CASE REPORT

Serotype 15C *Streptococcus pneumoniae* with Third Cranial Nerve Palsy: Unusual Serotype and Presentation

Fatimahtuz Zahrah Muhamad Damanhuri[1,2], Evelyn Aun[2], Revathy Arushothy[3], Thenmalar Kandasamy[1,2], Adillahtul Bushro Zaini[1], Siti Zulaikha Zakariah[4], Siti Norbaya Masri[4]

[1] Department of Pathology, Hospital Sungai Buloh, Jalan Hospital 47000 Sungai Buloh, Selangor. Ministry of Health Malaysia.
[2] Department of Medical, Hospital Sungai Buloh, Jalan Hospital, 47000 Sungai Buloh, Selangor. Ministry of Health Malaysia.
[3] Department of Bacteriology, Institute Medical Research (IMR), 50588 Jalan Pahang, Kuala Lumpur. Ministry of Health Malaysia.
[4] Department of Medical Microbiology and Parasitology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor.

ABSTRACT

We present a unique case of pneumococcal meningitis caused by serotype 15C, a non-vaccine serotype, which is long thought to be non-virulent. Our patient is a young lady with a known case of plaque psoriasis, presented with sudden onset of left oculomotor nerve palsy and severe headache two days prior to admission. The clinical features were initially mimicking of brain tumour and brain aneurysm. The diagnosis of pneumococcal meningitis was confirmed by the bacterial antigen test and genome detection using multiplex PCR from the CSF. The blood culture also grew *Streptococcus pneumoniae*. Serotyping was performed on the isolate using Neufeld's Quellung method and it was identified as serotype 15C. Psoriatic skin disease was identified as a potential source of this invasive infection.

Keywords: Invasive pneumococcal disease, Meningitis, Serotype 15C, *Streptococcus pneumoniae*

Corresponding Author:
Siti Norbaya Masri, MPath
Email: sitinorbaya@upm.edu.my
Tel: +6019-3091810

INTRODUCTION

Streptococcus pneumoniae is an encapsulated gram-positive diplococcus, which causes community-acquired pneumonia, meningitis and bacteraemia. It consists of 98 serotypes with less than 30 serotypes causing invasive pneumococcal disease (IPD) (1). The dominant serotypes causing pneumococcal meningitis among children 14, 6B, 19A, 6A, and 19F, that are covered by the pneumococcal vaccine, Prevenar 13 (PCV13) (1). In Malaysia, the incidence of IPD, including meningitis, is estimated at 3.8 per 100 000 cases each year (1). Pneumococcal meningitis can cause cerebral vascular event such as infarction and vasculitis although the incident is rare (2).

CASE REPORT

A 31-year-old lady with a known case of generalised plaque psoriasis defaulted treatment for 3 years presented with sudden onset drooping of left upper eyelid following two days history of fever and severe headache. She had no neurological symptoms, nor exposed to any persons with upper respiratory tract infection. On examination, there were multiple erythematous scaly plaques over both upper and lower limbs, some were excoriated. Cranial nerve examination revealed isolated left oculomotor nerve palsy; the left eyelid was in total ptosis, with failure of adduction. The left pupil was dilated and did not respond to light. Other cranial nerves were intact and there were no pyramidal signs noted. The Brudzinski's sign was also negative. Vital signs upon presentation were otherwise normal. She never took pneumococcal vaccine and was not on any medication.

This acute presentation of a "surgical third nerve palsy" suggests a space-occupying lesion such as brain tumours and the classical posterior communicating artery (PCOM) aneurysm as a differential diagnosis (Figure 1). Computed Tomography (CT) scan of the brain revealed a normal finding. Subsequently, a CT angiogram was performed; however, it showed no evidence of intracranial aneurysm or arteriovenous (AV) malformation. Laboratory investigation demonstrated leucocytosis with neutrophilia (white cell counts 31.6 $x10^9$/L, neutrophils 60%). She was started empirically with intravenous (IV) Ceftriaxone to cover for possible meningitis. The cerebrospinal fluid (CSF) biochemical

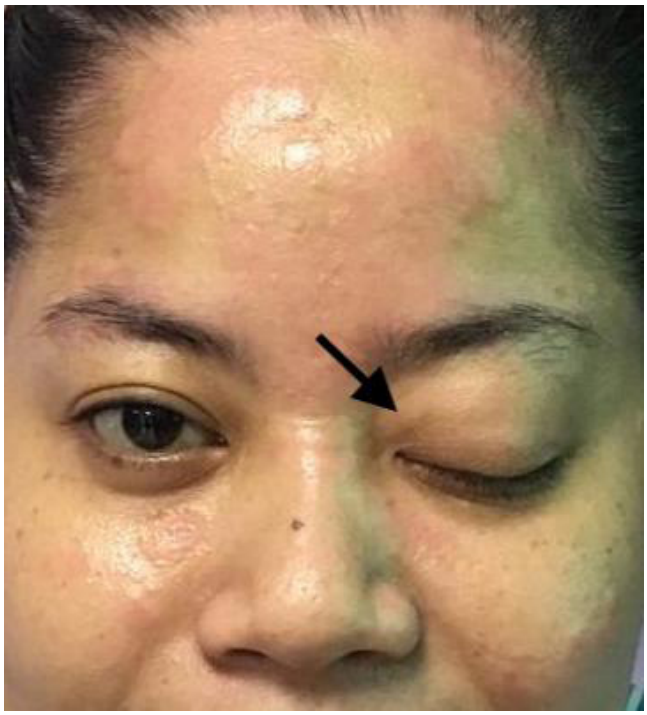

Figure 1: Left eye ptosis secondary to third cranial nerve palsy (arrow)

result showed features of bacterial infection with low glucose (0.08 mmol/L) and high protein (2.3 g/L). However, bacterial culture yielded no growth. Magnetic resonant imaging (MRI) of the brain showed multiple non-enhancing subcortical hyperintensities with patchy leptomeningeal enhancing lesions suggestive of infection-causing vasculitic infarcts at bilateral frontal lobes (Figure 2).

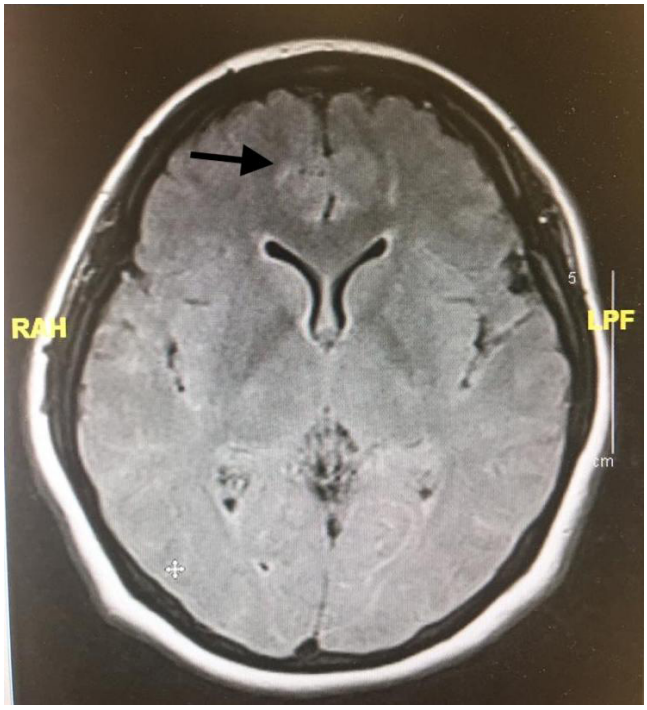

Figure 2: MRI brain at T2/FLAIR showed hyperintensities at bilateral frontal lobes (arrow)

The CSF bacterial antigen test and genome detection using multiplex PCR were positive for *S. pneumoniae*. The blood culture grew the same organism after a one-day incubation period and it was sensitive to penicillin (MIC 0.032 ng/ml) and ceftriaxone (MIC 0.016 ug/ml). The culture isolate was serotyped using Neufeld's Quellung reaction method (Statens Serum Institute, Copenhagen, Denmark) and identified as serotype 15C. The patient responded well to IV C-penicillin 4 mega unit, 4 hourly for 14 days. The full blood count showed normalised leukocyte count after seven days of antibiotic therapy. She was discharged after completion of a two-week course of antibiotic; albeit with residual left eye partial ptosis and a dilated pupil.

DISCUSSION

Serotype 15C *S. pneumoniae* is known as a non-invasive serotype and not covered by the available pneumococcal vaccine. To date, there is no published case report regarding non-vaccine serotype, causing IPD in a patient with underlying psoriasis. The emergence of infection by non-vaccine serotype *S. pneumoniae* after the introduction of PCV13 in 2010 is becoming a topic of interest in recent years. A study done in Japan among patients infected with non-invasive pneumococcus after the introduction of PCV13 showed that 72% of pneumococcal isolates were non-vaccine serotype (3). Meanwhile, a study was done by Shanez N. Ladnani et al., 2018 revealed a rapid increase in non-vaccine serotypes causing IPD in England and Wales with the incidence of 7.97 per 100 000 since the introduction of PCV13 in 2016/17. In Malaysia, despite the lack of immunisation policy of PCV, a recent study reported that 7.8% of IPD is due to non-vaccine serotypes (11A, 11C, 15A, 15B, 15C, 19B, 23A, 8, and 6C) in contrast to a study done by Hannah C. Mc Neil in 2016 reported that no non-vaccine serotype was isolated. This changing pattern is possibly due to natural serotype shift (1).

Even though the natural niche of *S. pneumoniae* in human is in the oropharynx (1), a recent study detected *S. pneumoniae* colonised in the skin of the healthy population (4). In this case, the underlying chronic inflammatory skin disease of plaque psoriasis is probably have predisposed the patient to pneumococcal infection. The skin lesion is associated with injury due to excoriation and inflammation of the skin layer. The disturbance of the normal integrity of the epidermal skin layer possibly facilitates the inoculation of *S. pneumoniae* into the squamous epithelial cells. The organisms subsequently invade the bloodstream and blood-brain barrier, leading to bacteraemia and meningitis (2).

The pneumococcal meningitis is associated with substantial morbidity and mortality. The cerebrospinal fluid (CSF) culture remains as the "gold standard" in diagnosing bacterial meningitis. However, culture technique may lack of sensitivity, particularly when

the patient is pre-treated with antibiotic prior to CSF sampling as occurred in this patient. The low yield of viable organism in addition to the fact that pneumococcus is relatively fastidious organism explain the culture-negative result but positive antigen and PCR tests. Molecular method is more sensitive and specific in diagnosing pneumococcal meningitis allowing early accurate diagnosis, particularly in CSF culture-negative meningitis (2).

Vasculitis is a rare sequela to bacterial meningitis. The non-classical feature of meningitis in our patient further made the diagnosis more challenging. The pneumococci undergo rapid multiplication and release immunogenic products, causing an inflammatory response of the blood vessel (5). The bacteria penetrate the vascular wall and cause vasculitis changes characterised by infarction, thrombosis and vascular narrowing (5) as seen in this patient's brain MRI that revealed vasculitic infarction of the bilateral frontal lobe. However, the exact mechanism of serotype 15C *S. pneumoniae* causing third cranial nerve palsy is still unclear due to the lack of reported cases.

CONCLUSION

This case demonstrates the indication of pneumococcal vaccine in patient with underlying chronic skin disease to prevent IPD. Identification of a high-risk group, case tracing and surveillance studies are important in monitoring the disease and to evaluate the effectiveness of the vaccine. Although the current PCV13 vaccine has significantly reduced IPD worldwide, serotype replacement by non-vaccine serotype should not be ignored as it has a potential to cause invasive disease. Hence a new vaccine with wider serotype coverage is still in demand.

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