A 70-year-old woman who had suffered from aseptic meningitis complained of chronic headache after dental treatment including tooth extraction. She developed a fever and respiratory failure. Based on chest computed tomography and head magnetic resonance imaging (MRI), she was diagnosed with osteomyelitis in the clivus accompanying moderate pituitary involvement, cavernous sinus thrombosis and septic pulmonary embolism. Both of the causal bacteria, *Fusobacterium nucleatum* and *Campylobacter rectus*, were isolated from her blood. Dual infection leading to clival osteomyelitis and cavernous sinus thrombosis has not been reported. It is important to perform enhanced MRI and blood culture for patients with chronic headache related to dental treatment.

Key words: *Campylobacter rectus*, cavernous sinus thrombosis, clival osteomyelitis, *Fusobacterium nucleatum*, septic pulmonary embolism

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Introduction

Osteomyelitis in the clivus and cavernous sinus thrombosis are very rare, and it is difficult to diagnose these complications since they lack any specific symptoms and their symptoms mimic those of aseptic meningitis. Although clival osteomyelitis is generally complicated with otitis externa caused by *Pseudomonas aeruginosa* (1), several cases without otitis externa have also been reported. In such cases, the causative organism is often determined from the patient's oral bacteria (2-9). Hormonal impairment due to spread of inflammation of the clivus may also occur.

We herein report a very rare case of clival osteomyelitis accompanying sinus thrombosis due to double oral bacterial infection.

Case Report

A 70-year-old woman who had a complaint of prolonged left temporal headache visited a hospital. She had had a tooth extracted two weeks before the headache developed (Fig. 1). She had a history of hypertension, but no other remarkable medical history. Based on the findings of cerebrospinal fluid (CSF) showing increased mononuclear-dominant cells but no isolation from the bacterial culture, she was diagnosed with aseptic meningitis. However, her headache was not ameliorated, and she was referred to and admitted to our hospital for the further examination of her chronic headache.

On the day of admission, her body temperature was 35.6°C. Jolt accentuation was positive, but there were no other neurological abnormalities. Laboratory data revealed increased levels of inflammatory markers as well as elevated values of white blood cell count (13,400/μL), erythrocyte

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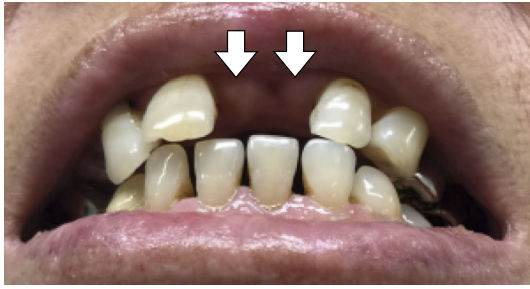


Figure 1. Image of the patient's mouth. The arrows indicate the extracted teeth.

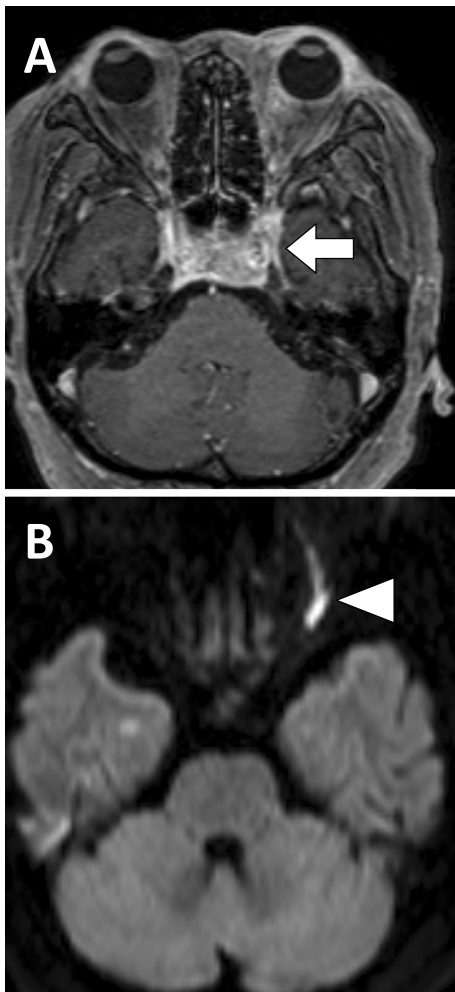


Figure 3. Head MRI. (A) Clival and cavernous sinus lesions with a contrast effect (arrow). (B) Diffusion-weighted images showing a highly intensified superior ophthalmic vein (arrowhead).

sedimentation rate (123 mm/h), C-reactive protein (CRP) level (28.81 mg/dL), and pro-calcitonin (3.07 ng/mL). On the night of admission, she had chills, shivering, a fever (39.7°C), and respiratory failure. Chest X-ray showed multiple macular ground-glass opacities (Fig. 2A), and computed tomography (CT) revealed multi-nodular shadows in the bilateral lungs and pleural effusion in the right lung (Fig. 2B). The administration of intravenous ampicillin/sulbactam and

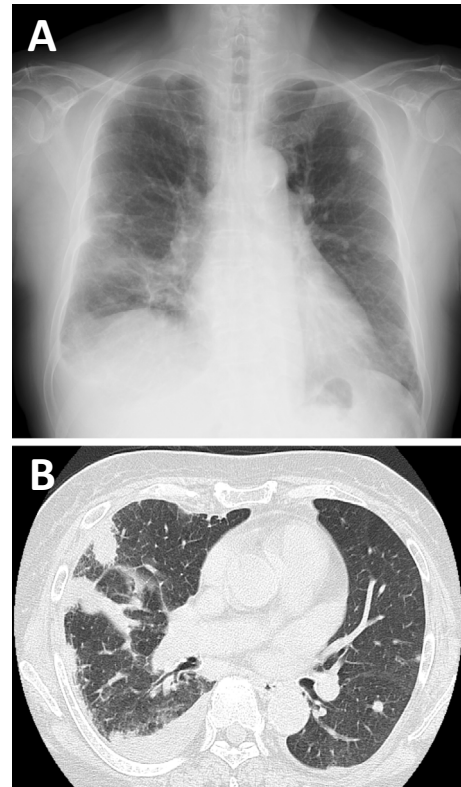


Figure 2. Chest X-ray (A) and CT findings (B).

oral fluconazole was commenced, presuming both septic pulmonary embolism caused by toothy infection and Cryptococcal pneumonia associated with meningitis. On the 3rd day after admission, swelling around her left eye suddenly occurred, and enhanced magnetic resonance imaging (MRI) was performed. MRI showed marked enhancement of the clival region and cavernous sinus in enhanced-T1 images (Fig. 3A, arrow) and also revealed highly intensified signals in the superior ophthalmic vein in diffusion images (Fig. 3B, arrowhead).

On the 4th day, *Fusobacterium nucleatum* and *Campylobacter rectus* were isolated from blood cultures, leading to a diagnosis of central skull-base osteomyelitis with cavernous sinus thrombosis as well as septic pulmonary embolism caused by oral infection. An antimicrobial susceptibility result was not obtained since the growth of the bacteria was poor. Since her general condition improved after the administration of ampicillin/sulbactam, ampicillin/sulbactam seemed to be effective. However, the serum CRP level on the 4th day had increased to 33.2 mg/dL. Based on the serum CRP level, the unknown antimicrobial susceptibility and the fact that exacerbation of clival osteomyelitis could be fatal, the antibiotics were switched to intravenous meropenem and metronidazole. Her headache, swollen left eye, fever, and inflammatory markers gradually improved, and she was discharged with continuation of oral antibiotics. On the 27th day, we performed a combined anterior pituitary function test to examine the pituitary involvement. The data showed delayed recovery patterns of all anterior hormones after stimulation despite the response levels of the anterior hor-

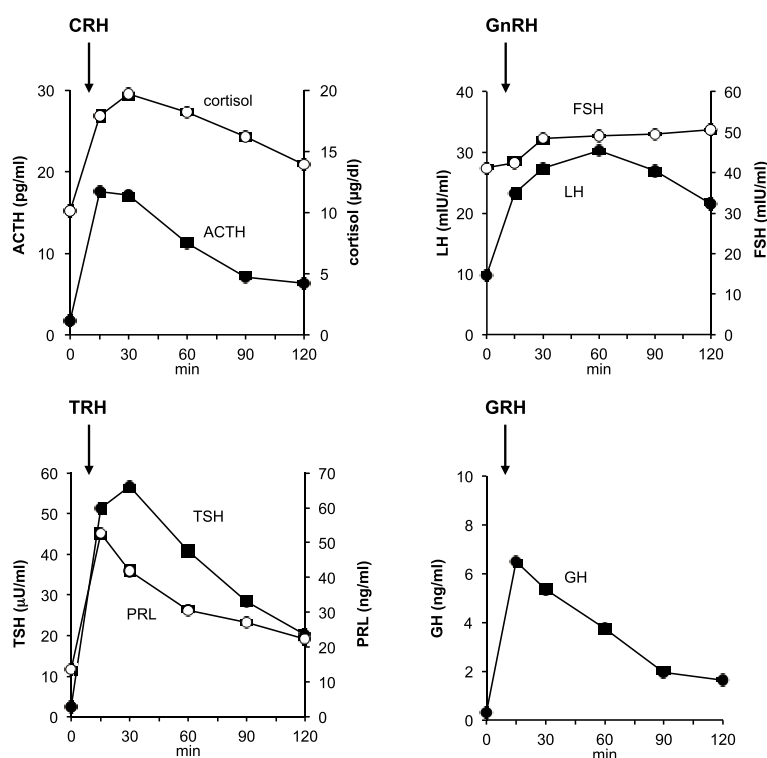


Figure 4. Combined anterior pituitary function test. Corticotropin-releasing hormone (CRH), thyrotropin-stimulating hormone (TRH), gonadotropin-releasing hormone (GnRH) and growth hormone-releasing hormone (GRH) were administered, and examinations of hormones, including adrenocorticotropin (ACTH), cortisol, thyrotropin (TSH), prolactin (PRL), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and growth hormone (GH), were serially performed.

mones examined being preserved, indicating the involvement of the hypothalamic region rather than pituitary damage (Fig. 4), although hormone replacement therapy was not clinically needed.

Discussion

The present patient complained of headache after tooth extraction, and she was followed up with a diagnosis of aseptic meningitis. However, based on the results of head MRI and blood culture, the cause of her headache was finally revealed to be clival osteomyelitis with cavernous sinus thrombosis due to an infection with *Fusobacterium nucleatum* as well as *Campylobacter rectus*. The patient developed sepsis with respiratory failure, and septic pulmonary embolism was also detected by chest X-ray and CT. Since clival osteomyelitis is often accompanied by aseptic meningitis, we should distinguish central skull-base osteomyelitis in patients with a prolonged history or in patients with neuropathy, even if a CSF test shows aseptic meningitis (2, 7, 8, 10). It is also necessary to perform a detailed examination of systemic infection for patients with a history of tooth extraction. Cryptococcal meningitis and pneumonia should also be considered for patients with chronic meningitis and multiple-nodular shadows in bilateral lungs (11).

This is the first case of central skull-base osteomyelitis in which double causative bacteria were detected. Since sys-

temic infection by multiple oral bacteria often occurs after dental events (12), systemic infection in the present case may have been caused by the tooth extraction. To our knowledge, besides cases due to the spread of otitis externa caused by *Pseudomonas aeruginosa*, there have been 14 reported cases of central skull-base osteomyelitis in which the causative organism was successfully determined (2-9, 13-18). Among those 14 cases, 8 were due to oral bacteria, including 4 cases caused by *Fusobacterium species* and 1 case caused by *Fusobacterium nucleatum*. The case in which the causative organism was *Fusobacterium nucleatum* was complicated with cavernous-sinus thrombosis, septic pulmonary embolism and Lemierre's syndrome, despite no related history of tooth extraction (7). Since infections with *Fusobacterium species* are often accompanied by thromboembolism, it is necessary to choose antibacterial agents against oral bacteria, including *Fusobacterium species*, and to immediately perform a radiological examination for thromboembolism when central skull-base osteomyelitis is suspected.

Our case was also complicated with *Campylobacter rectus* infection. There have been only three reports of intracranial infection by *Campylobacter rectus* (3, 19, 20) including cases of cavernous sinus thrombosis, rupture of an aneurysm caused by a subdural abscess, and multiple abscesses in the skull base and brain. To our knowledge, ours is the second reported case of central skull-base osteomyelitis and cavern-

ous sinus thrombosis related to *Campylobacter rectus* infection. Although its occurrence is quite rare, *Campylobacter rectus* should be considered as a potential cause of intracranial infection.

In the present case, related endocrinological damage due to clival osteomyelitis was suspected. Although MRI indicated pituitary involvement due to the infection, a pituitary function test showed a pattern of hypothalamic involvement rather than pituitary involvement. Although there have been no reports showing related endocrine damage due to central skull-base osteomyelitis, it is possible that inflammation of the clivus impaired the hypothalamic functions. If symptoms such as unexplained fatigue appear after treating clival osteomyelitis, it is necessary to search for endocrinal dysfunction.

It is therefore necessary to perform enhanced MRI and blood culture to rule out the possibility of central skull-base osteomyelitis and/or cavernous sinus thrombosis when a patient complains of chronic headache that cannot be explained by aseptic meningitis. When a patient has a history of tooth extraction, a detailed examination of the presence of systemic infection should be performed, and antibiotics against oral bacteria should be selected. Related hypothalamic and/or pituitary damage should also be suspected in such cases.

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

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