

## Twelve episodes of meningitis in the same patient!

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### Abstract

Recurrent bacterial meningitis is potentially life-threatening; resultant complications and adverse events during management take their extra toll on the patient. A rare case with 12 consecutive episodes of pyogenic meningitis, probably the maximum number ever reported in the literature, has been presented. A minor head injury but with no subsequent cerebrospinal fluid (CSF) leak during childhood was the index event in this patient. High resolution computerized tomography (HRCT) scan of the base of the skull clearly revealed a bony dehiscence missed on numerous previous imagings. Culprit micro organisms involved in recurrence were *Streptococcus pneumoniae* and *Neisseriae meningitides*. Though surgical repair would have been definitive treatment, medical management with pneumococcal and meningococcal vaccination and prophylactic penicillin have been used in this patient to prevent further recurrences.

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Recurrent Meningitis indicates pyogenic meningitis that has occurred on two or more occasions after an intervening period of full convalescence.<sup>1</sup> This is different from 'relapse' or recrudescence of meningitis, where the disease recurs without full recovery of the subject.

The central nervous system (CNS) is protected against microbial invasion by an effective blood-brain / cerebrospinal fluid (CSF) barrier and by an external covering of leptomeninges and skull. Thus, an effective pathogen needs either a defect in the external covering (e.g., dural leak, purulent mastoiditis) or must run the biological gauntlet of host defences to gain access into the CNS and cause an infection therein.<sup>2</sup>

Recurrent bacterial meningitis is not an extremely rare entity. In a study by Durand et al, 9% of patients with acute bacterial meningitis, many of whom had cerebrospinal fluid leak, had recurrent episodes<sup>3</sup>; in another study, 18.8% of patients with pneumococcal meningitis had recurrent episodes<sup>4</sup>.

### Case report

This 52 year old gentleman presented to the emergency room of Patan Hospital with the history of severe headache, nausea and neck pain of 3 hours duration. There had been no fever, vomiting, seizure or alteration of consciousness at the time of presentation.

On examination, the patient was conscious, but restless and ill looking. His pulse was 72/min,

respiration 22/min, BP 130/84 mm Hg, and temp 98.6 °F. There was no definite neck rigidity; Kernig's and Brudzinski's signs were absent. There was no focal neurological deficit, and examination of the cranial nerves including the fundi was normal. There was no abnormality in his cardiovascular, respiratory, and gastrointestinal systems.

With the history of sudden severe illness, and repeated episodes of meningitis in the past, it took no time for the emergency room doctor to suspect that this was another episode in the series. Immediate spinal tap showed 230 WBCs with 90% polys, glucose 63 mg/dl (blood sugar 73 mg/dl) and protein 48 mg/dl. He was immediately admitted, and ceftriaxone and dexamethasone started intravenously. The CSF later grew *Streptococcus pneumoniae* which was sensitive to the prescribed antibiotic. The patient improved uneventfully and was discharged after two weeks.

Prior to this admission he had already been admitted eight times to our hospital and three times to a hospital in South Korea with a similar illness. Each time a diagnosis of pyogenic meningitis had been made and treated with intravenous antibiotics.

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Out of the nine episodes for which he had been admitted to our hospital, *Streptococcus pneumoniae* was isolated on 5 occasions, *Neisseria meningitidis* on 2 occasions, the CSF was sterile on one and the report was missing from another occasion. Apart from these recurrent meningitic episodes and a recent left sided tubercular pleural effusion, he had never had major systemic infections like pneumonia, gastrointestinal, skin or urinary sepsis, and septicaemia.

The first episode of pyogenic meningitis occurred at the age of 28 years and subsequent episodes occurred at various intervals, but each time he improved without any sequel. The longest and shortest intervals between any two episodes were 2.5 years and 3 months respectively. He does not have a single neurological complication even after a dozen episodes of meningitis. This is interesting, as complication rate and case fatality is very high in pneumococcal and meningococcal meningitis. The patient had sustained a minor head injury at the age of 6, 22 years prior to the first episode of

meningitis. He had never had CSF rhinorrhoea or otorrhoea after the trauma, and never had symptoms of sinusitis, otitis or mastoiditis. The patient was not diabetic, and there was no clinical evidence to suggest immunodeficiency.

Investigations revealed a normal complete blood count with normal renal and liver function tests. Various investigations to look into the cause of recurrence revealed no clue. He was negative for HIV and had normal total immunoglobulin level. The USG of the abdomen showed an intact spleen and there were no Howell Jolly bodies in peripheral smear suggesting splenic dysfunction. A coronal CT scan and MRI of the head did not reveal any abnormality, and CT cisternogram did not reveal any leakage of the contrast material either. However, a recent High Resolution CT (HRCT) scan of the base of the brain showed a bony dehiscence at the floor of the anterior cranial fossa in the cribriform plate area, pointing out the cause for the recurrence.



**Fig 1:** HRCT of the base of the skull (coronal section) showing bony dehiscence at the floor of the anterior cranial fossa in the cribriform plate area.

As his meningitis was recurring without any apparent underlying cause, pneumococcal and meningococcal vaccination and penicillin prophylaxis was planned by the treating doctor, but initially he did not comply for several years. Currently, he is on prophylactic Penicillin V and has received both pneumococcal and meningococcal vaccinations. He had one further episode after these vaccinations; but none after the

addition of Penicillin V (last episode in Feb 2005). Neurosurgical repair has been postponed because of the differing opinions in the face of lack of expertise and resources, no recurrence after addition of antibiotic and vaccine prophylaxis, and above all the patient's own desire not to undergo surgery at the moment.

## Discussion

Episodes of recurrent bacterial meningitis are potentially life-threatening events. The repeated hospital admissions and multiple invasive investigations also take their toll on the patient both psychologically and financially. This is especially true if the underlying cause remains undetected even after a series of investigations.

Our patient probably had the maximum number of recurrences of meningitis ever reported in the literature. Each episode can cause serious neurological sequel and even death, and it is interesting to note that our patient did not have a single complication despite several episodes.

Recurrent bacterial meningitis has significant clinical implications as it signals the presence of an underlying pathology; this may either be an immunological disorder or a structural defect in the craniospinal axis. Defects or deficiency in antibody production, splenic malfunctions, human immunodeficiency virus (HIV) infection, early-phase complement deficiencies of classical (C1q, C1rs, C2, C4, and C3) or alternative pathway are associated with opsonophagocytic dysfunction, increasing the risk of invasive infections caused by polysaccharide-encapsulated organisms, particularly pneumococci<sup>5</sup>. Repeated attacks of pneumococcal meningitis and otitis media have been described in a four year old girl with low C3 and CH50 values<sup>6</sup>. Deficiency of the terminal complement components (C5-C8) may lead to recurrent *Neisseria meningitidis* (and *N. gonorrhoea*) infections, including meningitis<sup>7</sup>.

However, evaluation for immunodeficiency is not indicated in most patients with bacterial meningitis, particularly when the disease occurs in a previously healthy individual, when there is no history of other recurrent systemic infections, or risk factors for HIV infection are not present<sup>5</sup>. Our patient did not have any obvious immunological defects as evidenced by clinical examination and routine laboratory tests.

Bacterial migration occurs, through congenital or acquired pathways from the skull or spinal dural defects, into the central nervous system (CNS) and can cause recurrence of meningitis. Various structural defects like skull fracture with dural tear, CSF rhinorrhoea or otorrhoea, Mondini dysplasia with CSF fistula, stapedectomy, and lumbosacral defects have been found to be associated with recurrent meningitis. Although our patient had no CSF leak, the high resolution CT scan showed a focal bony dehiscence, communicating with the nasopharynx, in the right cribriform plate adjacent to the crista galli.

Bacterial specificity can lead to significant clues with regards to the cause of the recurrent meningitis: A pneumococcus or hemophilus suggests cranial dural defects, *E. coli* or other gram negative bacilli suggest spinal dural defects, and meningococcus suggests immunologic deficiency. Organisms associated with recurrent meningitis secondary to cerebrospinal fluid leaks are commonly found in the upper respiratory tract<sup>5</sup>. In our patient the responsible organisms were *Streptococcus pneumoniae* and *Neisseria meningitidis*, both normal bacterial flora of the nasopharynx. Meningococcus colonizes the nasopharynx of 5%-15% of individuals in areas of nonendemicity, and a larger proportion of individuals may be colonized during epidemics<sup>5</sup>.

Meningitis may occur after years of the incident trauma; Tokisato et al<sup>8</sup> reported a case of bacterial meningitis in a patient with CSF rhinorrhoea which took place 20 years after the initial head injury. The history of head injury dates back 22 years prior to the first episode in our patient, but he never had features of CSF leak. The diagnosis and detection of underlying structural lesion is difficult if there is no evidence of CSF leakage, especially in a resource-poor setting. Some cases in one study required repeated imaging and even explorative surgery to find out the anatomical lesion<sup>9</sup>.

The role of prophylactic antibiotics or immunization for the prevention of bacterial meningitis in patients with skull injuries has been controversial. In one patient with recurrent pneumococcal meningitis, one further episode occurred after immunization. In our patient also, the 12<sup>th</sup> episode occurred after both pneumococcal and meningococcal vaccination. It is thought that the organisms bypass the circulating serum antibodies by direct invasion of the meninges from the nasopharynx.<sup>10</sup>

In conclusion, the long clinical course of our patient highlights that CNS infection may develop long after the history of trauma and even in the absence of CSF leakage. Clinicians should be aware of the fact that routine imaging of the skull may not detect minor skull base abnormalities as evidenced in this case. Moreover, whenever a patient presents with unexplained meningitis it may be worthwhile to think about any factors that may have precipitated it.

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