An unusual case of neonatal meningococcal meningitis complicated by subdural empyema and hydrocephalus

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Neisseria meningitidis is a leading cause of pyogenic meningitis worldwide, as well as causing large epidemics in parts of Africa. With the dramatic decline in cases of *Haemophilus influenzae* B, *N. meningitidis* has emerged as one of the most common causes of acute bacterial meningitis in children and adults in South Africa. However, it remains an uncommon cause of meningitis in the neonatal period. Subdural empyema together with hydrocephalus has been infrequently described as a complication of meningococcal meningitis.

We report a rare case of neonatal meningococcal meningitis, complicated by subdural empyema and hydrocephalus. To the best of our knowledge only a few cases of neonatal meningococcal meningitis have been reported from South Africa, with none of these cases having the complication of subdural empyema.

Neisseria meningitidis remains an important cause of meningitis in children and adolescents worldwide.[1] Neonatal meningococcal meningitis is uncommon, with a prevalence of only 2/10 000 being reported by the Centers for Disease Control.[2] Subdural empyema development in the course of meningococcal disease in adults is rare, but seems to affect children more frequently.[3] *N. meningitidis* remains a major health problem despite effective antibiotics and vaccination.[4] A 10-year study at the Chang Gung Children's Hospital, Taipei, reported on the clinical spectrum of meningococcal infection in infants younger than 6 months of age; 7 of the 10 were neonates, and 4 of these had subdural empyema as a complication.[4] There has been 1 documented case of intra-uterine infection caused by *N. meningitidis*.[5]

Case report

A 3-week-old male infant was admitted with a 2-day history of fever, lethargy and poor feeding. His mother was known to be HIV-infected; her CD4 count was 264 cells/µl, and she had been started on zidovudine during the pregnancy. The baby was born by normal vaginal delivery at term, weighing 3 610 g. The immediate postnatal period was uneventful and he was commenced on nevirapine prophylaxis at birth. The family lived in a small, overcrowded informal dwelling with three other families, including an 8-year-old school-going sibling.

On examination the infant was poorly responsive with decreased tone, pallor and a temperature of 39°C. No skin rashes or petechiae were noted. Central nervous system examination revealed a full fontanelle but no focal neurological signs. Lumbar puncture was performed (Table 1), and other tests on admission included a full blood count, measurement of urea and electrolytes, liver function tests and measurement of C-reactive protein.

The polyvalent bacterial antigen test was positive for *N. meningitidis,* which was also confirmed on culture and identified as serotype W135 at the National Institute for Communicable Diseases.

The full blood count revealed a white cell count of 3.77×10^9/l (normal 5.5 - 18×10^9/l), a haemoglobin concentration of 7.8 g/dl (normal 11.5 - 16 g/dl) and a platelet count of 163×10^9/l (normal 150 - 400×10^9/l). The C-reactive protein level (295 mg/l) was markedly increased. Urea and electrolyte levels and the results of liver function tests were normal.

The infant was started empirically on intravenous ceftriaxone 500 mg daily, but developed generalised tonic seizures, with no loss of consciousness, 2 days after admission. The seizures were managed with lorazepam and phenobarbitone. A computed tomography (CT) scan of the brain showed dilatation of the ventricles in keeping with hydrocephalus as well as trans-ependymal fluid and rim-enhancing collections in both cerebral hemispheres compatible with empyema. A diagnosis of complicated meningitis with subdural empyema and hydrocephalus was made. On the basis of the cerebrospinal fluid analysis after 10 days of ceftriaxone (Table 1), neurosurgical advice was to continue intravenous ceftriaxone for 28 days and review thereafter.

The patient continued to have seizures, increased tone, scissoring and opisthotonus, and the occipitofrontal circumference increased from 41 cm to 44 cm. A repeat CT scan revealed an active communicating

Table 1. Cerebrospinal fluid findings on days 1, 10 and 28

CSF	Appearance	Microscopy, Gram stain	Cell count				Biochemistry			
			RBCs ($\times 10^{12}$/l)	Poly ($\times 10^9$/l)	Lymph ($\times 10^9$/l)	Culture	Globulin	Protein (g/l)	Glucose (mmol/l)	Cl (mmol/l)
Admission	Turbid	Pus cells ++ Gram -ve diplococci	0	266	28	*N. meningitidis*	+++	4.73	0.2	110
Day 10	Turbid	Pus cells ++ No organisms	0	1 270	110	No growth	+++	4.82	0.5	115
Day 28	Fibrin clot	Pus cells +	400	28	80	No growth	+	1.64	1.8	121

CSF = cerebrospinal fluid; RBCs = red blood cells; Poly = polymorphonuclear leucocytes; Lymph = lymphocytes; Cl = chloride.

hydrocephalus. A ventriculoperitoneal (VP) shunt was inserted, and a CSF specimen was obtained during the procedure (Table 1). The subsequent hospital stay and follow-up to 21 months was uneventful. The patient has delayed motor milestones with inability to walk. The VP shunt is still in place and functional, and the latest CT scan reveals ventriculomegaly but no hydrocephalus. His HIV test has remained negative at 18 months.

Discussion

Acute bacterial meningitis is particularly common during the neonatal period and is associated with high mortality and morbidity including long-term neurological sequelae.[5] Neonates are at increased risk of sepsis because of a relative deficiency in humoral and cellular immunity, as well as in phagocytic function. Infants born at less than 32 weeks' gestation receive little of the maternal immunoglobulin received by full-term infants.[6] Inefficiency in neonates' alternative complement pathway compromises their defence against encapsulated bacteria.[7] HIV-exposed uninfected infants are at higher risk of bacterial sepsis than HIV-unexposed infants as a result of deficiencies in innate immunity, incomplete maternal antibody protection, and increased environmental exposure to pathogens.[8-12] *N. meningitidis, Haemophilus influenzae* B and *Streptococcus pneumoniae* are responsible for the majority of cases of meningitis in children, but are uncommon causes of neonatal meningitis owing to protection from maternally transferred antibodies to the neonate.[1]

N. meningitidis exists as normal flora of the upper respiratory tract and is transmitted by direct contact or via droplets.[13] Studies in the USA and the UK indicate that between 5% and 10% of the population carry *N. meningitidis* in the nasopharynx at any given time.[14] The risk of acquiring infection with *N. meningitidis* is directly related to the nature and duration of contact.[15] Household overcrowding, coexisting viral infection and exposure to tobacco smoke increase the risk.[15] Our patient lived in a small, overcrowded dwelling, with three other families, and a positive contact could therefore not be excluded. The mother was not screened as a carrier.

Transient meningococcaemia is characterised by a short, febrile flu-like episode with a nonspecific rash.[16] When the bacteraemia is not cleared, clinically overt disease develops.

Meningitis is the most common clinical presentation of invasive meningococcal disease, but haemorrhagic skin lesions are present in 28 - 77% of patients and some present with severe persistent shock lasting for more than 24 hours or until death.[17]

Sub-Saharan Africa has a distinctive epidemiological pattern in which *N. meningitidis* occurs in yearly waves, and serogroup A has commonly been associated with these epidemics.[16] Other important clinical serogroups include B, C, X, Y, W-135 and Z. In South Africa, W135 was documented as the most predominant serogroup

in 2011.[15] However children aged under 1 year were at greatest risk of disease caused by serogroups B, W135 and Y.[15]

Neurological complications of bacterial meningitis in children include subdural effusion or empyema, cerebral abscess, hydrocephalus, focal deficits and seizures, which are often seen during the acute stage of the disease.[5] Sequelae occur in approximately 10% of patients with meningococcal meningitis, and permanent neurological deficits include hearing loss.[4] Subdural empyema occurs relatively more frequently in children than adults.[3] Mortality is reportedly less than 10% if patients are alert at the time of admission, but increases dramatically to 75% if the patient is already comatose.[3]

H. influenzae B used to be the commonest cause of subdural effusion, but has now been replaced by *N. meningitidis* because of the universal use of HIB conjugate vaccine.

No definitive guidelines exist regarding the duration of treatment for subdural empyema, but most series report 2 - 6 weeks of intravenous antibiotics.[18] The type of surgical procedure has little impact on outcome, provided it is performed early and allows for complete evacuation of the pus.[18] The optimal duration of antimicrobial therapy for subdural empyema is uncertain. Parenteral antimicrobial therapy is recommended for at least 3 weeks after neurosurgery, followed by 3 weeks of oral therapy.[4]

Conclusion

With the dramatic decline in cases of *H. influenzae* B as a direct result of widespread vaccination with the HIB conjugate vaccine, *N. meningitidis* has emerged as one of the most common causes of acute bacterial meningitis in children. However, it remains an unusual cause of acute bacterial meningitis in the neonatal period, probably because of the protective effect of maternal antibodies. Neonatal meningitis is associated with high morbidity and mortality. Subdural empyema together with hydrocephalus as a complication of meningococcal meningitis has been infrequently described in the literature. Despite the use of ceftriaxone in appropriate doses, to which the organism was fully susceptible, our patient deteriorated and developed complications of subdural empyema and hydrocephalus. Establishing the aetiological diagnosis, as demonstrated in our patient, was vital for correct management of the meningitis and the associated rare complication of subdural empyema and hydrocephalus.

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