Group B streptococcal meningitis in a middle-aged woman

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ABSTRACT

Group B streptococcal (GBS) infections are increasing in incidence as a cause of serious disease in the adult population. Risk factors for this infection include age, diabetes mellitus, liver disease, history of stroke, breast cancer and HIV infection, which are all becoming more common. We report a patient with severe GBS meningitis who made a good recovery following appropriate treatment, despite a delay in specific diagnosis of the organism. We believe this to be the first case of GBS meningitis in a non-pregnant adult in Australia or New Zealand to be reported in the literature.

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Group B streptococcus (GBS, *Streptococcus agalactiae*) is best known as a cause of neonatal meningitis and septicaemia.[1] Until relatively recently, GBS was not thought to be an important pathogen in non-pregnant adults. However, recent data suggest that GBS may pose a considerable threat to adult health, particularly in older people and those with medical comorbidities.[1-7] It has been noted that the proportion of the elderly population colonised with GBS is similar to the proportion among women of childbearing age, while at the same time the elderly population accounts for over 50% of the GBS mortality in the United States.[4]

We report the case of a 57-year-old woman with multiple medical comorbidities who developed severe GBS meningitis but made a good recovery. We believe this to be the first reported case of GBS meningitis in a non-pregnant adult within Australia and New Zealand.

Clinical record

A 57-year-old woman was found unresponsive at home by a friend and brought to the emergency department by ambulance. The woman had been seen well the previous evening. Her vital signs on arrival at the emergency department are shown in Table 1. On arrival, she was experiencing generalised tonic clonic seizures. She was intubated. Computed tomography of the brain showed a normal appearance. After initial stabilisation, she was transferred to the intensive care unit.

The patient had an extensive past medical history, including chronic alcohol abuse with secondary hepatic impairment, iron deficiency anaemia resulting in a recent hospital admission for congestive cardiac failure, and a history of psychiatric disorders, including paranoia and anxiety. She was also a long-term smoker.

Further examination revealed increased size of the left pupil (5 mm) compared with the right (3 mm), but equal reactivity to light. There was significant neck stiffness, limb rigidity and positive Kernig's and Brudzinski's signs. Reflexes were brisk throughout but more marked on the left side, with clonus and an upgoing plantar reflex noted on the left.

Initial serum biochemical testing revealed mild hyponatraemia and hypokalaemia, with normal renal function, mildly deranged liver function, and a compensated normal anion gap metabolic acidosis. A full blood count revealed anaemia, leukocytosis (with a predominance of polymorphs), and thrombocytopenia. Erythrocyte sedimentation rate and C-reactive protein concentration were both raised. A mild coagulopathy was noted (see Table 2). Blood was cultured.

Initially, the patient was commenced on meropenem (1 g 8-hourly), and acyclovir (750 mg 8-hourly). The anaemia and coagulopathy were corrected with 3 units of packed red cells, 4 units of fresh frozen plasma and 4 units of platelets. Hyperglycaemia was controlled with an intravenous insulin infusion, adjusted to maintain blood sugar levels within the range 4–6mmol/L. Sedation was maintained with morphine and propofol infusions, and a noradrenaline infusion was added to maintain a mean arterial pressure greater than 70 mmHg. A midazolam infusion was also commenced, as alcohol withdrawal was considered a possible contributing factor to the seizures.

On the evening of Day 1 of admission, the patient's temperature rose to 38.1°C. Blood was again taken for culture, and a lumbar puncture was performed. An electroencephalogram demonstrated no epileptiform activity, but low voltage theta and delta waves, consistent with diffuse encephalopathy. Examination of the cerebrospinal fluid (CSF) revealed: white cell count, $18\,000 \times 10^6$ cells/L (with a predominance of polymorphs) (RR $< 5 \times 10^6$ cells); protein, 3 g/L (RR, 0.15–0.5 g/L); and scant gram-positive cocci with leucocytes 3+ on Gram stain. No organisms were subsequently grown on culture of the CSF. Blood cultures grew penicillin-sensitive *S. agalactiae* in three of three bottles. Cultures of blood taken subsequently (after commencement of antibiotics) were negative. GBS meningitis was diagnosed.

On Day 2 of ICU admission, the patient developed respiratory difficulties. A chest x-ray revealed signs of acute pulmo-

Table 1. Vital signs on presentation

Variable	Result
Temperature (°C)	36.2
Heart rate (beats per min)	112
Blood pressure (mmHg)	107/79
Respiratory rate (breaths per min)	33
Oxygen saturation (%)*	100%
Blood glucose level (mmol/L)	7.6

* Breathing oxygen, 10 L per minute. ◆

Table 2. Initial blood test results

Variable	Result	Reference range
Haemoglobin (g/L)	85	115–160
White blood cell count ($\times 10^9$/L)	24.1	4.0–11.0
Platelet count ($\times 10^9$/L)	50	140–400
Sodium (mmol/L)	132	135–145
Potassium (mmol/L)	2.8	3.2–4.5
Urea (mmol/L)	7.3	3.0–8.0
Creatinine (μmol/L)	72	50–100
Albumin (g/L)	33	33–47
Bilirubin (μmol/L)	35	< 20
Alkaline phosphatase (U/L)	130	30–120
γ-glutamyl transferase (U/L)	336	< 50
Alanine aminotransferase (U/L)	50	< 40
Aspartate transaminase (U/L)	78	< 35
International normalised ratio	1.8	0.9–1.3
Activated partial thromboplastin time (s)	45	25–38
C-reactive protein (mg/L)	182	< 5
Erythrocyte sedimentation rate (mm/h)	84	< 19
pH	7.42	7.35–7.45
$PaCO_2$ (mmHg)	27	35–45
PaO_2 (mmHg)	84	75–100
Bicarbonate (mmol/L)	18	22–33
Lactate (mmol/L)	3.1	0.7–2.5
Anion gap (mmol/L)	11	4–13

nary oedema, which was thought to be neurogenic in origin, and the patient was started on a hypertonic saline infusion to maintain a serum sodium concentration > 145 mmol/L.

Once GBS meningitis was diagnosed, the patient was treated with ceftriaxone (2 g intravenously twice daily) and dexamethasone (10 mg 6-hourly). Her condition began to improve on Day 3 of admission. The propofol infusion was ceased on Day 3, and further sedation was achieved with morphine and midazolam infusions alone. Sedation was completely withdrawn on Day 5, and she was extubated on Day 6. Computed tomography of the head the following day demonstrated bilateral new areas of hypodensity in the frontal lobes, consistent with ischaemic brain injury. Increased tone was still noted in all limbs, with tone greater on the left compared with the right, and bilateral upgoing plantar reflexes. The patient was able to respond appropriately to questioning, although she remained disoriented. The improvement continued, and she remained afebrile from Day 7. She was transferred to the ward on Day 10, and to a rehabilitation facility on Day 42, requiring assistance with mobilisation and activities of daily living (such as toileting, dressing and feeding).

Discussion

GBS are gram-positive β-haemolytic facultative anaerobes, currently known to include at least eight strains with serologically distinct capsular antigens.[8] They are normally found to colonise both the gastrointestinal and genitourinary tract in up to 40% of adults.[2,4,8] Invasion of colonising GBS is enhanced by numerous pathogenic mechanisms, including adherent surface proteins, invasive capsular antigens, haemolysin expression, and complement inhibition.[8] The most commonly invasive strains in non-pregnant adults are thought to be types Ia and V, closely followed by type III, together comprising over 80% of invasive GBS.[2,4,6]

In our patient, no bacterium was isolated from CSF culture. This was probably because of the timing of the lumbar puncture, which was performed at least 12 hours after antibiotics were commenced. Various methods have been developed to identify organisms when conventional CSF cultures are negative, including immunological testing (latex agglutination), fluorescence labelling, polymerase chain reaction (PCR) testing and reverse line blot hybridisation.[9-11] Currently, none of these methods are routinely used in Australia for GBS identification. However, research is being conducted on a simple and economical method for rapid identification of GBS, involving PCR-based techniques.[9-11] In future, such techniques may enable more rapid diagnosis of this pathogen, and subsequently more rapid treatment.

The greatest risk factor for invasive GBS disease (based on population studies) is diabetes mellitus.[2-6] Other risk factors include increasing age, liver disease, stroke, cardiovascular disease, renal disease, breast cancer, and immunocompromise (including HIV infection).[1-7,12] The incidence of invasive GBS disease is increasing, with recent studies indicating a two- to fourfold increase over the past 20 years.[2-5] In light of the continuing increase in diabetes incidence in the adult population, along with many other risk factors for GBS disease, awareness of this organism as a pathogen is important. GBS infection is well documented in neonates and peripartum women,[1,3,5] and arguably this has been the

driving force behind current research into the organism. However, it is notable that two thirds of deaths from GBS infection occur in men and non-pregnant women.[3,4]

Meningitis (as documented in this case), is a relatively uncommon manifestation of GBS infection,[7,12-15] but the organism contributes to up to 4% of bacterial meningitis cases in adults,[2-4] with up to a third of patients dying as a result.[4,7] More commonly, GBS infection manifests as skin or soft tissue infections (up to ~40%) or bacteraemia of unknown source (up to ~40%), with significant associated morbidity and mortality.[1-6] Our case highlights the possible severity of GBS infection in the non-pregnant adult population, especially those with pre-existing comorbidities. It illustrates the speed with which the infection may progress, and the potential severity of its sequelae. Research is continuing on vaccines against GBS,[1] and, while the main purpose of such a vaccine is neonatal protection,[3] various authors have suggested that its use may also extend to adults at risk of invasive GBS disease.[1-5]

Treatment of invasive GBS disease is penicillin G, with the organism remaining universally sensitive.[2,4,6,8] Alternatively, cephalosporins, vancomycin, meropenem or imipenem may also be used.[2,4,8] Resistance to erythromycin and clindamycin is increasing,[2,4,6,8] and resistance to tetracyclines is found in about 90% of isolates.[8] In patients with penicillin allergy, the preferred drug for treating GBS infection is vancomycin,[2,8] owing to the large base of resistance to other non-penicillin antibiotics. Treatment should be continued for at least 14 days for GBS meningitis, with pneumonia, bacteraemia, and pyelonephritis requiring a minimum 10-day course, and endocarditis and osteomyelitis a minimum 4-week course.[8] It is also important to note that high CSF concentrations of antibiotic are required when treating GBS meningitis, which often necessitates large and frequent doses of antibiotics.[7,8]

Dexamethasone has been shown to be beneficial in decreasing morbidity and mortality in patients with bacterial meningitis, regardless of the causative organism.[16-18] This benefit has been shown when dexamethasone is given shortly before, or with, the first dose of antibiotics, and it has not been shown to cause significant side effects.[16-19] Notably in our patient, dexamethasone was given after antibiotics were commenced. Ultimately, her outcome was favourable, but the current evidence supports use of dexamethasone only before or with the administration of antibiotics.[17,18] Dexamethasone is currently the only adjuvant therapy with proven clinical efficacy.[16] However, further research is required in this area, especially on dosage, duration and timing.[17]

This case is important as a reminder to clinicians to consider GBS infection in patients who are at risk of this disease and have no obvious cause for their condition. We believe this to be the first reported case of GBS meningitis in a non-pregnant adult in Australia and New Zealand.

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References

1 Schuchat A. Group B streptococcus. *Lancet* 1999; 353: 51-6.
2 Farley MM. Group B streptococcal disease in nonpregnant adults. *Clin Infect Dis* 2001; 33: 556-61.
3 Farley MM, Harvey C, Stull T, et al. A population-based assessment of invasive disease due to Group B streptococcus in nonpregnant adults. *N Engl J Med* 1993; 328: 1807-11.
4 Edwards MS, Baker CJ. Group B streptococcal infections in elderly adults. *Clin Infect Dis* 2005; 41: 839-47.
5 Jackson LA, Hilsdon AS, Farley M, et al. Risk factors for group B streptococcal disease in adults. *Ann Intern Med* 1995; 123: 415-20.
6 Tyrrell GJ, Senzilet LD, Spika JS, et al. Invasive disease due to group B streptococcal infection in adults: results from a Canadian, population-based, active laboratory surveillance study – 1996. Sentinel Health Unit Surveillance System Site Coordinators. *J Infect Dis* 2000; 182: 168-73.
7 Domingo P, Barquet N, Alvarez M, et al. Group B streptococcal meningitis in adults: report of twelve cases and review. *Clin Infect Dis* 1997; 25: 1180-7.
8 Edwards MS, Baker CJ. *Streptococcus agalactiae* (group B streptococcus). In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. Philadelphia: Churchill Livingstone, 2005: 2423-31.
9 Ke D, Bergeron MG. Molecular methods for rapid detection of group B streptococci. *Expert Rev Mol Diagn* 2001; 1: 175-81.
10 Dmitriev A, Suvorov A, Shen AD, et al. Clinical diagnosis of group B streptococci by scpB gene based PCR. *Indian J Med Res* 2004; 119 Suppl: 233-6.
11 Kong F, Ma L, Gilbert GL. Simultaneous detection and serotype identification of *Streptococcus agalactiae* using multiplex PCR and reverse line blot hybridization. *J Med Microbiol* 2005; 54: 1133-8.
12 Tung BY, Kowdley KV. Spontaneous group B streptococcal meningitis in a patient with cirrhosis. *West J Med* 1996; 165: 229-30.
13 Barile AJ, Kallen AJ, Wallace MR. Fatal group B streptococcal meningitis in a previously healthy young adult. *Clin Infect Dis* 1999; 28: 151.
14 Waite DC, Alper EJ, Mady BJ. Adult group B streptococcal disease. *Ann Intern Med* 1996; 125: 152-3.
15 Dunne DW, Quagliarello V. Group B streptococcal meningitis in adults. *Medicine (Baltimore)* 1993; 72: 1-10.
16 van de Beek D, Weisfelt M, de Gans J, et al. Drug insight: adjunctive therapies in adults with bacterial meningitis. *Nat Clin Pract Neurol* 2006; 2: 504-16.
17 van de Beek D, de Gans J, McIntyre P, Prasad K. Steroids in adults with acute bacterial meningitis: a systematic review. *Lancet Infect Dis* 2004; 4: 139-43.
18 van de Beek D, de Gans J, McIntyre P, et al. Corticosteroids for acute bacterial meningitis. *Cochrane Database Syst Rev* 2007; 1: CD004405.
19 de Gans J, van de Beek D. Dexamethasone in adults with bacterial meningitis. *N Engl J Med* 2002; 347: 1549-56. ❑