Case Reports

Recurrent Meningitis in Association with Common Variable Immune Deficiency

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Recurrent meningitis in children is unusual and usually associated with a predisposing factor like immune-deficiency disorder or cranio-spinal defect. We report a case of recurrent meningitis in association with Common Variable Immune deficiency.

Keywords: *Common variable immune deficiency, Meningitis, Recurrence.*

Recurrent meningitis in childhood should always prompt a search for an underlying cause. Meningitis is usually acquired by the spread of blood-borne bacteria into the cerebrospinal fluid (CSF). However, if more than one episode has occurred, other possible routes of entry should be considered. Bacteria can gain entrance to the subarachnoid space by migration along congenital tissue planes or acquired anatomical pathways(1,2). Alternatively, the usual hematogenous spread may be facilitated by an immunological deficiency, which makes the host defences inadequate barriers against potential bacterial pathogens(1). We describe a child with recurrent episodes of bacterial meningitis who was investigated for both immunodeficiency and an anatomical defect.

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Case Report

An 8-year-old boy presented with pneumococcal meningitis. He responded to intravenous ceftriaxone and vancomycin. The previous year he had been treated for pneumococcal meningitis as well. He had made a good recovery from this illness and there had been no apparent sequelae. He had previously suffered from frequent ear infections with chronic discharge, and upper respiratory tract infections. He also had occasional bouts of diarrhea. He had chickenpox with severe scarring at 6 years of age. There was no significant family history, and his 3-year-old sibling was well.

Investigations were carried out for an underlying cause during his convalescence. A CT scan of the sinuses and mastoids demonstrated a persistent collection in the left mastoid antrum, representing chronic mastoiditis. In addition, the posterior wall of the antrum, separating the mastoid from the central nervous system, was very thin. Abdominal ultrasound scan showed normal splenic size.

Measurement of total immunoglobulins (Ig) revealed pan-hypogammaglobulinemia with IgG 1.5 g/L (normal range 5-15), IgM <0.1 g/L (0.5-2), IgA < 0.1 g/L (0.2-2.5), IgE < 2.0 IU/mL (<52). He also had abnormal specific antibody responses (Measles IgG-Negative, Mumps IgG–Negative, Rubella

IgG-positive, Tetanus IgG-negative, and Varicella Zoster virus IgG-positive). T lymphocyte subsets were normal. Complement studies were normal, an HIV antibody test was negative, and a nitroblue tetrazolium test was normal.

Genetic immune defects, such as X linked hypogammaglobulinemia were ruled out by molecular immunological studies, and a diagnosis of common variable immune deficiency was made. He was commenced on regular, 3-weekly courses of intravenous immunoglobulin, and penicillin prophylaxis. He has made a full recovery and is now making good progress.

Discussion

The incidence of recurrent meningitis has not been well studied. Kline reviewed the world literature from 1978-1988 and found 47 patients with recurrent meningitis(3). Of these patients, 33(70%) are <18 years old 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%(3). Drummond, *et al.*(4) reported 6 (1.3%) children with recurrent meningitis over an 11-year period after reviewing 463 cases of meningitis. Of these, two were diagnosed with temporal anatomical abnormalities, 2 with immunological deficiencies and no underlying etiology for recurrent meningitis was identified in the remaining 2 patients(4).

Children with immunodeficiencies are at increased risk from hematogenous spread of bacteria to the meninges. Although a number of immunodeficiency conditions may be associated with recurrent meningitis, the most common causes are immunoglobulin deficiency, complement deficiency and hyposplenia(1).

Recurrent meningitis has been reported in the immunoglobulin-deficient condition X-linked agammaglobulinemia as well as in selective deficiencies of IgG, IgA, and IgG2(5,6). Common variable immune deficiency (CVID) represents a heterogeneous group of disorders, which usually present in the 2nd or 3rd decades of life. Recurrent meningitis in association with CVID has not been reported before. Patients with CVID may have normal or decreased numbers of B cells. In contrast to X-linked agammaglobulinemia the immunoglobulin levels are low rather than absent. Clinical presentations are typical of humoral immune deficiencies, with poor responsiveness to antigens. Associated T-cell dysfunction has been reported, but nevertheless patients usually benefit from intravenous immunoglobulin replacement therapy.

Links between recurrent meningitis and deficiencies of both the classical and alternative complement pathways are well-described(1,5,7) In these deficiencies the most common pathogen is *N. meningitidis*. Splenic hypofunction is also associated with an increased risk of septicemia and meningitis with encapsulated bacterial pathogens. However, minor immunodeficiencies like selective IgA deficiency and IgG2 subclass deficiency are not rare, but not commonly associated with recurrent meningitis. The presence of minor antibody deficiency should not preclude the search for anatomical defect(8).

When CSF communicates with the middle ear cavity, the nose or the 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(9).

Congenital temporal bone anomalies like the Mondini malformation can also predispose to CSF fistulae(10). The Mondini malformation is a consequence of a disruption in the embryonic development of the inner ear during the 7th week of gestation. This results in a shortened cochlea, an enlarged vestibule, and sensorineural hearing loss, with a CSF leak at the modeolus. 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(4).

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 encephaloceles, dysplasia of the cribiform 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(2).

Conclusion

It is important to assess the etiology of recurrent meningitis to provide optimal management to prevent further recurrences. All children with more than one episode of meningitis should undergo a thorough evaluation by appropriate neuroimaging and immune function studies.

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