International Journal of Medical and Pharmaceutical Case Reports
5(5): 1-5, 2015; Article no.IJMPCR.19873
ISSN: 2394-109X, NLM ID: 101648033

SCIENCEDOMAIN *international*
www.sciencedomain.org

Cephalosporin Resistant Pneumococcal Meningitis in a Child-A Case Report

Appiah-Korang Labi[1*], Joan Woode[2], Nicholas T. K. D Dayie[3] and Eric S. Donkor[3]

[1]Department of Microbiology, Korle-Bu Teaching Hospital, P.O.Box 77, Accra, Ghana.
[2]Department of Child Health, Korle-Bu Teaching Hospital, P.O.Box 77, Accra, Ghana.
[3]Department of Medical Microbiology, School of Biomedical and Allied Sciences, College of Health Sciences, University of Ghana, P.O.Box KB 143, Accra, Ghana.

Authors' contributions

This work was carried out as collaboration between all authors. Author AKL conceived the idea for the report and participated in the coordination and writing of the manuscript. Authors JW, NTKDD and ESD contributed to the writing and review of manuscript. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2015/19873
Editor(s):
(1) Syed A. A. Rizvi, Department of Pharmaceutical Sciences, College of Pharmacy, Nova Southeastern University, USA.
Reviewers:
(1) Charbell Miguel Haddad Kury, Medicine School of the Municipality of Campos dos Goytacazes, State of Rio de Janeiro, Brazil.
(2) Izabela Korona-Glowniak, Medical University of Lublin, Poland.
(3) Anonymous, University of Sao Paulo, Brazil.
Complete Peer review History: http://sciencedomain.org/review-history/11718

Case Report

Received 1st July 2015
Accepted 6th August 2015
Published 7th October 2015

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.

**Corresponding author: E-mail: guylabi2@gmail.com, appiahl@yahoo.com;*

Keywords: Streptococcus pneumoniae; vancomycin; ceftriaxone; meningitis, Ghana.

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℃). 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 (25.69×10^9) with neutrophilia (20.98×10^9 granulocytes) (Table 1). Microscopy for malarial parasites was negative. CSF studies showed a white cell count of 173×10^6/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, cefuroxime 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℃) 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].

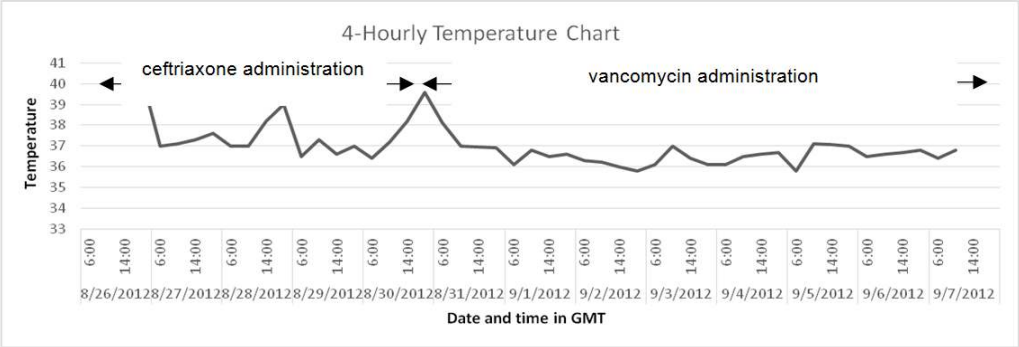

Fig. 1. 4-Hourly temperature chart of patient during admission

Table 1. Laboratory results

Test parameter	Value	Reference range
FBC		
Haemoglobin	9.9g/dl	11.0-18g/dl
Platelets	340×10^9/l	$150\text{-}450\times10^9$/l
WBC	25.69×10^9/l	$2.5\text{-}8.5\times10^9$/l
Neutrophils	20.98×10^9/l	$2.0\text{-}7.0\times10^9$/l
Lymphocytes	3.52×10^9/l	$1.0\text{-}3.0\times10^9$/l
Blood film for malarial parasites	No parasites seen	
CSF studies		
Appearance	Hazy	Clear & colourless
Glucose	1.7mmol/l	2.5-4.0mmol/l
Protein	0.76g/l	0.15-0.45g/l
Globulin	Positive	negative
RBS at LP	10.2mmol/l	
WBC count	173×10^6	$0\text{-}5\times10^6$
Gram stain	Gram positive cocci	
Latex agglutination	Positive for *S. pneumoniae*	

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, 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.

ACKNOWLEDGEMENTS

We thank staff of the Microbiology Unit of the Korle-Bu Teaching Hospital for their support.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Agrawal S, Nadel S. Acute bacterial meningitis in infants and children. Pediatr Drugs. 2011;13(6):385–400.
2. Kim KS. Acute bacterial meningitis in infants and children. Lancet Infect Dis. 2010;10(1):32–42.
3. Owusu M, Nguah SB, Boaitey YA, Badu-Boateng E, Abubakr A-R, Lartey RA, et al. Aetiological agents of cerebrospinal meningitis: A retrospective study from a teaching hospital in Ghana. Ann Clin Microbiol Antimicrob. 2012;11(1):28.
4. Holliman RE, Liddy H, Johnson JD, Adjei O. Epidemiology of invasive pneumococcal disease in Kumasi, Ghana. Trans R Soc Trop Med Hyg. 2007;101(4):405–13.
5. Mhlanga B, Toscano C, O'Loughlin R, Cohen R. Pediatric bacterial meningitis surveillance --- African region, 2002--2008. 2009;493–7. Report No.: 58(18).
6. Mace SE. Acute bacterial meningitis. Emerg Med Clin North Am. 2008;26(2): 281–317.
7. Enweronu-Laryea CC, Boamah I, Sifah E, Diamenu SK, Armah G. Decline in severe diarrhea hospitalizations after the introduction of rotavirus vaccination in Ghana: A prevalence study. BMC Infect Dis. 2014;14(1):431.
8. Weinberger DM, Malley R, Lipsitch M. Serotype replacement in disease after pneumococcal vaccination. The Lancet. 2011;378(9807):1962–73.
9. WHO | Bacterial Meningitis [Internet]. WHO. [cited 2013 Aug 30]. Available:http://www.who.int/nuvi/meningitis/en/
10. Bambeke DFV, Reinert RR, Appelbaum PC, Tulkens PM, Peetermans WE. Multidrug-Resistant *Streptococcus pneumoniae* Infections. Drugs. 2012; 67(16):2355–82.
11. Mills RO, Twum-Danso K, Owusu-Agyei S, Donkor ES. Epidemiology of pneumococcal carriage in children under five years of age in Accra, Ghana. Infect Dis. 2015;47(5):326–31.

12. Ministry of Health. Republic of Ghana Standard Treatment Guidelines. Sixth. Accra, Ghana: Ghana National Drugs Programme. 2010;362-365.
13. Grebe T, Hakenbeck R. Penicillin-binding proteins 2b and 2x of *Streptococcus pneumoniae* are primary resistance determinants for different classes of beta-lactam antibiotics. Antimicrob Agents Chemother. 1996;40(4):829–34.
14. Lonks JR, Durkin MR, Meyerhoff AN, Medeiros AA. Meningitis due to ceftriaxone-resistant *Streptococcus pneumoniae*. N Engl J Med. 1995;332(13): 893–4.
15. Van der Meer H, Van Zwol A, Spanjaard L, Van Furth M. An infant with meningitis caused by resistant pneumococcus: Infection despite vaccination. Netherland Med J. 2012;156(1).
16. Cenderello G, Pontali E, Torresin A, Milano G, Ansaldi F, Feasi M, et al. An unexpected *Streptococcus pneumoniae* strain. J Chemother. 2013;26(3):173–5.
17. Faella F, Pagliano P, Fusco U, Attanasio V, Conte M. Combined treatment with ceftriaxone and linezolid of pneumococcal meningitis: A case series including penicillin-resistant strains. Clin Microbiol Infect. 2006;12(4):391–4.
18. Ramírez P, Sahuquillo JM, Cortés C, Kot P, Bonastre JM. Linezolid as rescue therapy for pneumococcal meningitis. Intensive Care Med. 200724;33(5):924–5.
19. Tunkel AR, Hartman BJ, Kaplan SL, Kaufman BA, Roos KL, Scheld WM, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis. 2004;39(9):1267–84.

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/11718