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RESEARCH ARTICLE

A case study: Viral Pneumonia induced Acute Respiratory Distress Syndrome with super infection of ESBL producing Klebsiella pneumonia treated with Antibiotic Adjuvant Entity: Elores

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Abstract

Viral pneumonia is a rising concern worldwide, especially in children and young adults. Viral pneumonia can rapidly progress to Acute Respiratory Distress Syndrome (ARDS) which is a syndrome of acute respiratory failure with symptoms of dyspnea, tachypnea and progressive arterial hypoxia requiring mechanical ventilation. Gram-negative super-infection with *E. coli, Klebsiella spp., and P. aeruginosa* are common in mechanical ventilated patients, leading to increased hospital stay, cost of treatment, morbidity and mortality in children. Here we discuss a case of viral pneumonia induced ARDS with nosocomial infection (super-infection) of ESBL producing *K. pneumoniae*, in a patient hypersensitive to Meropenem and Colistin, treated successfully with newer antibiotic adjuvant entity: Elores

INTRODUCTION

Pneumonia is an inflammation of lung, caused by bacteria, viruses, and fungi infection. Viral infections contribute in substantial proportion of cases in childhood pneumonia. Re-infection with viral pneumonia is relatively uncommon during young adulthood. However, respiratory viruses are important etiological agents of pneumonia. Studies of community-acquired pneumonia (CAP) have reported viral etiology as much as 10–36% of the cases[1,2]. The common characteristics of viral pneumonia are bilateral diffused infiltration on chest X-ray, severe hypoxia (required mechanical ventilation), and deterioration of respiratory function[3].

Viral pneumonia can rapidly progres to an Acute Respiratory Distress Syndrome (ARDS) in children and young adults patients who are having influenza like symptoms followed by dyspnea and tachypnea. ARDS is a syndrome of acute respiratory failure that presents with progressive arterial hypoxemia, dyspnea and difficulty in breathing[4]. The possible mechanism of respiratory failure in viral pneumonia associated with ARDS is due to rapid replication of respiratory epithelium, direct injury of alveolar epithelial cells, with increased cytokines production which might cause diffused alveolar damage, a typical characteristic of ARDS[3].

ARDS generally can be induced by two types of virus: Respiratory viruses that cause community-acquired viral pneumonia and *Herpesviridae* that cause nosocomial viral pneumonia. Among the respiratory viruses, *Coronavirus* can cause severe ARDS. *Herpesviridae, Herpes simplex virus (HSV)* and C*ytomegalovirus (CMV*) cause nosocomial viral pneumonia that can evolve into ARDS[5].

Most patients with ARDS require mechanical ventilation, increasing the risk of nosocomial pneumonia[6]. Gram-negative rods such as *E. coli, Klebsiella spp., and P. aeruginosa* have been widely reported in ARDS patients who have been mechanically ventilated for 5 days or more in ICU. Mechanical ventilation in ARDS associated with

tracheal intubation followed by long stay in the ICU and reduced defense mechanisms facilitate bacterial growth. The incidence of nosocomial pneumonia in patients with ARDS ranges from 15% to 60%[7].

Here, we report a case of viral pneumonia with secondary infection of ESBL producing *K. pneumoniae* with ARDS successfully treated with Elores, an Antibiotic Adjuvant Entity.

Case presentation

A 17-year female patient with clinical symptoms of fever, cough and shortness of breath since 4 days and on treatment with antipyretic, multi-vitamin and anti-tussives, was referred to our emergency department. At the time of admission, patient presented chief complaints of fever since last 7 days, dry cough since 5 days, diffuse chest pain since 2 days and sudden onset of breathlessness since last 1 day. On physical examination, patient was conscious, oriented, responding, tachypneic and tachycardic with pulse rate 140 beats/min, blood pressure 110/60 mm Hg and oxygen saturation 78% on room air. Auscultation of the chest revealed bronchial breath sounds. Patient was evaluated and investigated thoroughly. The patient's chest X-ray showed bilateral diffuse consolidation. Biochemical and hematological profile were normal. Inflammatory markers such as TLC (total leukocytes count), Neutrophils, C-reactive protein and Procalcitonin levels were raised. Arterial blood gas showed severe hypoxia. Hence, based on patient condition and biochemical parameters, a provisional diagnosis of Virus induced ARDS with secondary infection was considered.

The patient was put on empirical intravenous antibiotic (ceftriaxone and a macrolide) along with oxygen therapy, IV fluids and other supportive care. All the routine samples were sent to the laboratory for culture sensitivity. Sample culture reports were sterile.

Orotracheal intubation was performed in view of refractory hypoxia after a failed attempt to oxygen and noninvasive ventilation. Two days following admission, patient was afebrile with decreased oxygen requirement on ventilation. Also showed improvement in terms of tachycardia, radiological and inflammatory markers, but, on the fifth day of post-admission, patient's condition deteriorated, with recurrent episodes of fever, tachycardia, tachypnoea, increased oxygen requirement of ventilator and increased volume of purulent secretions. The purulent secretion was sent for gram staining and culture sensitivity. Chest radio-graph revealed bilateral infiltration of lungs. All intravenous lines (Central Venous Pressure, arterial line and foley's catheter) were changed in view of cross infection or intravenous catheter-related infections. Two sets of blood samples, urine and endotracheal (ET) tube were sent for culture sensitivity study.

Patient was switched over to Piperacillin/Tazobactam and Fluoroquinolone based on hospital antibiogram, but no improvement was observed in the patient condition after 48 hrs. The culture sensitivity report from ET tube showed ESBL producing *K. pneumoniae,* sensitive to Elores [ceftriaxone + sulbactam with adjuvant EDTA], meropenem, colistin and tigecycline.

Based on the culture sensitivity, along with inflammatory markers, patient was put on meropenem with colistin. Hypersensitivity reaction was observed, meropenem and colistin infusion was stopped. Patients relatives were informed about the situation, challenge and risk associated in treating the patient. Considering the broad spectrum activity of Elores towards multi-drug resistance (MRD) Gram-negative pathogens and on the basis of culture and sensitivity report, Elores 3g BID with 90 minutes infusion was initiated. Improvement in the patient's condition was observed within 48 hrs and after 5 days of Elores therapy and post improvement in oxygen saturation, patient was weaned off from the ventilator and shifted to ward with supportive therapy. Patient was discharged on 9th day.

Discussion

Bacteria generally cause the most severe lung disease. Viral pneumonia are rare in healthy civilian adults. However, the prevalence of CAP due to viruses are reported between 10 - 36% of the cases[2]. The clinical features of respiratory viral infections include: high-grade fever, chills, dry cough, pharyngeal irritation, myalgias, malaise, and anorexia. Fever persists for an average of 3 days (range of 2 to 8 days). Cough is initially nonproductive and non-purulent and may persist for weeks. These manifestations are correlating to the present case.

In patients with viral pneumonia, infections became fatal if it progress rapidly to ARDS. These patients present with slowly increasing dyspnea and severe hypoxemia after 2 days of typical influenza symptoms. The cough is normally productive, bloody, sputum with few cells. Hypoxia increases progressively to the point of respiratory failure requiring intubation and mechanical ventilation, often after only one day of hospitalization. Bacteria, rickettsiae and viruses were the commonest infections causing ARDS. Tarun et al., highlighted a higher proportion of patients (78.%) with moderate ARDS to have an infectious etiology in India[6].

In the present case, patient presented with typical respiratory viral infection symptoms and rapidly developed respiratory failure. Chest X-ray revealed bilateral infiltration. These clinical features and laboratory findings correlating with viral pneumonia induced ARDS. Prompt initiation of appropriate oxygenation, ventilator support and antibacterial treatment in concurrent bacterial pneumonia, are critical for survival in patients with viral pneumonia[8]. Patient was put on empirical antibiotic therapy of ceftriaxone and a macrolide along with other supportive care. However, with relapse of infective signs and symptoms on the fifth day indicated nosocomial infection.

Mechanical ventilation judiciously used in patients with ARDS, prevents the risk of nosocomial pneumonia. The incidence of nosocomial pneumonia in patients with ARDS is reported in the range of 15% to 60%[2,9]. *Klebsiella spp.*, are majorly isolated in ARDS patients, receiving mechanical ventilation for 5 or more days.

In the present case, initial culture reports though sterile, showed ESBL producing *K. pneumoniae* isolate from ET tube culture samples on fifth day, thereby indicating the deteriorating immune system and nosocomial infection present in the patient. Based on culture and sensitivity results, meropenem and colistin were given. However, when these antibacterials failed to treat patient due to hypersensitivity, Elores was considered as an alternative safe and efficacious choice to treat the patient suffering from post hypersensitive reaction of carbapenem and colistin.

Elores an AAE with a novel combination of ceftriaxone/sulbactam/disodium edetate, combats antimicrobial resistance caused by ESBL/MBL producing strains due to multiple modes of action and has proven efficacy in VAP cases. Phase-III clinical trial on Elores reported clinical cure rate of 91.30% (42/46) and bacterial eradication 97.05% (33/34) in LRTI patients including pneumonia[10]. Manisa S *et al*., reported 82% sensitive and intermediate sensitive to ESBL producing clinical strains of *K. pneumoniae* majority isolates from sputum, ET tube, urine, tissue and pus[11].

Oxidative stress in Gram- negative bacteria infected lung tissue increases considerably. A study on pneumonia induced by *K. pneumoniae* pathogen on rats, showed reduced bacterial count, free radical scavenger property with reduced inflammatory response on Elores treatment, thereby indicating higher safety and tolerance[12]. Similarly, Chaudhary et al., showed Elores good antibacterial activity against ESBL/MBL producing *K. pneumoniae* (n=23) with lower MIC values of 4-8 μg/ml[13].

In the present case, patient responded to Elores within 24 hr of therapy and weaned from the ventilator within 5 days, indicating the importance of novel antibiotic adjuvant like Elores in situations where first line antibiotics have decreased antibiotic activity or increased adverse drug reactions.

Conclusion

Patients presenting with typical symptoms of respiratory viral infections should be aggressively treated to protect from ARDS and bacterial super-infections. Virus-induced ARDS with super-infection of ESBL producing bacteria may cause severe hypoxia with increased morbidity and mortality. Though the present case has statistical limitations, still Elores seems to be a better choice in terms of safety, efficacy and pharmacoeconomic parameters. New Antibiotic Adjuvant Entity: Elores may be a preferred choice in ESBL producing Gram-negative pathogens, resistant or hypersensitive broad spectrum antibiotics (in our case carbapenem or polymyxin B) along with aggressive supportive management treatment. Hence, Elores could be safer and alternative option to carbapenems.

References

1. Falsey AR and Walsh EE. Viral Pneumonia in Older Adults. Clin Infect Dis 2006;42:518–524.
2. Gupta D, Agarwal R, Aggarwal AN, et al. Guidelines for diagnosis and management of community- and hospital-acquired pneumonia in adults: Joint ICS/NCCP(I) recommendations. Lung India 2012;29):27–62.
3. Igusa R, Sakakibara T, Shibahara T, et al. Complicated secondary pneumonia after swine-origin influenza A virus infection in an immunocompetent patient. Tohoku J Exp Med 2012;226:117-20.
4. Matthay MA, Zemans RL. The acute respiratory distress syndrome: pathogenesis and treatment. Annu Rev Pathol 2011;6:147-63.
5. Luyt CE, Combes A, Trouillet JL, et al. Virus-induced acute respiratory distress syndrome: epidemiology, management and outcome. Presse Med 2011;40:561–568.
6. George T, Viswanathan S, Karnam AH, Abraham G. Etiology and Outcomes of ARDS in a Rural-Urban Fringe Hospital of South India. Crit Care Res Pract 2014;1-7.
7. Torsten T Bauer, Antoni Torres. Acute respiratory distress syndrome and nosocomial pneumonia. Thorax 1999;54:1036-1040.
8. Rello J and Pop-Vicas A. Clinical review: Primary influenza viral pneumonia. Crit Care 2009;13:235.

9. Bauer TT and Torres A. Acute respiratory distress syndrome and nosocomial pneumonia. Thorax 1999;54:1036–1040.
10. Chaudhary M and Payasi A. A randomized, open-label, prospective, multicenter phase-III clinical trial of Elores in lower respiratory tract and urinary tract infections. J Pharm Res 2013;6:409–414.
11. Sahu M, Sanjith S, Bhalekar P, Keny D. War Against Extended Spectrum Beta Lactamase and Metallo betalactamase Producing Pathogens- Novel Adjuvant Antimicrobial Agent Cse1034- An Extended Hope. J Clin Diagn Res 2014;8:20–23.
12. VD Kumar, Kumar P, Chaudhary M. Comparative Study of CSE 1034 and Ceftriaxone in *Pneumonia* Induced Rat. Clin Exp Pharmacol 2012;2:1-7.
13. Chaudhary M, Payasi A. Antimicrobial susceptibility patterns and molecular characterization of *Klebsiella pneumoniae* clinical isolates from north Indian patients. Int J Med Med Sci 2013; 46:1218-24.