

## Recurrent meningitis in children

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Recurrent meningitis indicates pyogenic meningitis occurring on two or more occasions after an intervening period of full convalescence<sup>1</sup>. This differs from 'relapse' or 'recrudescence' of meningitis, where the disease recurs without full recovery of the patient.

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 overcome host defences to gain access to the CNS and cause an infection<sup>2</sup>.

Incidence of recurrent meningitis has not been well studied. Kline reviewed the world literature from 1978-1988 and found 47 patients with recurrent meningitis<sup>3</sup> of whom 33 (70%) were under 18 years of age at the time of diagnosis. Predisposing factors included a congenital CSF fistula in 55% of cases, traumatic or surgical CSF fistula in 17%, immunodeficiency in 21% and unknown cause in 6%<sup>3</sup>. Drummond et al. reported 6 (1.3%) children with recurrent meningitis over an eleven year period after reviewing 463 cases of meningitis. Of these, two had temporal anatomical abnormalities and 2 had immunological deficiencies; no underlying aetiology for recurrent meningitis was identified in the other 2 patients<sup>4</sup>.

Recurrent meningitis in childhood should always prompt a search for an underlying cause as it is usually associated with a predisposing factor such as an immune-deficiency disorder or a cranio-spinal defect. Bacteria can enter the subarachnoid space by migrating along congenital tissue planes or acquired anatomical pathways<sup>5,6</sup>. Alternatively, the usual blood stream spread may be facilitated by an immunological deficiency, which makes the host defences inadequate barriers against potential bacterial pathogens<sup>5</sup>.

Although several immunodeficiencies may be associated with recurrent meningitis, the most common are immunoglobulin deficiency, complement deficiency and hyposplenism<sup>5</sup>.

Recurrent meningitis has been reported in X-linked agammaglobulinemia as well as in selective deficiencies of IgG, IgA, and IgG2<sup>7,8</sup>. It has also been rarely reported in children with common variable immune deficiency (CVID)<sup>9</sup>. Deficiency of the IgG2 subclass is not rare in young children and often resolves spontaneously. It is not commonly associated with recurrent bacterial meningitis, although a case of recurrent pneumococcal meningitis in a 3 year old boy with low concentrations of IgG2 specific pneumococcal antibodies has been described<sup>12</sup>. Furthermore, children with humoral immunodeficiencies often have infections in other sites such as ears, lung, and skin. The presence of a minor antibody deficiency should not preclude the search for a cranial defect<sup>13</sup>.

Links between recurrent meningitis and deficiencies of both the classical and alternative complement pathways are well described<sup>5,7,10</sup>. In these deficiencies the most common pathogen is *N. meningitidis*. Repeated attacks of pneumococcal meningitis and otitis media have been described in a four year old girl with low C3 and CH50 values<sup>11</sup>.

Splenic hypofunction is associated with an increased risk of septicaemia and meningitis with encapsulated bacterial pathogens.

When CSF communicates with the middle ear cavity, nose or nasopharynx, there is potential for CSF bacterial contamination and meningitis. Acquired traumatic temporal bone fractures are the most common cause of a CSF leak into the middle ear. A fracture of the temporal bone may result in a disruption of the tegmen with a concomitant tear in the middle fossa dura, resulting in CSF leak. Although a chronic CSF fistula can result from temporal bone fracture, the majority of CSF leaks heal spontaneously<sup>14</sup>.

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Congenital temporal bone anomalies such as the Mondini malformation can also predispose to CSF fistulae<sup>15</sup>. The Mondini malformation is due to a disruption in the embryonic inner ear development during the 7<sup>th</sup> week of gestation resulting in a shortened cochlea, an enlarged vestibule, sensorineural hearing loss and a CSF leak. CSF may leak into the middle ear at the deficient oval window. Congenital CSF leak may also occur within the bony labyrinth. A child with recurrent meningitis and congenital sensorineural hearing loss should be strongly suspected of having a translabyrinthine CSF fistula<sup>4</sup>. CSF fistulae can originate from the anterior skull base.

CSF rhinorrhea in children is more commonly due to developmental defects than trauma. Such defects include ethmoidal encephalocoeles, dysplasia of the cribriform plate and CSF leakage via an empty sella. Recurrent meningitis has also been reported in children with dermal sinus tract associated with a dermoid cyst within the lumbosacral spinal canal<sup>6</sup>.

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

Bacterial specificity can lead to significant clues regarding the cause of the recurrent meningitis: A pneumococcus or haemophilus 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 CSF leaks are commonly found in the upper respiratory tract<sup>15</sup>. Meningococcus colonizes the nasopharynx of 5-15% of individuals in areas of non-endemicity, and a larger proportion of individuals may be colonized during epidemics<sup>16</sup>.

The diagnosis and detection of the 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>6</sup>.

Investigation of patients with recurrent bacterial meningitis should include a complete history, stressing any previous head trauma or surgery on the nose, paranasal sinuses, or ear. An immune screen

should be carried out. To rule out a congenital abnormality of the ear resulting in sensorineural hearing loss, audiometry is important.

If CSF leakage is suspected, the positive identification of the leakage can take different forms. Traditional testing of nasal discharge or middle ear fluid for its glucose content is unreliable and should be replaced by testing for  $\beta$ 2-transferrin<sup>17</sup>, or  $\beta$ -trace protein (prostaglandin D synthase)<sup>18</sup>.

Thin section cranial computed tomography offers a relatively easy, reliable, and non-invasive method of delineating anatomical defects in recurrent meningitis<sup>19</sup>. Axial cranial computed tomography may fail to identify defects in the basal ethmoidal area and cribriform plate and so give false reassurance, whereas coronal thin sections show detailed anatomy of the anterior cranial fossa and identify most skull defects. Although the CT scan may demonstrate a bony defect and suggest the site of the CSF leakage, the additional technique of cisternography may be needed to positively identify the leak. CT cisternography is currently the most reliable technique for the accurate localization of CSF leakage and is replacing radioisotope cisternography as the preferred method in many centres<sup>20</sup>. MR imaging is a sensitive and accurate technique for detection of CSF leakage even in patients who are not actively suffering leakage at the time of evaluation<sup>21</sup>. It is also non-invasive, offers excellent anatomical detail and has no radiation risk.

The role of prophylactic antibiotics or immunization for the prevention of bacterial meningitis in patients with skull injuries is controversial. In one patient with recurrent pneumococcal meningitis, one further episode occurred after immunization. It is thought that the organisms bypass the circulating serum antibodies by direct invasion of the meninges from the nasopharynx<sup>22</sup>.

Immunologic deficiencies should be corrected where possible. Anatomic abnormalities must also be repaired. Anterior skull base defects are best repaired via a frontal craniotomy. Congenital and acquired CSF through the temporal bone can be approached either via a transmastoid or middle cranial fossa approach, as the situation dictates.

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