Vertebral osteomyelitis as a hidden cause of persistent meningeal irritation in a patient with pneumococcal meningitis
A case report

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Abstract
Rationale: Pneumococcal meningitis generally develops from bacteremia and is often complicated by multiple organ infection.

Patient concerns: A 62-year-old man with no previous medical history developed progressive disturbance of consciousness preceded by high-grade fever and headache for a few days.

Diagnosis: The patient was diagnosed with pneumococcal meningitis based on meningeal irritation, polymorphonuclear cell-predominant pleocytosis of the cerebrospinal fluid (CSF) and a positive pneumococcal urinary antigen test at a different hospital. Despite the administration of meropenem and vancomycin, his consciousness worsened, and the patient was transferred to our hospital. Marked nuchal stiffness was noted. The patient showed a disturbance of consciousness, with a Glasgow Coma Scale score of E3V2M5. No significant cranial nerve palsy, motor weakness or sensory impairment was observed. CSF examination showed polymuclear cell-predominant pleocytosis of 755/μL. Transthoracic echocardiography revealed infectious endocarditis.

Interventions: After the detection of penicillin-susceptible Streptococcus pneumoniae, the antibiotic regimen was changed to aminobenzylpenicillin 12 g/d and ceftriaxone 4 g/d, which improved the patient’s consciousness and CSF findings. However, marked neck stiffness and neck pain persisted; we performed a systemic investigation that revealed cervical vertebral osteomyelitis and aortic aneurysm.

Outcomes: After surgical treatment, the patient achieved complete remission of both conditions.

Lessons: We should consider vertebral osteomyelitis as a potential complication of meningitis when nuchal stiffness persists despite an improvement in meningitis.

Abbreviations: CSF = cerebrospinal fluid, IE = infectious endocarditis, WBC = white blood cell, CT = computed tomography, MRI = magnetic resonance imaging, PSSP = Penicillin-susceptible Streptococcus pneumoniae.

Keywords: bacterial meningitis, infectious aortic aneurysm, Streptococcus pneumoniae, vertebral osteomyelitis

1. Introduction
Bacterial meningitis is a neurological emergency, with high rates of neurological sequelae and mortality, especially when treatment is delayed.[1] Thus, bacterial meningitis requires systemic management, including appropriate antibiotic therapy in the early phase.[1][2] It can be acquired spontaneously as a community-acquired bacterial meningitis in community or as a complication of invasive procedures or head trauma in the hospital (nosocomial bacterial meningitis). As patients with bacterial meningitis often show concomitant multiple organ infections, it should be treated as a systemic disease.[1][2] We herein report a case of pneumococcal meningitis complicated by multiple organ infections. Notably, the systemic investigation revealed that complicated vertebral osteomyelitis was a hidden cause of sustained meningeal irritation in our patient.

2. Case report
A 62-year-old man who had not been vaccinated for Streptococcus pneumoniae developed high-grade fever and headache. He had no history of medical visits and was not on regular medication. Two days later, the patient was admitted to a hospital because of disturbance of consciousness. The patient was diagnosed with pneumococcal meningitis based on meningeal irritation, polymorphonuclear cell-predominant pleocytosis (92 cells/μL) with glucose levels of 0 mg/dL in the cerebrospinal fluid.
fluid (CSF) and a positive pneumococcal urinary antigen test. Laboratory tests showed a white blood cell (WBC) count of 8580/μL (neutrophils, 93.4%) and C-reactive protein level of 30.12 mg/dL. According to the Japanese guidelines for bacterial meningitis, treatment with meropenem and vancomycin was initiated. However, his consciousness worsened, and he was transferred to our hospital on the sixth day after onset. He was afebrile, and other vital signs were stable. His right wrist was swollen, and a cut on his right pollex pedis was found. Meningeal irritation including marked nuchal stiffness and Kernig’s sign was observed. The patient showed a disturbance of consciousness, with a Glasgow Coma Scale of E3V2M5. No significant cranial nerve palsy, motor weakness or sensory impairment was observed. Tendon reflexes were bilaterally normal and negative for Babinski sign. Laboratory tests showed elevated inflammatory reactions: white blood cell count, 13,300/μL; C-reactive protein, 1.82 mg/dL; erythrocyte sedimentation rate, 21 mm (1 hour); and procalcitonin, 2.26 ng/mL. The D-dimer level was 10.6 μg/mL. Renal failure or diabetes mellitus was not present. The anti-HIV antibody test was negative. CSF examination showed polymorphonuclear cell-predominant pleocytosis of 755/μL, a protein concentration of 976 mg/dL and a glucose level of 75 mg/dL (CSF/blood glucose, 0.56). The CSF was positive for pneumococcal antigen. An electrocardiogram showed sinus rhythm. Transthoracic echocardiography revealed infectious endocarditis (IE) in the aortic valve; however, no abnormalities were observed on chest computed tomography and brain magnetic resonance imaging (MRI) examinations on admission.

Meropenem 6g/d and vancomycin 2g/d were continued, and dexamethasone 29.7 mg/d was added for 4 days. Penicillin-susceptible Streptococcus pneumoniae was detected in serum and CSF cultures, and according to antimicrobial susceptibility tests, we downescalated the antibiotic regimen to amoxicillin/penicillin 12 g/d and ceftriaxone 4 g/d. After 3 weeks of antibiotic therapy, his consciousness had improved; however, muscle weakness in the lower extremities and left-sided hearing impairment were noted. At 21 days after admission, his marked neck stiffness and neck pain persisted despite the improvement of CSF findings, and Babinski sign became positive bilaterally. On cervical MRI, vertebral osteomyelitis at the C3/4 level was detected (Fig. 1). In addition, an infectious aortic arch aneurysm and Stanford B-type aortic dissection were noticed incidentally. Both vertebral osteomyelitis and infectious aortic aneurysm required surgical treatment. After the operations, his neck pain and meningeal signs disappeared. He was transferred to a rehabilitation hospital and returned to society 1 year after the onset of symptoms.

3. Discussion

We experienced a case of pneumococcal meningitis complicated by multiple organ infections. *Streptococcus pneumoniae* is the most common pathogen causing bacterial meningitis (60%) in adults despite the prevalence of pneumococcal vaccines. Pneumococcal meningitis shows poor prognosis, with a 20% to 37% mortality and 31% sequelae rate compared with other types of bacterial meningitis. Among the neurological sequelae, hearing impairment is the most common, followed by seizures, hydrocephalus, spastic/llacoid paralysis and other cranial nerve palsies. Weisfelt et al reported that the predictive factors of bacterial meningitis were as follows: older age, severe consciousness disturbance, tachycardia (>120 bpm), the presence of cranial nerve palsy, a CSF leukocyte count of less than 1000/μL and gram-positive cocci on CSF culture. Of those risk factors, our patient was of older age and had consciousness disturbance, cranial nerve palsy, a low CSF leukocyte count, and gram-positive cocci on CSF culture; the likelihood of an unfavorable outcome was approximately 80%.

About 40% of pneumococcal IE cases are complicated by pneumococcal meningitis. IE is a systemic infection that leads to the development of vegetation on the valves or endocardium and causes bacteremia, mycotic embolization and cardiac...
dysfunction. Delayed treatment can lead to multiple organ failure and unfavorable outcomes. *Streptococcus viridans*, *Staphylococcus aureus*, and *Enterococcus* spp. are the most common agents of IE, while *Streptococcus pneumoniae* accounts for less than 1%. Our patient with pneumococcal meningitis had multiple complications, such as vertebral osteomyelitis, aortic aneurysm and IE, presumably related to *Streptococcus pneumoniae* infection.

As his neck stiffness remained after the improvement of CSF findings, we suspected a comorbidity in the spine and performed a systemic investigation. Cervical computed tomography and MRI revealed vertebral osteomyelitis. Vertebral osteomyelitis, which can manifest as meningeval irritation signs and be complicated with meningitis, is a differential diagnosis of bacterial meningitis. \[9,10\] Table 1 shows the data of 13 reports which can manifest as meningeal irritation signs and be complicated with meningitis, is a differential diagnosis of bacterial meningitis.\[9,10\] Table 1 shows the data of 13 reports in which can manifest as meningeal irritation signs and be complicated with meningitis, is a differential diagnosis of bacterial meningitis.\[9,10\] Table 1 shows the data of 13 reports.

| Patient number, ref | Patient (age, sex) | Underlying disease | Other complications | Treatment | Outcome |
|---------------------|-------------------|--------------------|---------------------|-----------|---------|
| Kaufman (1980) | 58, NR | NR | IE | Abx, spine surgery | Died |
| Peterson (1987) | 77, M | Fall injury | None | NFPC+GM—PC+CP, spine surgery | Died |
| Heard (1992) | 61, F | None | IE | PC+CLDM p.o. | Improved |
| Chemil (1996) | 52, M | Alcoholism, CHF | Acute bronchitis | CTX+RFP—CTRX+RFP—pristinamycin+RFP | Improved |
| Turner (1999) | 79, F | None | IE | PC+GM | Improved |
| Poyani (2001) | 51, F | None | None | CTRX, CT guided drainage | Improved |
| Brouwer (2008) | 51, M | Depression | Vertebral osteomyelitis | PC+DEX—flucloroxacin | Improved |
| Brouwer (2008) | 39, F | Underwent operation of spondylitis | Vertebral osteomyelitis | AMPC+DEX—flucloroxacin | Improved |
| Suzuki (2013) | 9M/5F | Diabetes mellitus, 35.7%; malignancy, 14.3% | Epidural abscess, 14%; illoposus abscess, 21%; arthritis, 14% | One patient, β-lactam therapy | One patient (7.1%) died |
| Pires (2010) | 61, M | HT | None | CTRX+VCM+ABPC | Improved |
| Gaini (2017) | 66, F | Hypogammaglobulinemia due to MGUS | Pneumonia | CTRX+PCG+DEX—PCG, Mlg, Polysaccharide pneumococcal vaccination | Improved |
| Mitsutake (2018) | 69, M | HT, MGUS, COPD, AAA | Right psoas abscess, the dilution of AAA | CTRX+VCM+DEX, vascular surgery | Improved |
| Present case | 62, M | None | IE, AAA, arthritis of the right wrist | MEPM+VCM+DEX—CTRX+ABPC, neck surgery, vascular surgery | Improved |

AAA = abdominal aortic aneurysm, ABPC = ampicillin, Abx = antibiotics, AMPC = amoxicillin, CHF = congestive heart failure, CLDM = clindamycin, COPD = chronic obstructive pulmonary disease, CP = chloramphenicol, CTRX = ceftriaxone, CTRX+VCM = cefotaxime, DEX = dexamethasone, F = female, GM = gentamicin, HT = hypertension, IE = infective endocarditis, M = male, MEPM = meropenem, MGUS = monoclonal gammapathy of undetermined significance, NFPC = nafcillin, NR = not reported, PC = penicillin, PCG = pencycillin, RFP = rifampicin, VCM = vancomycin.

4. Conclusion
Bacterial meningitis can cause critical complications, and it should be regarded as a systemic infectious disease. To avoid delays in diagnosing complications, we should consider vertebral osteomyelitis as a potential complication of meningitis when nuchal stiffness persists despite an improvement in meningitis signs, and urgent surgical treatment should be performed when necessary.

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