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【 CASE REPORT 】

Aspiration of Cerebrospinal Fluid Rhinorrhea as a Cause of Non-resolving Pneumonia

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Abstract:

We herein report two cases of cerebrospinal fluid (CSF) rhinorrhea associated with lung infiltrates. One patient presented with symptomatic non-resolving pneumonia, while the other was asymptomatic. In both cases, the lung infiltrates completely resolved when CSF leakage had subsided. Pulmonary involvement in CSF rhinorrhea is under-recognized, and despite being the definitive treatment, surgery for CSF rhinorrhea is typically postponed due to the presence of lung infiltrates. However, meningitis is a serious complication due to a delay in surgical management. Physicians should be made aware that CSF rhinorrhea is a potential cause of intractable lung infiltrates.

Key words: CSF rhinorrhea, aspiration pneumonia, non-resolving pneumonia

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Introduction

Cerebrospinal fluid (CSF) rhinorrhea is a condition in which a disruption of the skull base leads to CSF draining through the nasal cavity, usually via the paranasal sinuses. Skull base disruptions can be secondary to trauma, tumor invasion, or intranasal or intracranial surgery. It rarely develops spontaneously and it is often associated with idiopathic intracranial hypertension (1, 2). Although some cases of CSF rhinorrhea resolve without intervention, many cases persist and require surgical intervention to stop the leakage. Persistent leaks not only cause bothersome symptoms such as nasal discharge, visual disturbance, olfactory disturbance, and headache, they also carry the risk of meningitis, which is potentially life-threatening (2, 3). Therefore, an early repair is recommended (4).

Pulmonary involvement of CSF rhinorrhea is rare, and only a few cases have so far been reported (2, 5, 6). We encountered two cases of pneumonia associated with CSF rhinorrhea. One patient who presented with symptomatic non-resolving pneumonia was partially responsive to antibiotics. Meanwhile, the other had asymptomatic persistent lung infiltrates, which were found incidentally on pre-admission chest computed tomography (CT) scans for coronavirus disease 2019 (COVID-19) screening. In both cases, the lung infiltrates resolved completely after CSF leakage had subsided or been controlled.

Case Reports

Case 1

A 30-year-old man with a medical history of allergic rhinitis (AR) presented to an urgent care clinic in a local hospital, complaining of high fever, dyspnea, and nasal discharge, which had started several days previously. Hypoxia was noted, and chest radiography demonstrated infiltrates in the bilateral lower lung fields. Chest CT showed bilateral infiltrates at the lung bases, with bronchial wall thickening and patchy upper lobe airway-centered ground glass opacities (Fig. 1A). Laboratory tests revealed leukocytosis (14,800 cells/μL) and an elevated C-reactive protein level (CRP, 23.08 mg/dL). He was admitted with a diagnosis of community-acquired pneumonia. Ceftriaxone and azithromycin were started, which were subsequently replaced with

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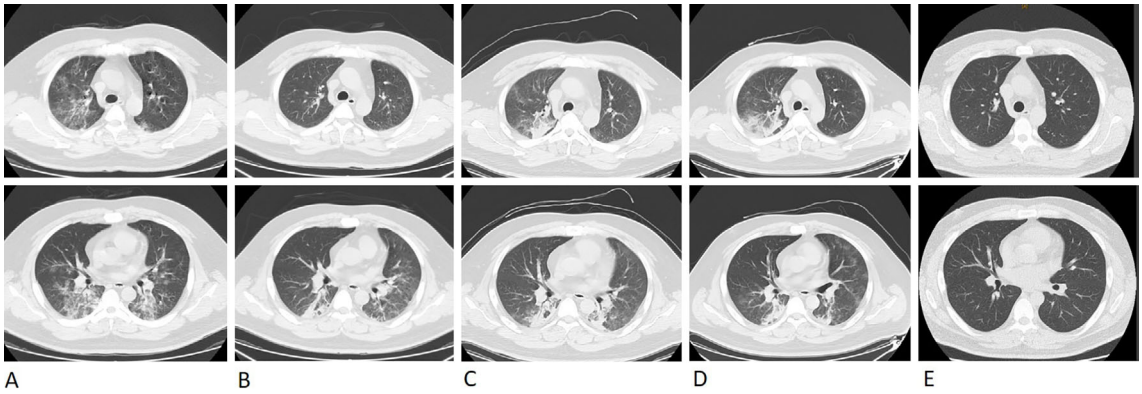

Figure 1. **A: At initial presentation, airway-centered patchy ground-glass opacities in the upper lobes and denser infiltrates in the bilateral lower lobes with bronchial wall thickening are noted. B: After antibiotic treatment. A partial improvement was observed. C: On readmission, 2 months later, ground glass opacities observed in (A) have progressed to consolidation. Ground glass opacities remain. D: After 2 weeks of glucocorticoid treatment, there is only a minimal improvement. E: After cessation of CSF leakage, complete clearing of the lung infiltrates is observed.**

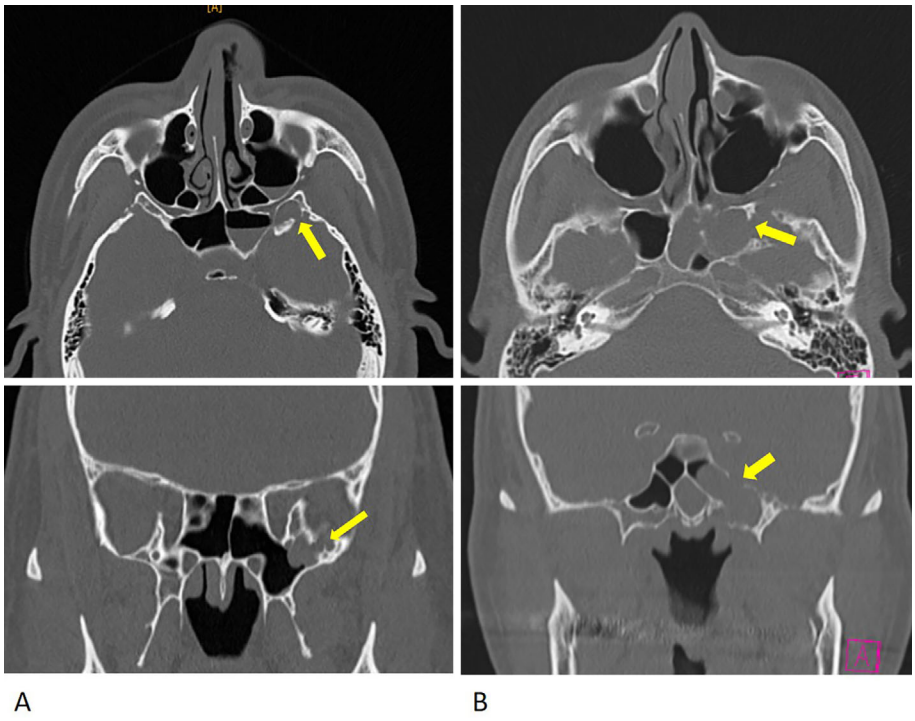

Figure 2. **Head CT of the case 1 (A) and the case 2 (B). The arrows indicate a bony defect in the lateral wall of the left sphenoidal cavity.**

levofloxacin because of persistent fever and hypoxia. The patient's clinical condition gradually improved; the hypoxia resolved and CRP decreased to 3.77 mg/dL. The patient was discharged after 3 weeks of antibiotic therapy. The lung infiltrates partly resolved, although a significant amount persisted at the time of discharge (Fig. 1B).

Nearly 1 month after discharge, the patient returned to the follow-up clinic. He reported a recurrence of cough and low-grade fever (approximately 37.5℃) soon after discharge. He also complained of persistent serous nasal discharge. No supplemental oxygen was required. A chest CT scan demonstrated persistent airway-centered ground-glass opacities and bibasilar consolidation (Fig. 1C). Blood tests revealed a recurrence of leukocytosis (12,900 cells/uL) and a mild elevation of CRP (3.91 mg/dL) as well as KL-6 (587 U/mL). Secondary organizing pneumonia following infection was suspected, and prednisolone 0.5 mg/kg/day was administered. The persistent nasal discharge was initially attributed to AR; however, no improvement was noted even with systemic glucocorticoid treatment. An otolaryngological examination revealed a serous discharge through the left sphenoid sinus ostium, with a glucose level of 103 mg/dL. CT confirmed a bony defect in the lateral wall of the left sphenoid sinus (Fig. 2A). Thus, a meningoencephalocele with CSF rhinorrhea was diagnosed. He reported a vehicular accident 5 years previously but denied any head trauma and any

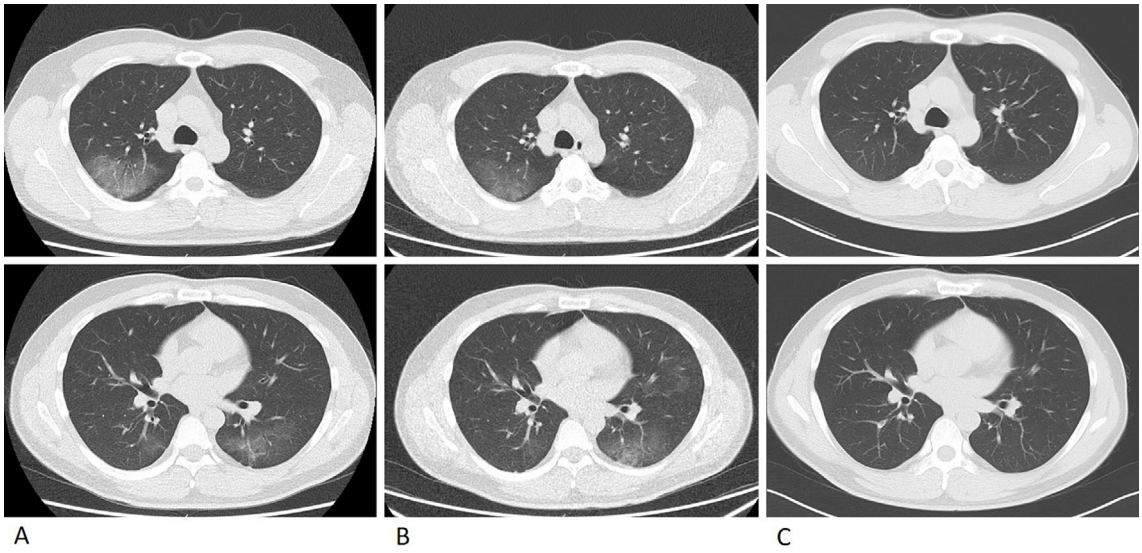

Figure 3. **A: Pre-admission screening CT. Patchy ground-glass opacities are noted. B: Two months after (A), there is an improvement in the upper lobe opacity and a mild worsening of the lower lobe opacity. C: Two months after the surgical repair of the CSF rhinorrhea, a complete clearance of the lung opacities is observed.**

changes in allergic rhinitis symptoms after the accident. The patient was referred to the otolaryngology clinic of our hospital for surgical repair.

On presentation, the association between lung lesions and CSF rhinorrhea was unclear, and a pulmonary service was consulted. Surgery was postponed until the pulmonary investigation was completed. A CT scan of the chest after 2 weeks of prednisolone therapy showed a minimal improvement (Fig. 1D), and prednisolone was discontinued due to the risk for infection. Serum β-D-glycan was negative. An autoantibody panel for interstitial pneumonia with autoimmune features (IPAF) was negative. A polymerase chain reaction (PCR) test for COVID-19 was negative. Bronchoscopy was performed, and bronchoalveolar lavage (BAL) fluid revealed neutrophil-predominant leukocytosis (leukocytes 405 cells/μL, neutrophils 18%, lymphocytes 9%, eosinophils 2%, and macrophages 71%). The lymphocyte CD4/CD8 ratio was 0.41. Cultures were negative, and a lung biopsy was not performed due to uncontrolled coughing.

The patient remained under observation while pulmonary investigations were non-diagnostic. He reported a gradual, spontaneous improvement in nasal discharge and other respiratory symptoms over a few months. A cessation of the CSF leak was confirmed when the patient underwent an endoscopic repair of the meningoencephalocele. Lung opacities on CT completely resolved 4 months after referral to our hospital (Fig. 1E).

Case 2

A 40-year-old man with a history of AR presented to a local ear nose and throat clinic complaining of persistent rhinorrhea that started after suffering head trauma as a result of falling down the stairs 2 months previously. CT of the paranasal cavities revealed a bony defect in the lateral wall of the left sphenoidal cavity (Fig. 2B), and the patient was referred to the otolaryngology clinic of our hospital. The β2-transferrin in the nasal discharge was found to be elevated (22.5 mg/dL). A meningoencephalocele with CSF rhinorrhea was diagnosed, and the patient was scheduled to undergo surgery. However, a pre-admission CT scan of the chest for COVID-19 screening revealed bilateral patchy ground glass opacities (Fig. 3A). Although a PCR test for COVID-19 was negative and the CT findings were not typical of COVID-19 pneumonia, the surgery was cancelled and a pulmonary consultation service was requested.

The patient denied any respiratory symptoms other than nasal discharge. There were no recently started medications or dietary supplements. Physical examination was unremarkable except for excessive nasal discharge. Laboratory examinations showed mildly elevated CRP (1.34 mg/dL), and the autoantibody panel for the IPAF was negative. Serum β-D-glycan was negative. The patient was observed without surgical intervention due to the unclear etiology of the pulmonary lesions. Follow-up CT imaging 2 months later did not show significant changes, although an improvement and progression of the lesions were simultaneously noted (Fig. 3B). Thus, surgery was performed. After the surgery, the lung lesions completely disappeared in the follow-up CT scan 2 months after surgery (Fig. 3C).

Discussion

Pulmonary involvement in CSF rhinorrhea is an underrecognized and rarely reported condition (2, 5, 6). Most patients complain of nonspecific respiratory symptoms, such as cough, sputum production, and dyspnea, in addition to nasal discharge (2, 5, 6). As in our first case, the presenting symptoms tend to involve respiratory issues. Nasal symptoms are easily overlooked or considered irrelevant or non-

specific. Physicians should maintain a high index of suspicion for CSF rhinorrhea when patients present with non-resolving pneumonia with persistent serous rhinorrhea, particularly when there is a preceding inciting event, such as head trauma. CSF rhinorrhea can be confirmed through measurements of glucose, which is high in CSF and low in nasal secretions, or β2 transferrin, which is found almost exclusively in the CSF (7). Additionally, imaging studies and otolaryngology examinations should also be performed.

Lung lesions are considered to be secondary to the chronic aspiration of leaked CSF (6). Supporting this view, a chest CT scan shows airway-centered ground glass opacities with or without bronchial wall thickening and a tendency of lower lobe predominance (2, 5, 6). In our patients, the upper lung zone was also involved. This may be a typical finding of aspiration pneumonia due to CSF rhinorrhea. Patients with CSF rhinorrhea without dysphagia are not expected aspirate when they are awake and upright. They are likely to aspirate when they are asleep and lying down. Aspiration in this position results in both upper and lower lobe posterior dominant distribution of lung opacities (8).

In case 1, BAL fluid demonstrated neutrophilic leukocytosis, which suggests a repetitive occurrence of acute inflammation resulting in the persistence of the lung lesions. We could not perform a lung biopsy, but the reported cases had bronchiocentric neutrophilic inflammation (2, 5, 6). These findings are in line with the main pathophysiologic mechanism of aspiration.

It is unknown whether CSF irritates the lung or the bacterial contamination of the aspirated CSF causes infectious pneumonia. However, both mechanisms are likely involved, as antibiotics partially ameliorated the patient's condition in case 1 and the lung infiltrates neither progressed nor regressed without antibiotic treatment in case 2. In case 1, we assume that there was preexisting but subclinical lung involvement before infectious complication resulted in acute respiratory symptoms, which eventually led to the medical attention.

Controlling CSF leakage is the definitive treatment for non-resolving pneumonia in CSF rhinorrhea aspiration. As in case 1, antibiotics help if symptoms of infection are present, but only temporarily. Although some CSF rhinorrhea cases resolve spontaneously, surgical repair is required for persistent leakage (2). Surgical delay should be avoided since unattended leaks are associated with a high risk of meningitis, as well as bothersome nasal symptoms and aspiration pneumonia (4).

Most of the reported cases and our presented cases were at a relatively young age (2, 5, 6). This probably reflects the prevalent age of basilar skull fracture, which is the most common cause of CSF rhinorrhea (9, 10).

In contrast with previously reported cases, case 2 is the first reported case of an asymptomatic pulmonary involvement in CSF rhinorrhea, which was detected through chest CT used for screening. Our institution, like several others, has implemented a pre-admission screening test using chest CT due to the ongoing COVID-19 pandemic. Since PCR testing is not 100% sensitive, CT aids in the identification of asymptomatic or pre-symptomatic COVID-19 patients. However, it is also expected to uncover other incidental findings, as in case 2. As reported in this study, CSF rhinorrhea aspiration was under-recognized as a cause of lung lesions, and surgery was postponed. Retrospectively, it was the delay in treatment that carried potential harm to the patients. The consulting internist should be aware of this possibility and provide appropriate guidance to the surgical team.

In summary, we herein reported symptomatic and asymptomatic cases of aspiration pneumonia due to CSF rhinorrhea. Antibiotics are indicated in cases of infection, but the definitive treatment is the management of CSF leakage. In the COVID-19 era, CT scans for screening may incidentally detect lung lesions in patients with CSF rhinorrhea. Physicians should be aware that CSF rhinorrhea can be a cause of intractable lung infiltrates and that timely, appropriate care must be provided to mitigate the risk of complications.

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

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