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Case report

Group B streptococcus meningitis complicated by periodic lateralising epileptiform discharges in an elderly patient with type 2 diabetes mellitus

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SUMMARY

Streptococcus agalactiae (group B streptococcus or GBS) is the most common cause of bacterial meningitis in infants, but is rarely the cause in adults. Across all non-pregnant adults it comprises 7% of bacterial meningitis cases, with a mortality rate of 56% in the elderly. Therefore, while rare, GBS should be a part of a patient's differential when initiating antibiotics in adults with chronic illnesses. We report a 78-year-old diabetic female admitted to the hospital with suspected meningitis. Lumbar puncture revealed grossly purulent cerebrospinal fluid (CSF) and she was started on antibiotics for empiric treatment of expected *Streptococcus pneumoniae*. Thirty-one hours post-sampling, the CSF culture results returned positive for beta haemolytic GBS and treatment was altered accordingly. The case was complicated by concomitant periodic lateralising epileptiform discharges which were treated simultaneously. After 14 days of hospitalisation, the patient was discharged to a skilled nursing facility for further recovery.

BACKGROUND

Group B streptococcus (GBS) is a rare cause of bacterial meningitis in adults, accounting only for 7% of cases.¹ However, recognising and appropriately treating GBS meningitis is important, especially in the population greater than 65 years of age due to its mortality rate approaching 56%, which is double the mortality of other types of bacterial meningitis.^{1,2} It is important for physicians to consider GBS meningitis in their differential diagnosis, especially in those with increased risk factors such as the elderly, diabetics, patients with malignancies, HIV, cirrhosis and advanced renal disease.^{3–6} GBS meningitis is found in both immunocompetent and immunocompromised patients, with little differentiation between the two. The majority of GBS infections remain sensitive to penicillin and its derivatives, as well as first and second generation cephalosporins and vancomycin.⁷ There is an increasing number of reports documenting resistance to penicillin, its derivatives as well as to macrolides, clindamycin and tetracyclines.⁸ There is some evidence to show that GBS is inherently resistant to trimethoprim-sulfamethoxazole as well.

Our patient did present with risk factors for GBS meningitis, including her age as well as having type 2 diabetes mellitus. Initially she was started

on broad spectrum antibiotics. After cerebrospinal fluid (CSF) isolates were identified, antibiotics were de-escalated. This case illustrates the importance of including GBS in the differential of chronically ill patients, especially those with concern for meningitis.

CASE PRESENTATION

The patient was a 78-year-old Caucasian woman, with a medical history including type 2 diabetes mellitus, hypertension and gout, who presented to the emergency department with disoriented speech, a temperature of 40°C (104°F), hypertension and tachycardic. There was an initial concern for heat stroke when she was admitted to the hospital considering the high temperature and humidity outside. She was admitted to the general medical floor where she rapidly deteriorated and developed respiratory distress with oxygen saturation declining to 86%. She was placed on non-invasive positive pressure ventilation (NIPPV) and transferred to the critical care unit (CCU). On CCU arrival, the patient's vital signs showed a temperature of 39°C (102.3°F) with her blood pressure spiking to 204/74 mmHg. She remained in sinus tachycardia at a rate of 124 beats/min and respiratory rate of 23 while on NIPPV. Physical exam findings revealed worsening mental status, severe nuchal rigidity and positive Brudzinski's sign (forced flexion of neck causes reflex hip flexion) and Kernig's sign (flexing at the hip and knee at 90° and subsequent knee extension is painful and patient resists).

On initial CCU history and chart review, it was found that she had no recent history of trauma or illness. She was taking amlodipine, atorvastatin, benazepril, calcium carbonate, glipizide, sitagliptin/metformin, insulin glargine and lisinopril at home. Her initial lab values showed multiple abnormalities, including hypokalaemia with a potassium of 3.3 mmol/L, glucose of 11.4 mmol/L mg/dL, Blood Urea Nitrogen (BUN) of 13.57 mmol/L, serum creatinine of 214.86 µmol/L, magnesium 0.64 mmol/L, phosphorus of 0.484 mmol/L, platelets at $86 \times 10^9/L$ and a white blood cell (WBC) at $12.44 \times 10^9/L$.

INVESTIGATIONS

Due to her constellation of symptoms and physical exam findings, meningitis was initially suspected.

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Reminder of important clinical lesson

Empiric ceftriaxone, ampicillin and vancomycin were started as well as intravenous dexamethasone. Empiric rifampin was added to provide coverage for coagulase negative *Staphylococcus* or *Streptococcus pneumoniae* that may be resistant to ceftriaxone. An emergent CT without contrast of the head was done which showed no herniation and was grossly normal. The lumbar puncture was then performed which drained grossly purulent CSF. CSF analysis and culture yielded 9.107×10^9 /L white blood cells (98% neutrophils), 0.0097×10^{12} /L red blood cells, 8.2 g/L protein, 4.4955 mmol/L glucose and 11.4 mmol/L lactic acid. This initial analysis confirmed our suspicion of bacterial meningitis and broad spectrum antibiotics were continued until further analysis was completed, which yielded 1+ streptococci from the CSF.

DIFFERENTIAL DIAGNOSIS

Bacterial meningitis can be difficult to diagnose. Less than 50% of adult patients who later test positive for the infection present with the classic triad of fever, neck stiffness and altered mental state.¹ The most common organisms causing bacterial meningitis vary depending on the age of the patient. For our purposes, the most common organisms (and their attack rate (AR) per 10 000 individuals) for our patient's age range include *Streptococcus pneumoniae* (AR: 1.5), *Listeria monocytogenes* (AR: 0.5), *Haemophilus influenzae* (AR: 0.2), GBS (AR: 0.2) and *Neisseria meningitidis* (AR: 0.1).⁴ A lumbar puncture is routinely performed to diagnose the specific strain causing the bacterial meningitis and to target antibiotic therapy accordingly. In our patient, the standard tests were performed after bacterial meningitis was suspected and the CSF analysis and culture confirmed the infection.

TREATMENT

On day two of admission, the patient was more arousable but still unable to communicate effectively. She was afebrile but remained in acute distress and developed new onset expressive aphasia. She continued to receive intravenous fentanyl for pain control and an insulin infusion, with goal blood glucose of 140–180 mg/dL. Despite repeated intermittent intravenous labetalol doses, she remained hypertensive throughout the day. On day two, despite increasing alertness, she had worsening pulmonary oedema and was unable to lie flat for any extended period, and was intubated and placed on mechanical ventilation in order to facilitate an MRI. Unfortunately, post-MRI, she was unable to be weaned from the ventilator due to both her neurological and pulmonary status.

On day three, the WBC count peaked at 15.03×10^9 /L. The final CSF culture result was beta haemolytic GBS with susceptibility to ampicillin, linezolid, penicillin G and vancomycin. Blood, urine and sputum cultures showed no growth at 3 days. On GBS identification, all antibiotics except ceftriaxone 2 g every 12 hours were discontinued based on the susceptibility data. The patient also began to develop signs of abdominal tenderness, seizure-like movements, such as twitching arms, and new left facial palsy. An emergent electroencephalogram (EEG) was ordered which demonstrated periodic lateralised epileptiform discharges with higher amplitude/frequency on the left side, as well as triphasic waves, which could be related to an encephalopathic process such as metabolic encephalopathy. Single antiepileptic therapy was initiated with levetiracetam 1000 mg intravenous twice daily; however that failed to stop seizure activity on subsequent EEGs and intravenous phenytoin 100 mg three times daily was added for double antiepileptic therapy. The

goal was to treat the patient and decrease or halt the number of discharge events. She was also started on a nicardipine infusion due to her persistent hypertension despite intravenous pushes of labetalol. It is difficult to isolate the source of her persistent hypertension, as she was mechanically ventilated for some time. She did not have any excessive hypercapnia, nor do we believe it was a Cushing's reflex, as she had tachycardia with hypertension and not relative bradycardia and vagal symptoms as one would expect. It is possible that the extent of her meningitis and its associated sympathetic overactivity, whether through pain or damage, was exacerbating and compounding her underlying hypertension and making it more difficult to treat.

A CT of her abdomen was also performed which showed thickening of the distal colon/rectum, correlating with infectious colitis, and she was subsequently started on intravenous metronidazole 500 mg every 8 hours for a total of 14 days.

OUTCOME AND FOLLOW-UP

Four days post-admission, the patient started to have improvement in her WBC to 14.07×10^9 /L, and continued to improve in the coming days. A weaning trial was attempted on day six due to improving mental and respiratory status. The patient passed with a shallow breathing index of less than 50, and was subsequently extubated successfully after 5 days on mechanical ventilation. On the same day, a repeat EEG showed improvements as well. On day ten, the patient was transferred out of the CCU to the medical floor.

Despite being transferred out of CCU to the general medical floor, she continued to have resistant hypertension, likely due to her meningoencephalitis, which continued to be managed with a nicardipine infusion. Eventually, with the addition of five new oral antihypertensive medications, she was weaned off the nicardipine infusion. Phenytoin was also tapered and eventually discontinued before discharge; however, the patient did remain on levetiracetam for 3 months. In total, the patient spent 14 days in the hospital before being discharged to a skilled nursing facility where she received another 11 days of high dose intravenous ceftriaxone. At the time of discharge, the patient had not reported any hearing loss.

DISCUSSION

Based on information collected in the USA between 1990 and 2007, 88% of adult GBS bacterial meningitis patients had at least one chronic condition, most commonly diabetes, which is in line with the risk factors identified earlier.³ In contrast, the most common cause of bacterial meningitis in healthy adults is *Streptococcus pneumoniae*.³ It is important for physicians who suspect bacterial meningitis to assess the risk factors of the patient, not only in terms of the condition itself but also for which organism it could be. It is also critical that patients with suspected meningitis, especially in the elderly population, are initiated on recommended empiric antibiotic therapy based on their age and co-morbidities. For patients over the age of 50 years old in the USA, per the Infectious Diseases Society of America guidelines, the current recommendation is vancomycin plus ampicillin plus a third generation cephalosporin (ceftriaxone or cefotaxime).⁹ Rifampin can be added if intravenous dexamethasone is also given. Starting empiric triple antibiotic therapy will cover for non-resistant GBS; however, due to emerging resistance patterns it is important that a CSF analysis is done and antibiotics tailored to the organism that is identified, or most highly suspected. To delay treatment invites worsening

morbidity and mortality and it is imperative that antibiotics are started as soon as possible.^{9 10}

Patient's perspective

I was working outside and it was warm. I went inside because I felt shaky and hot. It hit me quickly. I was sick in a hurry. I can honestly say I don't know where I picked up that infection. My recovery was very long. I had to spend some time at a skilled nursing facility after hospital discharge to help with my recovery. I did not have any hearing loss as a result of the infection.

Learning points

- ▶ Patients with chronic illness such as diabetes, cancer, pregnancy, acute renal or hepatic failure, or the elderly are at increased risk of group B streptococcus (GBS) meningitis, with a mortality rate of 56% in elderly patients.
- ▶ This case illustrates the importance of taking into consideration chronic illnesses in patients with suspected bacterial meningitis when physicians are determining antibiotic therapy.
- ▶ It is critical that empiric antibiotic therapy is started, especially in the elderly population, which will provide the broadest coverage and includes non-resistant GBS coverage. In the USA, per the Infectious Diseases Society of America, in the 50+ age group, triple antibiotic empiric coverage is recommended including vancomycin plus ampicillin plus a third generation cephalosporin. Other nations and regions will need to tailor their antibiotic regimens based on their own antibiograms.

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the concept for the article, was the treating physician for the patient and performed the interpretation of the results. AP did the planning and the interpretation of the results. Both NG and AP contributed to the revision of the document in response to the reviewers' comments and suggestions.

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