

Recurrent bacterial meningitis with cerebrospinal fluid rhinorrhea

Than Than Aye, Aye Aye Sann, Hpone Pyae Tun

ABSTRACT

Introduction: Recurrent bacterial meningitis is a rare clinical phenomenon, but a telltale sign of a mysterious foe. It is an occurrence of two or more episodes of bacterial meningitis by different organisms, or with the same organism and the episodes separated by an interval of at least three weeks.

Case Report: We present a case of a 29-year-old gentleman who presented with acute pyogenic meningitis due to *Streptococcus pneumoniae*. This is the second episode of confirmed bacterial meningitis in two years with another episode of meningitis ten years ago, which was treated as tuberculous. History of rhinorrhea was elicited on direct questioning and cerebrospinal fluid leak through cribriform plate was confirmed on magnetic resonance imaging. The current episode of meningitis was successfully treated with intravenous high dose cephalosporin and short course dexamethasone. The patient was referred to a neurosurgeon for closure of cerebrospinal fluid leak.

Conclusion: This case highlights the importance of a thorough clinical history and awareness of a seemingly unimportant symptom which can be an important diagnostic clue.

Keywords: Cerebrospinal fluid rhinorrhea, Cribriform plate defect, Pneumococcal meningitis, Recurrent meningitis

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INTRODUCTION

Recurrent bacterial meningitis is a rare clinical phenomenon, but a telltale sign of a mysterious foe. Meningitis is said to be recurrent if a person experiences two or more episodes of meningitis by different organisms or a second episode by the same organism which occurs more than three weeks after completion of treatment for the first episode [1]. This recurrence is clinically significant, and the pathogenesis is likely due to some defect in the host rather than the environment or the agent. It warrants a thorough search for the predisposing condition. These conditions can be categorized into three groups, namely (1) anatomical defects causing abnormal connections between cerebrospinal fluid (CSF) space and the skin, ears, or the nasal cavity, (2) immunodeficiency states, and (3) infections near the meningeal space.

The recurrent bacterial meningitis may be challenging to clinicians since it is not only a rare condition but also some underlying defects are subtle to diagnose, requiring specialized resources. In addition to treating the current illness, the physician is tasked with finding out and treating the predisposing condition. Otherwise, there will be another disaster. This process is quite challenging. It needs not only a science of structured and systematic approach but also an art of history taking.

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CASE REPORT

A 29-year-old gentleman presented to the emergency department of Grand Hantha International Hospital with seven days of low grade fever followed by a day of high fever and severe headache with nuchal pain. He vomited 3–4 times. There was no mental confusion nor convulsion. On examination, body temperature was of 101°F and there was marked neck stiffness. The Kernig's sign was also noted positive as the patient was painful when the knee was passively extended keeping the patient supine with hip flexed 90°. He was slightly drowsy, but no other neurological abnormalities were detected. There were no remarkable features of raised intracranial pressure. Other systems examination findings were unremarkable apart from tachycardia, presumably due to high fever.

In the past, he had a history of similar attacks of fever and headache ten years and two years before. The hospital discharge notes and medical documents were not available. According to his mother, the first episode was diagnosed as tuberculous meningitis for which he received nine months of anti-tuberculous therapy. The second episode occurred while he was in Singapore and it was diagnosed with bacterial meningitis and he recovered after two weeks of antibiotics.

On specific questioning whether he noticed any watery rhinorrhea recently, he admitted that it happened a week prior to this illness. They were spontaneously resolved, and he did not think it was an important issue. He was born as full term baby without neonatal complication and had no history of head trauma or head and neck surgery. Clinical diagnosis of recurrent acute meningitis was made.

A laboratory examination revealed an elevated C-reactive protein level of 40.5 IU/mL, erythrocyte sedimentation rate of 28 mm/first hour, and a white blood cell count of $21.09 \times 10^9/L$. Liver panels and renal panels were within normal limits. Procalcitonin was 0.55 µg/L, Hepatitis B antigen, hepatitis C antibody, human immunodeficiency virus and venereal disease research laboratory test for syphilis were negative. Serology tests for Dengue virus and its NS1 Antigen tests were negative. Urine for routine examination revealed no significant finding. Chest X-ray and electrocardiography were also normal. Computed tomography (CT) of the head showed only a cystic lesion most likely to be arachnoid cyst in the right cerebellopontine angle.

A cerebrospinal fluid (CSF) examination revealed a slightly turbid appearance and pleocytosis (390 white blood cells/mm³, 80% neutrophils), and total protein elevation (93 mg/dL); glucose was 81 mg/dL. Cerebrospinal fluid culture was negative. But Film Array tests for Meningitis/Encephalitis Panel of CSF revealed *Streptococcus pneumoniae*. The same organism also grew in blood culture. Cerebrospinal fluid for acid fast bacteria and polymerase chain reaction (PCR) test for tuberculosis were negative. For exclusion of agammaglobulinemia, immunoglobulin and complements system C3, C4

assay were done and these were within normal limits. Cerebrospinal fluid autoimmune Encephalitis Panel results were also normal.

The patient was therefore treated with high-dose ceftriaxone together with a few days of dexamethasone. This leads to a remarkably good response. The high dose ceftriaxone was extended up to two weeks. Because of three episodes of acute meningitis with history of watery rhinorrhea, CSF leakage was suspected as the cause of rhinorrhea. Therefore magnetic resonance imaging (MRI) of the brain was performed to locate the site of CSF leakage. This revealed a tiny opening in left side of cribriform plate causing CSF flow through this opening (Figure 1). He made a full recovery and was referred to a neurosurgeon for repair of the opening.

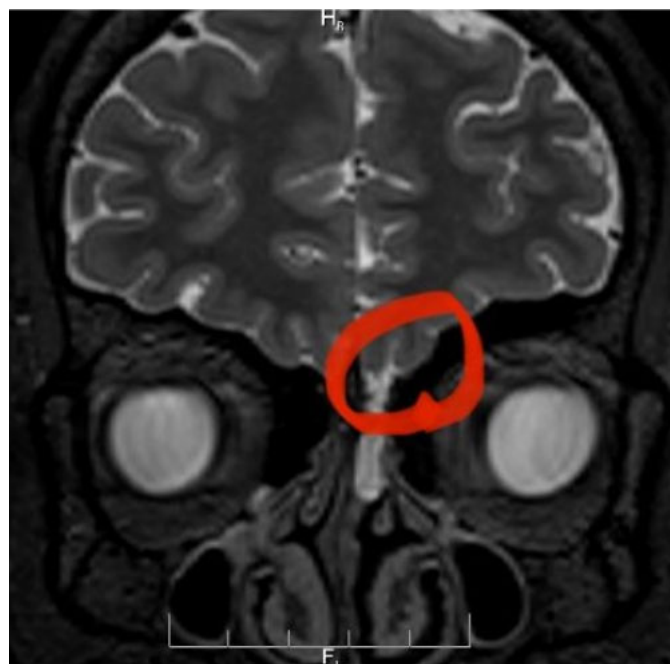


Figure 1: T2-weighted MRI brain showing CSF leak in left cribriform plates, circled in red.

DISCUSSION

Recurrent bacterial meningitis is a rare clinical phenomenon, with an estimated yearly incidence of 0.12 per 100,000 adults [2]. Approximately 5–6% of community acquired bacterial meningitis tends to be recurrent [1]. These recurrent attacks are usually less severe and have more favorable prognosis [1, 3]. The most commonly identified predisposing conditions for recurrent bacterial meningitis are ear or sinus infection (37%), CSF leakage (32%), and immunocompromised states (14%) [2]. *Streptococcus pneumoniae* is the most common causative organism in recurrent meningitis [1]. The other less commonly identified organisms are *Haemophilus influenzae*, *Neisseria meningitidis*, *Escheria coli*, *Staphylococcus aureus*, *Salmonella*, *Proteus*, *Enterococci* species, and *Klebsiella pneumoniae*. Some organisms are more commonly found with certain

predisposing conditions, e.g., *N. meningitidis* with complement deficiency, respiratory pathogens like *S. pneumoniae*, *H. influenzae*, and *N. meningitidis* with CSF leakages.

The diagnostic workup of a patient with recurrent bacterial meningitis is quite challenging to clinicians since it can be caused by a myriad of predisposing conditions, many of which are subtle to diagnose and require specialized resources. Tebruegge and Curtis suggested a systematic tiered approach to investigate recurrent meningitis, in which detailed history and examination stand as central and most important primary step [1]. If history and examination does not provide a clue, they suggested starting with locally available and less invasive tests. In our case, CSF rhinorrhea was elicited only by direct questioning with a suspicious mind.

Cerebrospinal fluid rhinorrhea is caused by abnormal CSF flow due to disruption in the barrier between sinonasal cavity and anterior or middle cranial fossa [4]. It predisposes to ascending infection of CNS from respiratory tract. Cerebrospinal fluid rhinorrhea can be due to traumatic (due to head injury and basal skull fracture), iatrogenic (sinonasal and brain surgery), or spontaneous/idiopathic. Our case has no history of head injury or surgical procedures. Without identifiable antecedent cause, it is most likely spontaneous CSF leakage. Spontaneous CSF rhinorrhea is more commonly found in obese patients with obstructive sleep apnea and due to its association with features of benign intracranial hypertension (BIH), some consider this as a variant of BIH [5, 6]. However, in our case, we could not identify features suggestive of BIH. The congenital defect in cribriform plate has been reported in literature in an infant [7]. However, our case presented late in adulthood and it is uncertain whether it is a late presentation of congenital defect or a spontaneous CSF rhinorrhea in adult. With limited information, we cannot also interpret the relevance of the first episode of meningitis, which was treated as tuberculous. It may have been unrelated event or the very first episode of pyogenic meningitis, which was empirically treated also for tuberculosis.

Diagnosis of CSF rhinorrhea requires two steps: demonstration of CSF leak and its localization. Beta 2 transferrin test in nasal secretion is the gold standard test for demonstration of CSF leak [8]. Beta 2 transferrin is exclusively found in CSF and its detection in nasal secretion has almost 100% sensitivity and 95% specificity for CSF rhinorrhea. However, this test is not readily available in some countries like ours. Traditionally, glucose oxidase test strips were used to detect CSF glucose in nasal secretion, which usually does not contain glucose. However, its sensitivity and specificity are low. Baker et al. [9] proposed a modified glucose testing algorithm, in which detection of glucose in nasal secretion might be clinically useful after exclusion of blood stained rhinorrhea, hyperglycemia and upper respiratory tract infection. Localization of CSF leakage site can be done

by either invasive tests like intrathecal fluorescein, CT cisternography or contrast enhanced magnetic resonance cisternography, or non-invasive tests like high-resolution computed tomography (HRCT) or magnetic resonance cisternography [10]. Magnetic resonance cisternography can directly visualize the fistulous tract and has sensitivity of 94% and specificity of 77%. In some practices like in Iran, direct visualization of CSF leak through endoscopy with maneuvers to increase CSF pressure is used due to limited resources for more sophisticated tests [11].

The international consensus panel on spontaneous CSF rhinorrhea strongly agrees that CSF leak should be closed as immediately as possible, instead of using watchful waiting or CSF pressure lowering therapy [12].

CONCLUSION

If a person experiences two or more episodes of bacterial meningitis, it is important to find out and treat the underlying predisposing condition. They can be abnormal connections between CSF space and noses, ear, or skin, immunodeficiency states or para-meningeal infections. Cerebrospinal fluid rhinorrhea may look trivial for the patient and should be carefully elicited by direct questioning in every patient with recurrent meningitis.

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Author Contributions

Than Than Aye – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Aye Aye Sann – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Hpone Pyae Tun – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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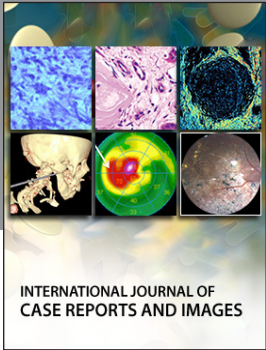
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