Management of meningococcal disease

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Abstract

Despite introduction of effective vaccines, meningococcal disease remains a life-threatening illness with significant mortality, morbidity and long term sequelae. Prompt recognition and early treatment with antibiotics and recognition and aggressive management of complications such as shock and raised intracranial pressure are imperative. This article summarizes clinical features, presentation, pathophysiology and diagnostic tests; and focuses in detail on the course and management of the disease. As meningococcal infection has two main manifestations: septicaemia with associated shock; and meningitis, this article mainly addresses management of meningococcal septicaemia and meningitis.

Keywords meningococcus; meningitis; sepsis; shock

Introduction and background

Meningococcal infection, first described by Vieusseaux in 1805 as epidemic cerebrospinal fever, is a disease with significant mortality, morbidity and long term sequelae. *Neisseria meningitidis*, the responsible pathogen is a Gram-negative diplococcus that is a common commensal organism of the human nasopharynx. There are 13 serogroups known to exist, some encapsulated and some unencapsulated. The polysaccharide capsule is associated with pathogenicity. The serogroups A, B, C, Y and W-135 are those most commonly implicated in disease.

The commonest age for disease is in children younger than 5 years. However, disease occurs throughout childhood, and the incidence increases again in adolescence and young adults.

Introduction of conjugate vaccines for serogroup C in much of the developed world has led to a dramatic reduction in the incidence of disease due to serogroup C meningococcus. However, disease due to the other serogroups remains an important cause of morbidity and mortality in both the developed and developing world.

While conjugate vaccines for serogroups A, C, W-135 and Y are available, vaccines widely effective against serogroup B are yet to be developed. One reason for this is that the serogroup B meningococcal capsule is a homopolymer of sialic acid, which is poorly immunogenic in humans due in part to its homology with mammalian neural cell adhesion molecules.

Roughly 10% of the population is colonized with commensal, non-encapsulated *Neisseria*, some of which confer protection against virulent strains. It is described that recent (less than 10 days) acquisition of a pathogenic strain in a susceptible host may lead to invasive disease. Person to person spread occurs by the respiratory route.

There are three main clinical manifestations of disease: meningitis, sepsis and pneumonia. Pneumonia is primarily a disease of the elderly and will not be discussed further.

There may be rapid onset and progression of disease, and death may follow within hours. In as many as 10–15% of survivors, there are persistent sequelae including neurological defects, deafness, amputation of limbs or digits or skin scarring.

Prompt recognition and early aggressive treatment with antibiotics and the recognition of complications such as shock, raised ICP and seizures are imperative.

Risk factors

Risk factors can be stratified into the categories shown in Table 1.

In general meningococcal epidemiology can be divided into endemic infections and epidemic outbreaks.

Endemic disease usually occurs in developed countries, and is usually low level, with an incidence of 1–3 cases per 100,000. The highest prevalence of disease usually occurs during the winter months, associated with increases in the rate of viral upper respiratory infection.

In the developing world, such as in sub-Saharan Africa, epidemic outbreaks occur with an incidence up to 10–100 times higher than that in endemic disease. The predominant organism in this region is serogroup A. Epidemic disease usually occurs during the dry season.

The risk of meningococcal disease is inversely related to age. 49% of cases occur in children less than 2 years of age. In epidemics, older children are more likely to be infected.

Crowding especially among military recruits, or university students is considered a major risk factor.

An association between smoking and increased rate of meningococcal carriage has been demonstrated. Passive smoking has

Risk factors for invasive meningococcal disease

- Geographical location – e.g. meningitis belt sub-Saharan Africa
- Seasonality: winter season in moderate climate zones, dry season in sub-Saharan Africa
- Age (<5 and 15–24 years)
- Overcrowding: poor housing/military/university dormitories
- Active/passive cigarette smoking
- Prior viral respiratory infection (e.g. influenza A virus, RSV infection)
- Inherited complement deficiency
- Close (family/household) contact with index case

Table 1

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been implicated in increasing the risk of meningococcal disease in children.

A recent infection with respiratory viruses has been documented to increase susceptibility to meningococcal infection. Respiratory viruses may disrupt the epithelial barrier and facilitate invasion of virulent meningococci.

In general, antibodies and complement are important in protection from meningococcal infection, and deficiency of either is associated with an increased risk of disease. Terminal complement component and alternative pathway deficiencies have been reported as predisposing to meningococcal disease (Table 2).

Presentation

Although the classical petechial/purpuric rash in a child with fever is highly suggestive of meningococcal disease, up to one-fifth of children have no rash or a non-specific maculopapular rash on presentation. Less specific features such as: fever, cold peripheries, tachycardia and abnormal skin colour present early. The characteristic haemorrhagic petechial/purpuric rash occurs much later than non-specific clinical features and may present up to 24 h after illness onset.

Laboratory findings

Microbiological confirmation is important for disease identification and institution of public health measures. Definitive diagnosis of meningococcal disease is established by isolation of *N. meningitidis*, or its products from a normally sterile body fluid such as blood or CSF. Meningococci are exquisitely sensitive to many antibiotics, with penicillin-resistant strains only rarely reported. Therefore, following administration of antibiotics, culture is rarely positive. Polymerase chain reaction (PCR) assays in whole blood or CSF detect nucleic acids of the pathogen and the test is very specific and sensitive.

Non-specific laboratory tests such as white blood cell count (WBC) and C-reactive protein (CRP) may be elevated suggesting bacterial infection. However, a low/normal WBC and relatively low CRP are adverse prognostic factors in patients with diagnosed meningococcal disease.

Lumbar puncture

A lumbar puncture to diagnose the presence of meningitis is important for the confirmation of meningococcal meningitis. However, the procedure may be dangerous in shocked patients or in patients with raised intracranial pressure (ICP) (Table 3).

Host factor susceptibility and severity

Complement deficiency
Hypogammaglobulinaemia
Hyposplenism
Various genetic factors associated with inflammatory response and coagulation pathway control

Table 2

Contraindications to performance of lumbar puncture

Clinical or radiological signs of raised intracranial pressure	• Reduced or fluctuating level of consciousness (Glasgow Coma Scale score less than 9 or a drop of 3 or more) • Relative bradycardia and hypertension • Focal neurological signs • Abnormal posture or posturing • Unequal, dilated or poorly responsive pupils • Papilloedema • Abnormal 'doll's eye' movements
Cardiovascular instability/shock	• Tachycardia and/or hypotension • Respiratory distress • Toxic/moribund state • Altered mental state or decreased conscious level (GCS < 9).
Extensive or spreading purpura	• Coagulopathy • Platelets < 100 • On anticoagulant therapy
After convulsions until stabilized	
Infection at proposed site of LP	

Table 3

A lumbar puncture should be performed in any stable patient where meningitis needs to be excluded, as long as no contraindications are present.

An urgent cranial CT scan is only justified in a patient with focal neurology or in a patient with unclear cause of coma. It should only be performed once the patient has been stabilized, and patients should be transferred to the CT scanner by an experienced team with full monitoring to detect deterioration. It is dangerous to transfer an unstable critically ill patient to the CT scanner.

Progression

Meningococcal disease in children usually presents in two major clinical syndromes, which determine priorities in management. It should be remembered that these two syndromes may overlap and often occur simultaneously.

Systemic meningococcal disease may become fulminant due to an overwhelming host inflammatory response. The patient rapidly progresses to shock, multi-organ failure and death unless rapid and aggressive resuscitation and organ support is carried out. This presentation occurs in approximately 20% of patients with meningococcal disease, but is associated with a high mortality and morbidity rate (Table 4).

Meningitis is the most common manifestation of meningococcal disease. It often follows a longer period of low-grade bacteraemia and a less fulminant course, with patients exhibiting signs of meningeal irritation. The clinical signs and symptoms of meningitis are headache, fever, vomiting, neck stiffness, positive