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RESEARCH ARTICLE

Acute left lung abscess caused by multidrug- resistant *Pseudomonas aeruginosa* treated with Elores: A case study

Arpit Jain

1. Sr. Consultant-Medicine, Artemis Hospital, J-Block, Mayfield Garden, Gurgaon, Haryana-122002, India

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Corresponding Author

Arpit Jain

Abstract

In this study we report a case of 63-year-old woman with symptoms of pyrexia, malaise, shortness of breath, cough with expectoration and anorexia was admitted to our hospital, showing a homogenous opacity in the left lower mid zone along the peripheral upper zone on a chest radiography was diagnosed with lung abscess of the left side (destroyed lung). Culture reports of brochoscopically obtained lung parenchyma, bronchoalveolar lavage (BAL) and endotracheal aspirates revealed pulmonary abscess caused by multidrug resistant (MDR) *Pseudomonas aeruginosa*. The current management of acute lung abscess is difficult. Based on culture and sensitivity report patient was put on intravenous Elores (Ceftriaxone/Sulbactam /Disodium edetate- a non-antibiotic adjuvant) and injection amikacin, with support of intravenous (IV) anti-pyretics, IV fluids, nebulization, physiotherapy for postural drainage and other supportive measures, who recovered well.

INTRODUCTION

Lung abscess is described as a circumscribed assortment of pus within the lung that results in formation of a cavity. It develops when a bacterial infection causes necrosis and produces cavities in the localized area of lung parenchyma[1,2] Antibiotic therapy is the main stay for treatment of lung abscess. About 90% of patients with lung abscess are recovered by antibiotic therapy. Surgical resection is rarely used when medical treatment fails.[2]

Management of lung abscess has always been a great challenge to physicians, especially in treatment of multi drug resistant organisms; aerobic *(Klebsiella, Pseudomonas, Nocardia, Escherichia coli, Staphylococcus, Haemophilus)* and anaerobic bacteria *(Peptostreptococcus, Bacteroides, Fusobacterium species*).[3,4,5]

P. aeruginosa, an uncommon pathogen in lung abscess is difficult to eradicate because of it's ability to develop resistance to multiple class of antibiotics during the course of treating an infection [**6**]. *P. aeruginosa* has developed various mechanisms for resistance development; production of extended spectrum β-lactamases (ESBL) and metalo-β-lactamases, target site or outer membrane modification and over expression of efflux pump.[7] ESBL mediated resistance to cephalosporins[8], carbapenems and β-lactams and β-lactamase inhibitor combination have been increasing worldwide.[9,10,11] Anti-pseudomonal drugs are getting resistance especially in ESBL and MBL mediated resistance among *P. aeruginosa*.[12] Delay in treatment for ESBL and MBL producing *P. aeruginosa* has been associated with complications of bacteremia and sepsis, with higher mortality.[13] Thus despite the development of newer treatment modalities in antibiotics treatment and surgical interventions, mortality associated with lung abscess is still significantly higher, ranging from 15%-20%.[1]

We present a case of left lung abscess treated with a newer antibiotic adjuvant entity: Elores (Ceftriaxone/Sulbactam/Disodium edetate), for ESBL/MBL producing MDR *Pseudomonas aeruginosa.*

CASE REPORT

A 63 year old female patient was admitted to Artemis Hospital, Gurgaon with symptoms of pyrexia, malaise, shortness of breath, cough with expectoration and anorexia since 9 days. Her past history was remarkable for tuberculosis, chronic obstructive pulmonary disease (COPD) and rheumatoid arthritis, with no known drug allergies. As per the National Tuberculosis Control Program, our patient had taken anti-tuberculosis treatment; DOTS (Directly Observed Treatment Short- Course) and was cured post treatment. On examination patient was conscious and oriented, but appeared unwell. Physical examination revealed, patient to be febrile (38.1 ºC), tachycardia (heart rate of 110/min), blood pressure of 100/60 mm hg and SPO_2 of 90% . Review of the systems was remarkable: respiratory system showed decreased air entry on left side with creps, while cardiovascular system, abdominal and central nervous system were non remarkable. Patient was investigated. Haematology report showed deranged values for hemoglobin (10.4 g/dL), platelet count (685 x 10' 9/l) and lymphocytes (14 %) while rest of the parameters were in normal range. Biochemical parameters showed quantitative C-reactive protein (CRE) on a higher side (19.2 mg/dL) with deranged Liver Function Test (LFT): S albumin : 2.2g/dL, S. globulin : 4.7 g/dL, SGOT: 40.3 IU/L, SGPT: 44.8 IU/L, y- glutamyl-4-nitroanilide (GGT): 46 IU/L and Renal Function Test (RFT): S. Sodium :131.8 mEq/L, S. Potassium : 3.4 mEq/L, S. Chloride: 96.7 mEq/L. Radiological investigation revealed, homogenous opacity in the left lower mid zone along the peripheral upper zone. Pulmonology opinion was taken. Based on the investigation (clinical, hematological, biochemical and radiological findings) the patients was diagnosed with lung abscess of the left side (destroyed lung).The patient and her relatives were informed of the disease process and different treatment modalities (including the need of surgery). Surgery review was done. Diagnostic bronchoscopy was performed for obtaining lung parenchyma and bronchoalveolar lavage (BAL). Patient was put empirically on intravenous (IV) infusion of Elores [Ceftriaxone plus Sulbactam plus Disodium edetate (CSE)] 3 g twice a day (BD) of 90 minutes along with Inj. Amikacin 1g IV once a day with support of IV anti-pyretics, IV fluids, nebulization, physiotherapy for postural drainage and other supportive measures. Brochoscopically obtained lung parenchyma, BAL, along with endotracheal aspirates were sent for culture and sensitivity, which revealed ESBL and MBL producing multi drug resistant *Pseudomonas aeruginosa*. The MDR characteristic was attributed to the ESBL/MBL producing nature of *P. aeruginosa*, identified through culture and sensitivity test. Thus, based on culture and sensitivity and the lowest MIC findings, Elores 3g iv BD dose of 90 minutes infusion was continued for 21 days while Inj. Amikacin was stopped after three days. Supportive measures were continued. Our patient improved gradually. Chest radiogram on the 18th days of treatment showed considerably decreased homogenous opacity and improved lung function. Patient was put on oral antibiotics and advised regular follow-up and discharged.

DISCUSSION

P. aeruginosa presents a serious therapeutic challenge for treatment of community-acquired and nosocomial infections. It is difficult to eradicate because of it's ability to develop resistance to multiple classes of antibiotics during the course of treating an infection. Epidemiological outcome studies have shown that infections caused by MDR *P. aeruginosa* are associated with significant increases in morbidity, mortality.[16] Hence selection of the appropriate antibiotic to initiate therapy is essential in optimizing the clinical outcome.

In our current case study, MDR *ESBL/MBL producing P. aeruginosa* identified. To our knowledge, no case of lung abscess caused by MDR ESBL/MBL producing *P. aeruginosa* has been reported till date, treated with intravenous infusion. Only a few non multi-drug resistant lung abscess cases have been reported in the literature.[14, 15, 5] Few notable cases reported are; pulmonary abscess and empyema due to *P. aeruginosa*[15], bilateral lung abscess due to *P aeruginosa* infection after open heart surgery in an infant [14] and lung abscess due to MDR *P. aeruginosa* was treated with oral antibiotic.[5]

Lung abscess are treated by prolong antibiotic use in medical treatment, with duration ranging from 1 month to 3 months. The current management of acute lung abscess is clinical, with the use of antibiotics, postural drainage and general care. Though, prolonged antibiotics therapy is the cornerstone when dealing with lung abscess, but when resolution is not satisfactory, tube drainage or surgical implication should be intervened[1,17], but surgery is usually less recommended as a treatment modality in lung abscess due to reports of high mortality and morbidity. Poor prognostic factors affect the overall success rate of the treatment. Patients diagnosed with wide abscess cavity (>6 cm), immune compromised, geriatric age group, partially consciousness and/or infection with certain aerobic pathogens (*K. pneumoniae, P. aeruginosa, S. aureus)* tend to increase the treatment failure rate.[3,l,18]

Adults with lung abscess typically present with manifestations of pulmonary infection, including fever, cough, sputum production, difficulty in breathing, chest pain, hemoptysis. Evidence of chronic lung abscess disease

manifest as night sweats, weight loss and anemia. Most patients present with putrid sputum or note a sour taste to the sputum. Patients with Gram-negative lung abscess are generally present in the acute phase of the infection[4,19] The diagnosis of lung abscess is primarily based on the physical symptoms, hematological, biochemical examination and chest radiography. Sputum, blood, or pleural fluid culture sensitivity may suggest for causative pathogens. Specimens for culture can be obtained by transtracheal aspiration, while bronchoscopy can be performed in patients with an atypical presentation.[19]

In the current case study, patient presented with symptoms of pyrexia, malaise, shortness of breath, cough with expectoration. Based on clinical evaluation, hematological and bacteriological investigations was started with empirical antibiotic therapy with Elores infusion and injection amikacin along with support of IV anti-pyretics, IV fluids, nebulisation, physiotherapy for postural drainage and other supportive measures. Elores was chosen as an empirical antibiotic therapy in our patient based on established safety, efficacy and broad-spectrum activity against ESBL/MBL producing MDR pathogens. In-vitro study on Elores, have shown enhanced susceptibility to *P. aeruginosa* by its synergistic effect and action on multiple resistant mechanism of bacteria.[7] 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.[20]

One study published in 2013, conclude that more than 14% *P. aeruginosa* are produced both ESBL and MBL, study also conclude that prevalence of ESBL, MBL and ESBL+MBL in *P. aeruginosa* has been increasing which leads to a therapeutic challenge. When comparison of the antimicrobial susceptibility levels, 74 to 94% isolates positive with either ESBL, MBL and ESBL+MBL were susceptible to Elores. The enhanced susceptibility of ceftriaxone plus disodium edetate plus sulbactam (Elores) against *P. aeruginosa* is likely to be associated with synergistic activity of components. Presence of disodium edetate in Elores enhanced permeability of ceftriaxone and sulbactam and thereby enhancing activity against ESBL microbes synergistically. Disodium edetate would also chelate the divalent ions required for the activity of MBLs thus de-activating the MBLs which in turn enhanced susceptibility of Elores towards MBLs producing organisms.[12] Presence of disodium edetate helps Elores to down regulate the expression of efflux pump (MexAB-OprM) of *P. aeruginosa* as well as altering the outer membrane permeability which in turn increased penetration of drugs inside the bacterial cells and enhancing bactericidal activity.[7]

In our case, patient gradually responded to Elores. Chest radiography was done on the 21st day of treatment showed reduced homogenous opacity. Improved lung function was also noted. Patient was put on oral antibiotics, advised regular follow-up and discharged. The usual duration of medical treatment for lung abscess varies from one month to three months, but our patient recovered in 21 days of antibiotic treatment, without surgical intervention.

CONCLUSIONS

Lung abscess is a circumscribed collection of pus in the lung, which leads to formation of a cavity. Patient in the current case was diagnosed with left lung abscess with causative organism MDR *P. aeruginosa*, presenting a serious therapeutic challenge in clinical practice. MDR *P. aeruginosa* is difficult to eradicate because of it's ability to develop resistance to multiple classes of antibiotics during the course of treating an infection Prolonged antibiotics therapy has been the cornerstone when dealing with lung abscess along with other supportive therapies include IV anti-pyretics, IV fluids, nebulization, physiotherapy for postural drainage.

Based on our study, we would recommend to adopt a multidisciplinary approach in treating lung abscess. Elores is well tolerated and more efficacious in treating MDR *P. aeruginosa* than routinely used anti-pseudomonal antibiotics. Elores may be considered as an empiric treatment for MDR *P. aeruginosa* for clinical success and microbiological eradication in clinical practice.

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