Recurrent Bacterial Meningitis and Impaired Host Defences

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SUMMARY: Recurrent pyogenic meningitis is uncommon. Its aetiology is often associated with impaired host defence mechanisms. Two such examples are discussed. Case 1 resulted from an anatomical defect and Case 2 a defect of the complement system.

Introduction

Recurrent bacterial meningitis suggests a compromised host immune system (1), and where the source is pneumococcal anatomical defects are common. Fifty percent of such cases will have a cranial or inner ear defect (2). Moreover, 80% of central nervous system infections in patients with cranial and anatomical defects will be due to *Streptococcus pneumoniae* (3).

Coronal thin section cranial Computed Tomography (CT) has been found to be a useful investigation in such cases (1), allowing definitive surgical repair and obviating the need for vaccination or prophylactic antimicrobials.

Deficiencies of the complement cascade are also associated with recurrent meningitis and when the defect lies in the terminal components, *Neisseria meningitidis* is often the organism responsible (5).

In cases of recurrent meningococcal meningitis, therefore, a search should be made for evidence of defective complement function since in such cases immunity may be improved by vaccination and antimicrobials.

Two cases are described which illustrate these points.

Case Reports

Case 1

A 40 year old white male presented requesting further investigations. He had suffered 4 attacks of culture-proven pneumococcal meningitis at the ages of 14, 15, 32 and 37 years. He had also suffered pulmonary tuberculosis aged 16 years and measles, chicken-pox and jaundice as a young child. He had received pneumococcal vaccine at the age of 34 years. During his most recent admission with meningitis cerebrospinal fluid (CSF) analysis, microscopy, culture and pneumococcal antigen assay had confirmed the diagnosis. Conventional computed tomography of the

Fig 1. Thin section direct coronal computed tomographic scan showing defect to the left of the midline in the anterior ethmoidal region.

head had been reported as normal. Thereafter he had been commenced on prophylactic penicillin and advised to have annual pneumococcal vaccination.

Further enquiry revealed two episodes of trauma of possible relevance. Aged 4 years, he had been involved in a road traffic accident when he had sustained bilateral periorbital bruising and may have been concussed. Aged 11 years he had fallen from an aerial runway pulley-ride sustaining a nasal fracture. On neither occasion had there been evidence of more serious injury. Specifically there was no history of CSF leak or of anosmia.

Physical examination at this stage revealed no systemic or neurological abnormalities. Normal laboratory investigations included a full blood count; differential white cell count; blood films; erythrocyte sedimentation rate; serum urea and electrolyte estimation; liver function tests; blood glucose; serum protein electrophoresis and serum immunoglobulin estimations. Chest X-ray revealed old calcification in the right upper lobe but was otherwise normal. Skull and facial X-rays were normal. He underwent direct coronal 2mm section CT scanning of the anterior cranial fossa and this re-

vealed a small defect at the left of the midline in the anterior ethmoidal region (Fig 1).

This was identified at craniotomy and closed with an autologous pericranial graft. Post-operatively he made an uneventful recovery with preservation of his sense of smell.

Case 2

A 20 year old male presented acutely with a one day history of headache, fever and vomiting. Physical examination revealed a pyrexia of 39.5 and a confluent macular rash over the trunk and legs. Neck stiffness was noted but no other neurological disturbance was apparent. No impairment in conscious level was apparent. Ear, nose and throat examination was unremarkable. Lumbar puncture showed normal pressure and gram staining revealed numerous polymorphs but no bacterial identification could be made. CSF protein was 2.1 g/L and the CSF glucose was low (2.2 mmol/L).

Treatment was commenced with intravenous benzylpenicillin and chloramphenicol and culture of the CSF subsequently grew *Neisseria meningitidis* group Y Type 14.

He made an uneventful recovery.

During convalescence, further history was obtained of past episodes of meningococcal meningitis (group B) in 1980 and 1982 with a possible history of meningococcal septicaemia aged 15 months. In addition, one of his five siblings had died of meningitis five months prior to this admission.

Further questioning revealed that the family had been investigated for immunodeficiency and three out of six children found to be deficient in the C7 component of the complement cascade.

His immunological status was checked and homozygous C7 deficiency confirmed.

He had been previously vaccinated against meningococcus groups A and C.

Discussion

The past history of trauma and the implication of *Streptococcus pneumoniae* in each episode of meningitis in Case 1 suggested an anatomical rather than an immunological defect. This was supported by the normal haematology and biochemistry results. The value of thin section direct coronal cranial CT scanning in identifying such defects is now well documented (1, 4) and allowed definitive diagnosis of the underlying defect in this case.

The patient had received pneumococcal vaccination probably 14-valent, but nonetheless suffered a further bout of pneumococcal meningitis 3 years later. A new 23-valent vaccine (Pneuvax-2), has recently been licensed for use in the UK. Its use has been recommended for those with special risk of pneumococcal disease due to several other causes but makes no mention of those with an underlying anatomical defect (6). Others have reported the ineffectiveness of vaccination and antimicrobial prophylaxis in such patients (1).

In summary, recurrent pneumococcal meningitis should prompt a search for remedial underlying anatomical cause. The best imaging technique for this is currently thin section direct coronal cranial CT scanning.

Deficiency of complement components and the subsequent effects on impaired resistance as in Case 2 have been extensively reviewed (5, 7, 8). The prevalence in the general population is estimated to be around 0.3% (9).

Homozygous patients with deficiencies of terminal complement components (C5C9) show an increased susceptibility to infection with meningococci and have several epidemiological characteristics that differ markedly from their complement-competent counterparts with later age of presentation, greater relapse rate, differing sero-group prevalence and, interestingly, decreased mortality in the hypo-complementaemic population (5).

Screening of selected populations fulfilling some of these criteria have shown deficiencies of terminal complement components in up to 25% of patients presenting with meningococcal disease (9) and have confirmed the increased susceptibility of recurrence.

Heterozygotes for deficiency of C7 and indeed other terminal complement components appear free from clinical disease (Thompson R A, Personal Communication May 1991). Also a patient with multiple normal but measurable complement component deficiencies who suffered recurrent meningococcal episodes has been described (10).

As far as management of these cases is concerned, a high index of clinical suspicion is required particularly in patients presenting with the above epidemiological characteristics. Initial management of hypocomplementic individuals with meningitis is, of course, unchanged. However, long term management remains a problem.

There are theoretical reasons why complement factor replacement may not work, namely short half-life and the development of antibodies (5).

Vaccination with quadrivalent vaccine against groups A, C, Y, and W135, is a logical step although the efficacy of this vaccine is unlikely to be of equivalence to that in normal populations since the essential problems of synthesis of the membrane attack complex persist, owing to absent terminal complement factors.

Opsonization and phagocytosis may however be improved by the cleavage products of the complement cascade proximal to the block and this may be of some clinical benefit by generating C3(a) and C5(a) with their attendant chemotactic values.

The place of prophylaxis in individuals with recurrent meningococcal disease and deficient complement components remains to be proven. One study failed to reveal an increased incidence of spread in the households containing multiple complement-deficient patients within 30 days of presentation of the index case, a

though the same study did suggest an increased spread relative to normocomplementemic households with an index case (11).

The siblings of the patient in Case 2 have, to our knowledge been immunised and advised of their increased risk of meningococcal disease.

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