Extended Spectrum Beta Lactamase (ESBL) Producing *Neisseria meningitidis* – Isolated from a Case of Pneumonia

O. Sasikumari, Angel Mary George, and K. L. Sarada Devi

**ABSTRACT**

*Neisseria meningitidis* (meningococci) is the most common cause of bacterial meningitis in all age groups. Invasive meningococcal disease manifesting as meningococcal pneumonia is a very rare clinical condition. Here we have a 72 year old male who presented with meningococcal pneumonia and sepsis following a flu like illness. It is notable that he did not develop the syndrome of meningococcemia or its associated complications. This patient was treated with injections of Piperacillin-Tazobactum and Azithromycin because of the unusual antibiotic resistance pattern of the organism. He recovered completely without any sequelae. The meningococci isolated was an ESBL (extended spectrum beta lactamase) producing strain, hence it was resistant to Penicillin and third generation Cephalosporins which are usually used for the treatment of meningococcal infections. This strain was also resistant to Ciprofloxacin. This poses a threat to the community as well, especially because Ciprofloxacin is used as a prophylactic drug by the contacts of the patient and the laboratory workers dealing with the patient’s clinical samples.

**Keywords:** Meningococci; meningitis; ESBL; Ciprofloxacin; Azithromycin; pneumonia.

I. INTRODUCTION

*Neisseria meningitidis* (meningococci) is the most common cause of bacterial meningitis in all age groups. Meningococcal pneumonia is a rare clinical condition, but it is the most common non neurological organ disease caused by this pathogen. Meningococcal pneumonia usually affects the elderly (> 65 years). More than 90 % isolates of *Neisseria meningitidis* are susceptible to Penicillin. In resistant cases third generation Cephalosporins are used, but here we have a case where the organism was resistant to Penicillin, third generation Cephalosporins and Ciprofloxacin.

II. CASE REPORT

A 72 year old male patient presented with history of fever, dry cough and rhinorrhea of four days duration following which he developed purulent expectoration and severe dyspnoea. He was a known case of COPD (chronic obstructive pulmonary disease). A provisional diagnosis of COPD with acute infective exacerbation was made and he was admitted in the Government Medical College, Thiruvananthapuram which is a tertiary care centre in Kerala, South India. His blood pressure was 90/60 mmHg and the pulse rate was 96/minute. He was nebulized with Levosalbutamol and Ipratropium. Injections of Methyl prednisolone were given as supportive measures to combat shock. The patient was immediately started on intravenous Ceftriaxone, Azithromycin and Linezolid. The patient’s hematological investigations were done along with chest X-ray. His sputum sample and blood samples were also sent for Microbiological investigations.

Chest X-ray showed right lower zone consolidation and right middle zone pneumonitis (Fig. 1).

Fig. 1. Chest X-ray of the patient.
The hematological values showed polymorphonuclear
leucocytosis. There was no thrombocytopenia. Other
parameters like renal function, liver function, electrolytes etc.
were within normal limits. Later Oseltamivir phosphate tablet
was also started for the patient.

A. Microbiological Investigations of the Sputum Sample

Macroscopic appearance – Sputum was purulent.

B. Gram Stain of the Sputum

There were plenty of pus cells. Normal flora was absent.
There were plenty of gram-negative cocci in pairs seen both
intracellular and extracellular (Fig. 2).

![Fig. 2. Gram stain of sputum showing intracellular and extracellular gram-
negative cocci in pairs.](image)

Ziehl Neelsen staining of the sputum did not show the
presence of acid-fast bacilli. The sputum was cultured on
Blood agar, Chocolate agar and MacConkey agar.

C. After 24 hours of Incubation

Blood agar and Chocolate agar showed predominant
growth of grey moist minute colonies of 0.5 to 1 mm size.
There was no hemolysis on blood agar. Normal flora was
absent. There was no growth on MacConkey agar.
Gram stain of the growth showed Gram negative diplococci.

The following biochemical reactions were done to identify
the isolate:

- Catalase – positive;
- Oxidase –positive;
- Nitrate -not reduced to nitrite;
- Fermentation of glucose- fermented;
- Fermentation of maltose-fermented;
- No growth at 22 °C.

The common gram-negative cocci of clinical isolates from
which Neisseria spp has to be differentiated are-Acinetobacter spp and Moraxella spp. Some features which
can help in a preliminary identification of the organism are
given in Table I.

Based on the morphology, cultural characteristics
andbiochemical reactions, the isolate was provisionally
identified as Neisseria meningitidis

Microbiological investigations of the blood samples (two
samples) of the patient also yielded pure growth of Neisseria
meningitidis. Since the study centre was a resource limited
setting, the isolate was sent to the public health laboratory of
Thiruvananthapuram. They identified the isolates as
Neisseria meningitidis by Vitek-2 and PCR. Despite these
findings the patient did not show any features of meningitis
or the syndrome of meningococccemia

| TABLE I: IDENTIFICATION OF GRAM-NEGATIVE COCCI |
|-----------------------------------------------|
| Biochemical reaction/other features of identification | Neisseria spp | Acinetobacter spp | Moraxella spp |
|---------------------------------------------------|----------------|------------------|---------------|
| **Morphology and arrangement**                    |                |                  |               |
| Diplococci seen both inside and outside the pus cells |                |                  |               |
|Absent                                            |                |                  |               |
|Coco bacilli scattered or arranged in groups. Not seen inside pus cells |                |Present           |               |
| **Growth at 22°C**                               |                |                  |               |
|Absent                                            |                |Present           |Present        |
|Coco bacilli scattered or arranged in groups. Not seen inside pus cells |                |Present           |Present        |
| **Catalase**                                      |                |                  |               |
|Positive                                          |                |Positive          |Positive       |
|Negative                                          |                |Positive          |Positive       |
| **Oxidase**                                      |                |                  |               |
|Positive                                          |                |Negative          |Positive       |
|Negative                                          |                |Positive          |Reduced to nitrite |
| **Nitrate**                                      |Not reduced     |Not reduced       |Reduced to nitrite |
| **Fermentation of glucose**                       |+               |+/-               |              |
| **Fermentation of Maltose**                       |+               |-                |              |
| **DNAase**                                       |-               |                 |+              |

The antibiotic sensitivity tests were done as per CLSI
(Clinical and Laboratory Standards Institute) guidelines. The
isolates from the sputum and blood samples showed the same
antibiotic sensitivity pattern. They were sensitive to
Azithromycin, Rifampicin, Gentamicin, Meropenem,
Chloramphenicol and Piperacillin-Tazobactum. The
organism was resistant to Penicillin (MIC 0.7) and third
generation Cephalosporins-Cefotaxim and Ceftriaxone (MIC
0.2) showing that it was an ESBL producing strain ESBL
production by meningococci is a very rare phenomenon. The
organism was also resistant to Ciprofloxacin (MIC 0.2). E-
test was done in the treating centre. MIC was confirmed with
Vitek 2 antibiotic sensitivity card.

The treating centre is one of the nodal centres for AMR
(antimicrobial resistance) surveillance of the country, so this
unusual antibiotic resistance pattern was immediately
informed to NCDC (National centre for disease control), New
Delhi. The isolate was sent to NCDC, and they also
confirmed the resistance pattern using molecular methods

D. Treatment

The patient was treated empirically with Injections of
Ceftriaxone, Azithromycin and Linezolid. After getting the
antibiotic susceptibility test reports, Ceftriaxone was stopped,
and the clinicians started injection Piperacillin-Tazobactum.
Oseltamivir phosphate tablet was also given from the second
day of admission. The parental treatment was given for
seven days after which the patient recovered completely
without any sequelae.

III. DISCUSSION

Studies conducted by J. A. Castro-Rodriguez et al in Chile
[3] showed that many respiratory viruses like Respiratory
syncytial virus, Influenza virus, Para influenza virus and
adenovirus have temporal association with meningococccal
disease. The case discussed here also gives a clinical history
similar to flu like symptoms following which he developed
severe respiratory infection. Though the patient was not
investigated for a viral etiology, he was given Oseltamivir
phosphate tablet which could have added to the recovery of

DOI: http://dx.doi.org/10.24018/ejmed.2021.3.3.908
such an elderly patient. In all the studies quoted by J. A. Castro-Rodriguez et al and in their own studies, they have discussed that 10% of the population are carriers of Meningio cocci, hence any viral infection causing abrasion to the respiratory tract will promote the entry of Meningio cocci into the blood. A primary respiratory infection and sepsis due to meningiococci without meningitis is a rare clinical presentation.

Cases of Meningococcal pneumonia seen over 25 years (1974 to 1998) were studied by Winstead JM et al [4]. It was a remarkable study in which they traced only 58 cases from literature showing that this is a rare clinical presentation. The blood cultures were positive for 42(79.3%) cases. All these cases with bacteremia did not develop the syndrome of meningococcemia or its associated complications, similar to our case here. In their study 80% cases were treated with Penicillin and the rest with Cephalosporins.

The meningococcal isolate obtained in our case was resistant to Penicillin and third generation Cephalosporin, Ceftriaxone showing that ESBL producing meningococci has also emerged. This is indeed a new threat to the community because majority of cases of meningococcal infections are treated with Penicillin or third generation Cephalosporins. The isolate was also resistant to Ciprofloxacin which is the common chemo prophylactic drug given to prevent the spread of infection to all the contacts of the patient and laboratory workers dealing with the clinical samples of the patient.

IV. CONCLUSION

The antibiotic resistance pattern of meningococci is changing with time. ESBL producing and Ciprofloxacin resistant strains are emerging, posing a threat for the treatment and chemoprophylaxis of Neisseria meningitidis.

DECLARATION OF INTERESTS

There are no conflicts of interest

ACKNOWLEDGEMENT

We sincerely thank the Public Health laboratory of Thruvananthapuram for helping us to identify the isolate of our case. We also extend our gratitude to the National center for disease control, who helped us to confirm our findings.

REFERENCES

[1] Rosenstein NE, Perkins BA, Stephens DS, Popovic T, Hughes JM, Meningococcal disease. N Engl J Med 2001;344(18): 1378-88.
[2] Matthias Vossen, Dieter Mitteregger, Christoph Steininger-Meningococcal pneumonia, Vaccine (2016) 4364-4370.
[3] J.A. Castro-Rodriguez, L. Jakubson, O. Padilla, D. Gallegos, R. Fasce, P. Bertrand, I. Sanchez, and C. Perret, Many respiratory viruses have temporal association with meningococcal disease, Allergology and Immunopathology (Allergologia et Immunopathologia), 2015-09-01, Volume 43, Issue 5, pp. 487-492, Copyright © 2014 SEICAP.
[4] Winstead JM, McKinsey DS, Tasker S, De Groote MA, Baddour LM, Meningococcal pneumonia: characterization and review of cases seen over the past 25 years. Clin Infect Dis. 2000 Jan;30(1):87-94.