A Case Report of Community Acquired Pneumonia Due to Multi-drug Resistance Pseudomonas aeruginosa Treated with Elores

Danish Menon¹*

¹Noble Hospital, 153, Magarpatta City Road, Hadapsar, Pune 411013, India.

Author’s contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Case Study

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ABSTRACT

Community-acquired pneumonia (CAP) is a common and potentially serious illness associated with considerable morbidity and mortality, particularly in patients infected with Multidrug resistance (MDR) Gram-negative bacilli. After S. pneumoniae, Pseudomonas aeruginosa is the second most common pneumonia causing pathogen followed by K. pneumoniae and S. aureus in India. An alarming rise in the incidence of bacteria resistant even to last resort of antibiotics in recent years, forced clinicians to change antibiotic treatment options in pneumonia. Here we discuss a case of CAP infected with MDR Pseudomonas aeruginosa which is resistant to carbapenems and successfully treated with a new antibiotic adjuvant entity (AAE); ELORES (Ceftriaxone + Sulbactam with adjuvant Disodium edetate).

Keywords: CAP; MDR; Pseudomonas aeruginosa; AAE; ELORES.
ABBREVIATIONS
CAP, Community-acquired pneumonia; AAE, Antibiotic adjuvant entity; MDR, Multidrug-resistant; COPD, Chronic obstructive pulmonary disease; DM, Diabetes mellitus; ESR, Erythrocyte sedimentation rate; AFB, Acid fast bacilli; FOB, Faecal occult blood; BAL, Bronchoalveolar lavage; ANA, Antinuclear antibody; RFT, Renal function test; ESBL, Extended-spectrum beta-lactamases; MBL, Metallo-beta-lactamase; LFT, Liver Function Test; OprD, Outer membrane porin Protein.

1. INTRODUCTION

Community-acquired pneumonia (CAP) is a common and potentially-serious illness worldwide. Increasing CAP associated morbidity and mortality is observed in patients with co-morbid conditions. In India, the scenario of CAP associated morbidity and mortality is not different from the rest of the world [1]. The bacteriological profile in CAP differs geographically and seasonally within the same country. In India too, geographical distribution of CAP differs considerably, e.g. *Streptococcus pneumoniae* predominates as etiological agent in Shimla and Delhi, whereas *Pseudomonas aeruginosa* dominates in Ludhiana, Karnataka and Srinagar [2,3].

*Pseudomonas aeruginosa* is an opportunistic pathogen, mostly involved in nosocomial infections, but now is being commonly observed in community acquired pneumonia. *Pseudomonas aeruginosa* presents a serious therapeutic challenge with its ability to develop resistance to multiple class of antibiotics [4].

Moreover, MDR *Pseudomonas aeruginosa* mediated resistance to cephalosporins, carbapenems, β-lactams and β-lactamase inhibitor combination have been increasing worldwide [5-8]. Chaudhary et al., reported increasing resistance of anti-pseudomonal drugs to ESBL and MBL enzymes. Delayed management of ESBL and MBL producing *Pseudomonas aeruginosa* has been associated with complications of bacteremia and sepsis with higher mortality [9,10].

Pneumonia is increasingly common among patients of COPD, DM, renal failure and in congestive heart failure [2]. Here we are reporting a case of CAP due to MDR *Pseudomonas aeruginosa* and successfully treated with ELORES.

2. CASE PRESENTATION

A 26-year-old female patient, admitted in our hospital for chief complaints of intermittent cough with sputum since 7 to 8 days, fever on and off, right side pleural chest pain, dyspnea on exertion since 4 to 5 days and generalized weakness. Patient had history of Stevens-Johnson Syndrome with allergic history to tetracycline and ibuprofen at the age of four, with no previous history of diabetes or hypertension. On general examination, patient was febrile (98.60 F), thin built, eye lashes were absent, pulse 80 beats/minute, blood pressure- 120/80 mmHg and with respiratory rate of 36 breaths per minute. Systemic examination revealed, respiratory system: Right infrascapular bronchial breathing sound, cardiovascular system: Normal S1 S2, per abdomen soft and non tender, central nervous system: Conscious and oriented. A chest X-ray was advised and report revealed pneumonia of the right middle and lower lobe. Patient was further investigated for routine blood tests for hemogram, ESR, sputum, acid fast bacilli (AFB), faecal occult blood (FOB). Bronchoalveolar (BAL) and sputum sample was sent for routine microscopy. Gene expert study along with antinuclear antibody (ANA) blot assay was advised. Laboratory reports showed hemoglobin 9.5 g/dL (low), white blood cells 11000 per mm3, platelet count 2.4 lakhs/Cumm, erythrocyte sedimentation rate (ESR)- 21 mm/hr, renal function test(RFT) and liver function test (LFT) were within normal limits. Tuberculin test (T.T), sputum acid fast bacilli (AFB) and antinuclear antibody (ANA) blot test were negative. Based on the available laboratory reports and hospital antibiogram, patient was empirically put on Elores 3 g B.I.D intravenous infusion with other supportive medications. The schematic representation of the clinical course for the management of CAP is depicted in Fig. 1. The antimicrobial susceptibility testing towards the isolated pathogen was carried out according to CLSI guidelines [11] and was noted that the *Pseudomonas aeruginosa* isolated from sputum and BAL was MDR with intermediate sensitivity to meropenem, imipenem- cilastatin, cefepime, piperacillin-tazobactam, ceftazidime and sensitive to Elores and colistin (Table 1). The treatment with Elores was continued on the basis of culture and sensitivity report and based on improving condition of the patient. Elores was
continued for 7 days and repeat chest X-ray, culture and sensitivity of sputum sample was advised. Chest radiography revealed significant resolution of pneumonic patches. Sputum sample showed no growth for *Pseudomonas aeruginosa*. Patient was discharged and advised to continue the Elores therapy along with supportive medications to reduce the chances of recurrence. Follow up was advised post 6 days of discharge. No relapse with marked improvement in general condition was noted when the patient visited out patient department on 7th day post discharge.

3. DISCUSSION

Community-acquired pneumonia (CAP) is an acute infection of the lower respiratory tract occurring in a patient who has not resided in a hospital or healthcare facility in the previous 14 days. In patients with CAP, *S. pneumoniae*, atypical pathogens and enteric Gram-negative organisms are responsible for the infection. The current study presents the case of a 26-year-old female with CAP due to MDR *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* is responsible for infection in some patients with severe CAP [12].

![Fig. 1. Schematic representation of clinical course for the management of community acquired pneumonia caused due to MDR *Pseudomonas aeruginosa*](image)

| Day - 1 | Admitted in hospital  
|         | Physical examination  
|         | Lab tests, X-ray, culture sensitivity test (C/S), suspected pneumonia  
|         | Empirical therapy with ELORES 3g B.I.D  
| Day - 3 | Received C/S reports, identified MDR *P. aeruginosa* in Sputum & BAL  
|         | ELORES 3g B.I.D continued based on C/S report  
| Day - 7 | Patient condition improved, reconfirmed with C/S report and X-ray  
|         | Discharged and follow-up visit after 6 days  
|         | Advised to continue ELORES 3g B.I.D with Follow-up after 7 days  
| Day - 14 | On follow-up day found no recurrence of infection  
|         | Antibiotic therapy discontinued  

Table 1. Antimicrobial susceptibility pattern of isolated *Pseudomonas aeruginosa* against different antibacterial drugs

| S. no. | Drugs                  | Zone diameter (cm) | Inference (R/S/I) |
|--------|------------------------|--------------------|-------------------|
| 1      | Meropenem              | 16                 | I                 |
| 2      | Imipenem - cilastatin | 18                 | I                 |
| 3      | Cefepime               | 17                 | I                 |
| 4      | Piperacillin - Tazobactam | 20             | I                 |
| 5      | Ceftazidime            | 17                 | I                 |
| 6      | Colistin               | 16                 | S                 |
| 7      | Elores                 | 29                 | S                 |

*Note: R, resistant; S, Susceptible; I, Intermediate resistance.*
Most Community Acquired Pneumonia are bacterial in origin. CAP due to Gram-negative bacilli occurs through micro aspiration. Constant exposure to contaminated air and frequent aspiration of nasopharyngeal flora make lung parenchyma susceptible to virulent microorganisms. Apart from this, chronic systemic disorders reduce the level of salivary fibronectin thereby increase colonization of Gram-negative bacilli in oropharynx and other lower respiratory tract [13].

The causative pathogen in this case was MDR *Pseudomonas aeruginosa* isolated from sputum and BAL samples, with intermediate sensitivity to meropenem, imipenem-cilastatin, piperacillin-tazobactam, ceftazidime and cefepime with sensitive to Elores and Colistin. Over the past three decades, numerous studies have reported a higher incidence of Gram-negative organisms in culture positive pneumonia, of which *K. pneumoniae* and *Pseudomonas aeruginosa* are considered the most common pathogens for CAP [3].

*Pseudomonas aeruginosa* is increasingly difficult to eradicate due to it’s significant intrinsic resistance to variety of antimicrobial agents. Antimicrobial resistance of *Pseudomonas aeruginosa* may be due to β-lactamases chromosomal, plasmid or integron encoded, alterations in outer membrane permeability (loss of OprD protein), over expression of efflux pump or development of biofilms during prolonged therapy [4].

Based on hospital antibiogram patient was empirically put on Elores (3 g B.I.D) IV infusion with supportive medications. Based on culture and sensitivity reports Elores was continued for treating MDR *Pseudomonas aeruginosa*. Elores was chosen as a suitable treatment of choice based on established safety, efficacy, broad-spectrum activity against ESBL/MBL producing pathogens and hospital antibiogram. In vitro study on Elores, have shown enhanced susceptibility to *Pseudomonas aeruginosa* by its synergistic action to tackle multiple resistant mechanism of bacteria [4]. Similarly a randomized, open-label, prospective, multicenter phase-III clinical trial on Elores showed clinical cure rates of 91.30% and bacterial eradication rates 97.05% in patient with lower respiratory tract infections [14]. Enhanced sensitivity of Elores to MDR *Pseudomonas aeruginosa* is achieved through synergistic activity of ceftriaxone, sulbactam and Disodium edetate which enhances bacterial cell permeability followed by chelation of divalent ions present in MBL enzymes for activation. ATP concentration in Gram-negative bacteria controls the rate of rRNA transcription initiation, thereby affecting protein synthesis and therefore growth rate. It is thus likely that, addition of Disodium edetate to antibiotics as a non-antibiotic adjuvant helps in down regulating protein expression responsible for mexAMexB-OmpM, which in turn is responsible for efflux over expression in *Pseudomonas aeruginosa*. [4,9].

In the present case, we observed Elores multi-target activity on *Pseudomonas aeruginosa*, culture sensitivity along with hospital antibiogram evidence supported and justified the use of Elores as an effective empirical therapy.

4. CONCLUSION

The rising incidence of CAP due to MDR pathogens increase morbidity and mortality. Clinical practitioners face difficult challenges in treating MDR non-fermentor pathogen like *Pseudomonas aeruginosa* with currently available antibiotic choices. Such a scenario highlights the importance of hospital antibiogram in empiric antibiotic selection and newer treatment options for treating MDR *Pseudomonas aeruginosa*. The present case shows antibiotic adjuvant entity Elores to be safe and efficacious in considering a drug of choice in treating MDR *Pseudomonas aeruginosa* due to its effect on multiple resistance mechanisms like efflux down regulation and activity against MBL enzymes.

CONSENT

The present retrospective case collection was done in the hospital. However, telephonic permission was obtained from the patient to publish the case with a commitment of not disclosing her identity, to which patient agreed.

ETHICAL APPROVAL

Author has declared that no ethical approval is required/ applicable for the present retrospective study.

COMPETING INTERESTS

Author has declared that no competing interests exist.
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