Spinal cord infarction and tetraplegia—rare complications of meningococcal meningitis

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A previously healthy 25-yr-old female developed flaccid areflexic tetraplegia, with intact cranial nerve function, 36 h after the diagnosis of bacterial meningitis. Polymerase chain reaction studies of cerebrospinal fluid and blood were positive for Neisseria meningitidis, serogroup B. Magnetic resonance of the cervicothoracic spine revealed increased signal intensity and expansion in the lower medulla, upper cervical cord and cerebellar tonsils. Neurosurgical consultation recommended hyperventilation, dexamethasone and regular mannitol therapy rather than decompressive intervention. The clinical course over the following 12 days was complicated by the development of progressive central nervous and multisystem organ failure with disseminated intravascular coagulopathy. Autopsy revealed cerebral oedema with cystic infarction extending from the medulla to the upper cervical cord and cerebellar tonsils. Flaccid areflexic tetraplegia with spinal cord infarction has not been reported following bacterial infection in an adult. The clinical implications would suggest complete central nervous system evaluation of patients recovering from meningococcal meningitis, since spinal cord lesions, although uncommon, do occur. In those very rare situations where a patient develops significant peripheral neurological deficits, urgent magnetic resonance imaging is warranted, to rule out an infective focus or an underlying anatomical anomaly.

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Potentially pathogenic meningococci are present in 2–10% of the asymptomatic, healthy population.¹ These organisms tend to colonize the nasopharynx as a result of the high carbon dioxide tension and humidity, and the presence of specific receptor substances synthesized in the nasopharynx, to which they adhere.² Invasiveness depends solely on the amount of host-specific anti-meningococcal bactericidal antibody. A history of recent upper respiratory tract infection is common.

Neisseria meningitidis is the most common pathogen associated with acute bacterial meningitis in young adult populations.¹ The prevalence of bacterial meningitis depends on seasonal and geographic factors. In Ireland in 1997 the incidence was reported to be 5.1 per 100 000 population, one of the highest in Western Europe.³ Reported cases peak in the winter months between December and March. The most common serogroup, B, for which there is no commercially available vaccine, has a 9% mortality rate.³

There are very few clinical reports of spinal cord injuries associated with purulent meningitis, although there have been isolated reports of arachnoiditis with secondary vascular compromise to the spinal cord.⁴ The arachnoiditis is a result of a vasculitis with or without capillary thrombosis, or focal haemorrhage within the cord.

Drowsiness, lateralizing neurological signs or cranial nerve palsies may be indicative of severe cerebral oedema or other complications, such as hydrocephalus or venous sinus thrombosis associated with bacterial meningitis. Flaccid areflexic tetraplegia with spinal cord infarction has not been previously reported as a complication following N. meningitidis infection in an adult.

Case report

A previously healthy 25-yr-old female presented to another hospital in a comatose state. Information obtained at the time of presentation indicated she had been drinking alcohol the previous evening, and the following day she had complained of malaise, headache and vomiting, which was attributed to the consequences of alcohol intoxication.
Twelve hours later she was unresponsive, and the Glasgow comatose score was 3 on presentation. Physical examination revealed a peripheral temperature of 38°C, heart rate 106 beats min⁻¹ and arterial pressure 150/80 mm Hg. The pupils were dilated, unequal and unreactive to direct and consensual light. Deep tendon reflexes were absent in the left upper and lower extremities as were plantar responses bilaterally. Laboratory investigations included haemoglobin 12.1 mmol litre⁻¹, white cell count 35×10⁹ litre⁻¹, serum urea 2.5 mmol litre⁻¹, serum creatinine 59 µmol litre⁻¹ and serum glucose 7.6 mmol litre⁻¹. Initial management included the administration of benzylpenicillin 2.4G and cefotaxime 3G intravenously and tracheal intubation with intermittent positive pressure ventilation.

The patient was transferred to this hospital for urgent computer tomographic (CT) brain scan. The differential diagnosis included acute meningitis and subarachnoid haemorrhage. Non-contrast CT of brain revealed no intracerebral space-occupying lesion and there was no evidence of raised intracranial pressure. The pupils were of equal size and were reactive to light. The cerebrospinal fluid (CSF) was turbid at lumbar puncture. Subsequent microscopy confirmed severe, predominantly polymorphic, pleocytosis. Gram stain revealed the presence of Gram-negative diplococci. No organism was cultured, possibly because high-dose antibiotics had been given 2 h previously. Polymerase chain reaction studies of CSF and blood were positive for N. meningitidis, serogroup B.

Patient management included sedation, hypocapnic (PₐCO₂ 4.0–4.5 kPa) artificially controlled ventilation and cefotaxime 2G intravenously every 4 h. The clinical course over the following 12 h was complicated by pupillary dilation and haemodynamic instability attributed to brain stem compression or cerebral oedema and was treated with mannitol and inotropic agents. Repeat non-contrast CT examination demonstrated patent basal cisterns.

Twenty-four hours later, following withdrawal of sedation, the patient was alert and obeyed commands by moving her eyes and tongue. However, neurological assessment at 36 h revealed flaccid areflexic tetraplegia consistent with a lesion at the level of C1, with intact cranial nerve function. A magnetic resonance (MR) scan was performed urgently to rule out a subdural or epidural pyogenic collection. Sagittal views of the cervicothoracic spine revealed increased signal intensity and expansion in the lower medulla, upper cervical cord and cerebellar tonsils. There was tonsillar ectopia with enhancement of the surrounding meninges. The CSF at the foramen magnum was effaced, indicating compression. The fourth ventricle was patent. Neurosurgical consultation recommended dexamethasone and regular mannitol therapy rather than decompressive surgical intervention.

The subsequent clinical course was complicated by the development of pyrexia (temperature 40°C) and leucocytosis (white cell count 28×10⁹ litre⁻¹) 6 days later. No organisms were isolated on cultures. Repeat MR imaging showed persistent abnormality within the structures of the foramen magnum, with effacement of CSF. During the following 24 h, the patient became progressively obtunded and unresponsive with the onset of seizure activity. Inotropic support was initiated to treat haemodynamic instability. Antibiotic treatment was extended to cover possible central nervous system (CNS) Listeria monocytogenes or fungal infection. Over the final 6 days of her illness, she developed progressive CNS and multisystem organ failure and disseminated intravascular coagulation.

Autopsy revealed cystic infarction extending from the medulla to the upper cervical cord. An area of infarction, of similar age, was noted bilaterally in the cerebellar tonsils. The brain was very oedematous. There was no evidence of active CNS infection or residual meningitis. Fibrin deposition at the base of the brain indicated recent meningitis. The cerebellum had widespread hypoxic changes, but the pons was normal. The lungs showed evidence of acute respiratory distress syndrome, and the kidneys showed changes associated with acute tubular necrosis. Autolytic changes were reported in the adrenal glands and liver.

Discussion

Nasal mucosal colonization with N. meningitidis may be followed by consequences ranging from transient bacteremia with no sequelae, to the rare entities of chronic meningococcaemia, clinical meningitis or fulminant meningococcaemia. The incidence of coexisting meningitis and meningococcaemia can range from 12% to 61%. Interestingly, the presence of meningitis has been shown to reduce the risk of meningococcaemia proving fatal. Improved survival rates in recent years have been attributed to increased awareness of the disease, combined with aggressive supportive therapy with volume replacement, artificial ventilation, inotropic support and renal replacement therapy. Third-generation cephalosporins are the recommended first-line agents in acute bacterial meningitis until sensitivity reports are available because of reported resistant strains of Streptococcus pneumoniae in the United Kingdom and mainland Europe.

The development of flaccid areflexic tetraplegia with intact cranial nerve function, 36 h after N. meningitidis infection, suggested the possibility of a subdural or epidural empyema or transverse myelitis at the craniocervical level. MR imaging excluded extrinsic cord compression while the increased signal intensity and expansion in the lower medulla, upper cervical cord and cerebellar tonsils on sagittal views of the cervicothoracic spine suggested transverse myelitis. There was also MR evidence of tonsillar ectopia with enhancement of the surrounding meninges. Transverse myelitis is an extremely rare, monophasic, inflammatory demyelinating illness, with a reported annual incidence of 1.3–4 per million population. Characteristically, acute inflammation of the spinal cord results in flaccid paraparesis or tetraparesis, with a defined sensory level. To
date, the only case report of transverse myelitis complicating bacterial meningitis was in a preterm neonate with group B infection. Transverse myelitis is normally associated with viral infections such as herpes, varicella, Epstein–Barr virus or hepatitis A. It has also been reported in systemic bacterial or atypical infections such as syphilis, mycoplasma or Lyme disease. Although most inflammatory in origin, predisposing conditions include multiple sclerosis and anterior spinal artery occlusion. The differential diagnosis of acute flaccid paralysis would also include Guillain–Barré syndrome, poliomyelitis, central pontine myelinolysis and acute cerebellitis.

Autopsy findings suggested that the cause of tetraplegia in this case was infarction of the craniocervical spinal cord. Histopathological findings dated the spinal cord infarction to approximately 12 h after admission when clinical signs of brainstem compression were noted. MR imaging about this time showed increased signal intensity within the medulla and upper cord and effacement of CSF at the foramen magnum, indicating significant compression of these structures. Of note, there was no mass effect in the supratentorial compartment and fossa, with persistent patency of the fourth ventricle.

The presence of pre-existing tonsillar ectopia may have predisposed this patient to subsequent spinal cord infarction. This anatomical anomaly is well described. In normal asymptomatic patients, the mean position of the cerebellar tonsils ranges from 8 mm above the foramen magnum to 5 mm below it. Up to 14% of the adult population have tonsils extending slightly below the foramen magnum; 5 mm below it is taken as the normal cut-off point. This degree of ectopia is, under normal circumstances, of no clinical significance. If the tonsils are lower than 3 mm, this constitutes a Chiari I malformation—an anomaly with inconsistent clinical findings, which tends to manifest itself in early to middle adult life.

Acute bacterial meningitis superimposed on such anatomy may exacerbate the degree of tonsillar ectopia, because of local tonsillar oedema and the mass effect from the inflammatory process occurring at the foramen magnum level, thus compressing the enclosed structures. The consequent vascular compromise, with ischaemia and infarction of the upper cervical cord and cerebellar tonsils, might be manifest clinically by flaccid areflexic tetraplegia. CT imaging of the base of the skull may have limited application in such patients, because the structures of the foramen magnum may not be adequately seen. MR imaging is recommended as the investigation of choice in any patient with evidence of craniocervical pathology.

Glucocorticoids are now extensively used, especially in the paediatric population, in the treatment of meningitis. There is evidence that they reduce the indices of meningeal inflammation in the CSF, and attenuate the rise in levels of tumour necrosis factor if given before the administration of ceftriaxone to patients with Haemophilus influenzae and S. pneumoniae meningitis. Two studies have suggested that steroid-treated patients have improved neurological and audiological outcomes in meningococcal meningitis. Most studies advocate administering dexamethasone at, or before, the first dose of antibiotic, in order to attenuate the rise in cytokines associated with antibiotic-induced bacteriolyis.

Decompressive surgery was considered as a treatment option in this patient, but was not subsequently performed. To perform foramen magnum decompression on such an unstable patient requires supportive risk–benefit data to be available. However, case reports have described beneficial patient outcomes following emergency decompressive surgery of the craniocephalic region, particularly in cases of spontaneous epidural haematoma. Critical factors for neurological recovery include the vertebral level of cord pathology, extent of pre-operative sensorimotor deficit and time interval between presentation and surgery. Thirty-six hours has been claimed to be the critical operative interval. Emergency surgery should be performed, irrespective of the neurological dysfunction, in cases of spinal epidural abscess.

Furuya and colleagues published clinical trial data on patients with symptomatic cerebellar tonsillar ectopia and compared them to patients with asymptomatic ectopia and to matched controls. The subjects were evaluated with MR studies and precise neurotological examination. Depending on clinical and MR findings, posterior fossa decompression surgery was performed. After the operation, all patients displayed improvement in symptoms and less severe neurotological abnormalities. The authors concluded that tonsillar ectopia, per se, could cause neurological symptoms which were surgically treatable.

References

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