ABSTRACT

Meningitis caused by Streptococcus pneumoniae is associated with severe morbidity and mortality. The occurrence of multi-drug resistant strains of S. pneumoniae is associated with treatment failure of pneumococcal infections. We present a case of multidrug resistant pneumococcal meningitis in a 10 month-old patient. The patient was admitted to the Department of Child Health of the Korle-Bu Teaching Hospital with high grade fever and irritability. She received an 8-day course of vancomycin after empirical treatment failure with ceftriaxone. Subsequently, she was discharged without complications on follow-up. Although resistance to ceftriaxone among Streptococcus pneumoniae in Ghana is rare, our report highlights an instance where an unusual ceftriaxone resistant isolate may be encountered as a cause of invasive disease leading to treatment failure.

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1. INTRODUCTION

Meningitis is inflammation of the protective membranes (meninges) covering the brain and spinal cord. Bacterial meningitis is associated with severe morbidity and mortality worldwide with Streptococcus pneumoniae contributing to a significant proportion of the disease burden [1–6]. The clinical presentation of meningitis caused by S. pneumoniae is similar to other bacterial causes of acute meningitis and include severe headache, photophobia, neck stiffness and fever. Currently, pneumococcal conjugate vaccines have been introduced into the vaccination programmes of many countries including Ghana [7]. However, the vaccines are unlikely to eliminate pneumococcal disease since only a few pneumococcal serotypes are covered by the vaccines [8]. Thus antimicrobial therapy remains important in the era of pneumococcal vaccination. The risk of developing complications is high with S. pneumoniae meningitis and the management of disease is challenged by the existence and spread of multi-drug resistant strains [1]. Here, we report a case of a 10 month-old patient presenting with multi-drug resistant pneumococcal meningitis.

2. Case Description and Diagnosis

A ten month old baby weighing 8.5 kg, presented at the paediatric emergency with a history of fever of 3 days duration. There was no associated cough, diarrhoea, vomiting or loss of appetite. Her mother had administered oral cefpodoxime and arthemether-lumfantrine at home without any improvement. There was no significant past medical or family history of ill health. Her developmental milestones were normal, and she had a complete immunization history including the pneumococcal conjugate vaccine (PCV-13). When examined, she was mildly pale, and febrile (40.2°C). Her respiratory rate was 24 cycles per minute with vesicular breath sounds, and the heart rate 210 beats per minute with normal heart sounds. She was irritable with a supple neck and a negative Brudzinski sign. A working diagnosis of severe malaria, meningitis, sepsis and urinary tract infection was initially made. The patient was admitted and the following tests ordered; Full blood count, blood film for malaria parasites, blood culture, cerebrospinal fluid (CSF) culture and biochemistry, urine culture and biochemistry and a chest x-ray. Empirical treatment was started using intravenous artesunate 200 mg statum and repeated after 12 hours, ceftriaxone 850 mg daily, suppository acetamenophine 125 mg 12 hourly and intravenous fluids. Forty eight hours into treatment, her temperature had come down with one spike during the period (Fig. 1).

Full blood count showed leukocytosis (25.69×10⁹) with neutrophilia (20.98×10⁹ granulocytes) (Table 1). Microscopy for malarial parasites was negative. CSF studies showed a white cell count of 173×10⁶/L mostly polymorphonuclear cells, low glucose (1.7 mmol/l), increased protein of 0.76g/l (Table 1). CSF and blood culture were both positive for Streptococcus pneumoniae. The isolates were resistant to 1 µg oxacillin disc (signifying resistance to penicillin), amoxicillin-clavulanic acid, cepuroxime and ceftriaxone but was susceptible to erythromycin, moxifloxacin and vancomycin. Chest x-ray and urine analysis were normal. Intravenous artesunate was stopped and a decision to persist with ceftriaxone was taken in conjunction with a medical microbiologist, as the patient’s condition had improved on ceftriaxone. However, a note was made to change treatment to vancomycin should the fever recur or patient’s condition worsen. Seventy two hours after admission, the fever (39.6°C) recurred (Fig. 1) with associated irritability.

Treatment was changed to intravenous vancomycin (128 mg 8 hourly). On vancomycin, the temperature peaks dropped sharply and remained normal till the patient was discharged home after 14 days of admission. Vancomycin was administered for a total of 8 days. Subsequent follow up of the patient showed she was in good health without any complications.

3. DISCUSSION

Bacterial meningitis continues to be associated with significant morbidity and mortality worldwide, despite improved antimicrobial therapy and vaccination strategies [1,2]. It is estimated that bacterial meningitis accounts for 170, 000 deaths worldwide [9]. Seventy five percent of the disease burden occur in children under five years of age [1]. If left untreated bacterial meningitis has a mortality rate of almost 100% [2].
Table 1. Laboratory results

<table>
<thead>
<tr>
<th>Test parameter</th>
<th>Value</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FBC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>9.9g/dl</td>
<td>11.0-18g/dl</td>
</tr>
<tr>
<td>Platelets</td>
<td>340×10⁹/l</td>
<td>150-450×10⁹/l</td>
</tr>
<tr>
<td><strong>WBC</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>25.69×10⁹/l</td>
<td>2.5-8.5×10⁹/l</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>3.52×10⁹/l</td>
<td>1.0-3.0×10⁹/l</td>
</tr>
<tr>
<td><strong>Blood film for malarial parasites</strong></td>
<td>No parasites</td>
<td></td>
</tr>
<tr>
<td><strong>CSF studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Hazy</td>
<td>Clear &amp; colourless</td>
</tr>
<tr>
<td>Glucose</td>
<td>1.7mmol/l</td>
<td>2.5-4.0mmol/l</td>
</tr>
<tr>
<td>Protein</td>
<td>0.76g/l</td>
<td>0.15-0.45g/l</td>
</tr>
<tr>
<td>Globulin</td>
<td>Positive</td>
<td>negative</td>
</tr>
<tr>
<td>RBS at LP</td>
<td>10.2mmol/l</td>
<td>0-5×10⁶</td>
</tr>
<tr>
<td>WBC count</td>
<td>173×10⁶</td>
<td></td>
</tr>
<tr>
<td>Gram stain</td>
<td>Gram positive</td>
<td>cocci</td>
</tr>
<tr>
<td>Latex agglutination</td>
<td>Positive</td>
<td>S. pneumoniae</td>
</tr>
</tbody>
</table>

In Ghana, surveillance data indicates *S. pneumoniae* is the most important cause of meningitis [3]. Currently, it is estimated that up to 40% of *S. pneumoniae* display multi-drug resistant phenotypes [10], which is highly variable among countries. In Ghana, a recent study reported MDR prevalence of 87% among pneumococcal carriage isolates [11]. In this case report however, the pneumococcal isolate was resistant to four of the seven antimicrobials tested which highlights the extent of pneumococcal antimicrobial resistance in Ghana. In Ghana, pneumococcal meningitis is treated with ceftriaxone [12]. Like other beta-lactam antibiotics, this drug inhibits bacterial cell wall synthesis by binding to penicillin binding proteins (PBPs) and the mechanism of pneumococcal resistance is by mutations in PBPs 1a and 2x [13]. Evidence from recent pneumococcal studies in Ghana show the absence of pneumococcal resistance to ceftriaxone in the country [11]. This case report however, shows the possible emergence of pneumococcal resistance to ceftriaxone in Ghana. This has important implications for antibiotic treatment of invasive pneumococcal disease in the country. Like our case, a patient in the USA with meningitis caused by intermediate penicillin resistant pneumococcus relapsed after initial response to treatment with ceftriaxone [14]. He was subsequently treated successfully with vancomycin after the isolate was found also to be ceftriaxone resistant. Similarly, in the Netherlands, a meningitis case report in 2012 also highlighted the isolation of a pneumococcal strain that was resistant to ceftriaxone but susceptible to vancomycin [15]. In Italy however a patient with meningitis caused by a ceftriaxone resistant pneumococcus was treated with linezolid and levofloxacin instead of vancomycin [16]. Although levofloxacin as an agent for treating multi-drug resistant pneumococcal meningitis is not well documented, others have suggested that linezolid may replace vancomycin in the management of such cases [17,18].

The Infectious Diseases Society of America recommends ceftriaxone and vancomycin for empirical treatment of meningitis caused by intermediate penicillin susceptible pneumococcal isolates [19]. This is because penicillin concentration levels in the brain are not adequate to kill pneumococcus with intermediate susceptibility. Thus, it is important that minimum inhibitory concentrations are performed for penicillin resistant pneumococcal isolates, which we could not do in this case investigation due to lack of funds. Our findings underscore the need
for surveillance of ceftriaxone resistant pneumococci in Ghana and susceptibility testing of the antibiotic if it is to be used in treating pneumococcal infections in Ghana. With the emergence of pneumococcal resistance to ceftriaxone in Ghana, the indications are that vancomycin will be used in the treatment of invasive pneumococcal infections caused by highly resistant strains like the one in this case report. However, vancomycin is a very expensive drug and not affordable by many Ghanaians. Currently, on the Ghanaian market the cost of 1g of vancomycin is GHC 147 (USD 40) while that of ceftriaxone is GHC 107 (USD 29).

In the Netherland case report, the pneumococcal strain was serotyped and was found to be serotype 19A, a non-vaccine serotype [15]. In our case report we were unable to serotype the pneumococcal strain isolated due to lack of facilities and funds. We however, strongly believe that the pneumococcal strain is a non-vaccine serotype related to introduction of the 13-valent pneumococcal conjugate vaccine in Ghana in 2012, since the patient had received this vaccine.

4. CONCLUSIONS

Our case report shows the emergence of pneumococcal resistance to ceftriaxone which is the mainstay for treating invasive pneumococcal disease in Ghana. There is the need for surveillance of ceftriaxone resistant pneumococci in Ghana and susceptibility testing of the antibiotic if it is to be used in treating pneumococcal infections in Ghana. It is also important that clinicians are aware of the emergence of pneumococcal resistance to ceftriaxone in the country. Our case report highlights the importance of prompt recognition of the clinical signs of meningitis despite the introduction of various vaccination programmes against the disease.

CONSENT

All authors declare that written informed consent was obtained from the parents of the child.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES


