

Multiple Antimicrobial-Resistant Bacteremia and Fungal Infection Pneumonia in Elderly Patient: A Case Study



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ABSTRACT

Introduction: The spread of multidrug-resistant bacterial pathogens has become alarming globally. Extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* (*E. coli*) have been recognized as a major multidrug-resistant bacteria implicated in hospital and community-acquired infections worldwide.

Case: We present the case of an elderly male, 74-year-old, with multiple comorbidities, who came to the hospital with main symptoms of cough. Three months previously, he was diagnosed with pneumonia. Nevertheless, he was treated as an outpatient, with Cefixime prescribed as an oral antibiotic. His non-contrast chest CT Scan showed opacities at the upper zone, middle zone and lower zone of the left lung and the lower zone of the right lung. The patient's symptoms and imaging expertise strongly suggest a pulmonary infection. Sputum culture and sensitivity test result eventually confirmed positive *E. coli* isolates demonstrated resistance to Augmentin, Ceftazidime, Gentamicin, Ampicillin sulbactam, Aztreonam, Cefotaxime, Cefepime. Fungal culture by sputum specimen revealed growth of *Candida*, non-*Candida albicans*. Concurrently, history of hospitalization and antibiotic treatment exposure are considered risk factors for the acquisition of multidrug resistance in this patient. Furthermore, corticosteroids in elderly patients are alleged as a risk factor of fungal infection.

Conclusion: The increasing case of antimicrobial resistance in elderly patients is challenging for the clinician. Culture and sensitivity tests performed before starting antimicrobial treatment in hospitalized geriatric patients can reduce unnecessary and inappropriate antimicrobial use. Fungal test is considered to be done in a susceptible case of the elderly patients. The rapid diagnosis followed with prompt initiation of appropriate antibiotic and antifungal therapy is urgently required.

Keywords: Pneumonia, geriatric, antibiotic, resistance, fungal.

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INTRODUCTION

The elderly individual is becoming the most common patient in clinical practice due to the increasing average life span. Aging is classified as biological aging, psychological aging, social aging, chronological aging and functional aging.¹ Biological aging involves the loss of cells over time. With biological aging, tissues and organs are less likely to function efficiently. The body's ability to repair itself slows down, and the immune functions decline, making the body more prone to infection.² Chronological aging is the number of years a person has lived so far. Old age denotes the decrease in an individual's environmental compliance ability out of her or his control and chronologically defines individuals aged 65 years and older.³

Community-acquired pneumonia (CAP) is a major public health problem with high morbidity, mortality and short- and long-term sequelae.^{4,5} In fact, the microbial etiologies are not identified in all cases. For years, antibiotics have saved many lives by being the main therapy for bacterial infections disease.

A recent systematic analysis study found that three infectious syndromes dominated the global burdens associated with antimicrobial resistance in 2019: lower respiratory and thorax infections, bloodstream infections, and intra-abdominal infections.⁶ Their raw data shows that up to 70% - <80% of third-generation cephalosporin-resistant *Escherichia coli* was found in South East Asia.

Fungal infection in the elderly is also an expanding clinical problem with higher

mortality in this group.⁷ Each year, over 1.6 million deaths occur due to invasive fungal infections.⁸ In the USA, 25,000 cases of coccidioidomycosis and 25,000 cases of histoplasmosis are diagnosed each year.⁴ Paracoccidioidomycosis caused by a dimorphic fungus *Paracoccidioides brasiliensis*, is to cause about 4000 life-threatening in Brazil, which carries a mortality rate of 5-27%.⁴ There are over 8000 cases of Penicillosis due to *Penicillium marneffeii* in Southeast Asia. It is pertinent to mention that 90% of the invasive fungi have been encountered in the immunocompromised patient.⁴ The high mortality due to invasive fungal is of great concern. Here we present a case of an elderly who was infected with antimicrobial-resistant *Escherichia coli* and fungal infection.

CASE PRESENTATION

A 74-year-old male came to the hospital on November 2021 with the main symptoms of cough. Three months previously, he was initially diagnosed with pneumonia at another clinic. Nevertheless, he was treated as an outpatient basis. At that moment, he was prescribed Cefixime as an oral antibiotic. He has gradually worsened over the past three months. The patient has a past medical history of hypertension, polyneuropathy, rosacea and right iliac artery occlusive disease. He underwent angioplasty with four stents of the right iliac artery. He had been hospitalized multiple times and received antibiotic treatment several times during the hospitalization. His current regular medications are Candesartan, Aspirin, Pravastatin and topical Metronidazole cream (as rosacea's treatment).

Based on the initial consultation, the cough was not getting better for the past three months, followed by fatigue, shortness of breath, and decreased appetite. Initial examination revealed that the oxygen saturation was lower than normal, 90% on room air. Blood pressure was 150/90 mmHg, heart rate 108 times per minute, respiratory rate was 24 times per minute, appeared weak, but still able to talk in a full sentence. No fever was recorded. On physical examination, rales can be identified clearly upon auscultation. He was then hospitalized for having further investigation and treatments. The blood test revealed Leukocytosis and high C-reactive protein (CRP) level. His non contrast chest CT scan revealed sign of pneumonia. Taken together, patient's symptoms and imaging expertise strongly suggest a pulmonary infection, pneumonia. Polymerase chain reaction (PCR) SARS CoV-2 test was performed to rule out COVID-19 infection during the pandemic, revealing negative results. Tuberculosis tests were performed by sputum analysis and Interferon-Gamma Release Assays (IGRA) test; both results were negative. Ceftriaxone was administered intravenously as an empiric antibiotics treatment. Other symptomatic medications were also administered with bronchodilators, corticosteroids and others.

Meanwhile, sputum culture and

sensitivity tests and the fungal sputum analysis test were performed. Progress of treatment was not impressive. Further investigation ruled out other differential diagnoses, such as pulmonary embolism (PE). The D-dimer test was within the normal limit, followed by low Well's score criteria for PE.

Sputum culture and sensitivity test result revealed confirmed positive *E. coli* isolates demonstrated resistance to Augmentin, Ceftazidime, Gentamicin, Ampicillin sulbactam, Aztreonam, Cefotaxime, Cefepime. No resistance was detected to Bactrim, Meropenem, Amikacin, and Piperacillin tazobactam. *Escherichia coli* is highly resistant to Cephalosporin gene III. Antibiotic therapy was modified accordingly. Fungal culture

by sputum specimen revealed growth of *Candida*, non-*Candida albicans*.

Meropenem was started intravenously, and blood culture was performed before administration of Meropenem. It came back with no bacterial growth eventually. Antifungal was administered with Fluconazole intravenously and Nystatin oral.

Daily observation showed improvement. Oxygen supplementation was tapered down gradually and stopped. No fever was recorded during admission. He was able to be discharged from the hospital.

Follow-up treatment as an outpatient on December 2021 revealed that the patient was in good condition, and no other worsening symptoms were apparent.



Picture 1. Patient's non contrast Thorax CT Scan showing opacities at upper zone, middle zone and lower zone of left lung and at lower zone of right lung.

Table 1. Microbiology examination of culture and sensitivity

Examination	Culture and sensitivity test
Specimen	Sputum
RESULT	
Gram stain	Epithelial (+1); Leucocytes (+2); Gram negative bacilli (+1); Gram positive cocci (scanty); yeast (scanty)
CULTURE RESULT	<i>Escherichia coli</i>
SENSITIVITY TEST RESULT	
• Augmentin	R
• Bactrim	S
• Ceftazidime	R
• Gentamycin	R
• Meropenem	S
• Amikacin	S
• Ampicillin Sulbactam	R
• Aztreonam	R
• Cefotaxime	R
• Cefepim	R
• Peciprillin tazobactam	S

Table 2. Microbiology examination of fungal culture

Examination	Fungal Culture
Specimen	Sputum
RESULT	
KOH	Yeast (found)
CULTURE RESULT	Candida non Candida albicans

DISCUSSION

Prior stay in healthcare settings is a risk factor for acquiring multidrug-resistant gram-negative bacteria (MDR-GNB).⁹ A study revealed this relationship is dose-dependent: length of hospital stay in the last year was associated with MDR-GNB carriage upon ICU admission, increasing the risk by 1% per day of previous hospital stay.⁹ In this patient presented, patient with multiple comorbidities, had been hospitalized numerous times, exposed and received several antibiotics during the hospitalization period previously. Concurrently, history of hospitalization and antibiotic treatment exposure is considered risk factors for the acquisition of multidrug resistance in this patient.

An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America in 2019 recommends not to obtain sputum Gram stain and culture routinely in adults with CAP managed in the outpatient.

They recommend obtaining pretreatment Gram stain and culture of respiratory secretions in adults with CAP managed in the hospital setting who are classified as severe CAP, especially if they are or are being empirically treated for Methicillin-resistant *Staphylococcus aureus* (MRSA) or *P. aeruginosa*; or were previously infected with MRSA or *P. aeruginosa*, especially those with prior respiratory tract infection; or were hospitalized and received parenteral antibiotics in the last 90 days.¹⁰

Appropriate antibiotic needs to be modified according to the study result. The duration of treatment for community-acquired pneumonia in current guidelines suggests a short 5-day course of antibiotics. Only patients without clinical improvement receive extended antibiotic therapy and further diagnostic approach.¹¹

A recent Spain study of Multidrug-resistant Gram-negative bacteria (MDRGNB) shows that the most

frequently isolated pathogens were *Escherichia coli* (57%).⁹ The most frequent resistance mechanism was the production of extended-spectrum beta-lactamases (ESBL). It also mentioned that 7% of screening cultures upon ICU admission were positive for MDRGNB, mainly ESBL-producing *E. coli* and *K. pneumoniae*.⁹

The production of β -lactamases was the main cause of β -lactam resistance, especially among gram-negative bacteria, including *E. coli*. The high prevalence of multidrug-resistant *E. coli* among the ESBL-producing isolates implies not only β -lactam antibiotics but resistance to other classes of antibiotics. Study shows that the most commonly used antibiotics could explain why ESBL-producing isolates are found to be resistant to the classes of antibiotics.¹² Beta-lactam antibiotics are among the most commonly prescribed drug classes with plenty of clinical indications. β -lactam antibiotics constitute a broad class of antibiotic agents that contain β -lactam rings in their molecular structure. These agents include Cephalosporins, Monobactams, Penicillins and Carbapenems.¹³ These antibiotics act by inhibiting the synthesis of the bacterial cell wall. Bacteria have developed a resistance mechanism against these antibiotics, usually mediated by the enzymes β -lactamases. It hydrolyses the β -lactam ring of the β -lactam antibiotics rendering it inactive.⁶

There are two basic ways to overcome the effect of hydrolytic activity of beta-lactamases. The first method involves getting molecules that inactivate or inhibit beta-lactamases. Sulbactam, Clavulanic acid and Tazobactam-lactamase are the three inhibitors used in clinical application.¹³ The second way to overcome the effect of hydrolytic activity of beta-lactamases is getting a new beta-lactam antibiotic that possesses a great affinity for the β -lactamases and cannot be hydrolyzed or poorly hydrolyzed by it. This has been the original rationale behind extended-spectrum Carbapenems or Cephalosporins. A common example of this principle is the development of compounds such as Doripenem and Ceftobiprol.¹³

In this case, the sputum fungal analysis test result revealed the growth of *Candida*,

non-*Candida albicans*. Most *Candida* infections are mainly acquired due to overgrowth and subsequent invasion by indigenous *Candida* species of the host. The primary factor in the colonization of *Candida* is adherence to host surfaces; this process is controlled and induced by several cell-signaling cascades in both the fungus and the environment.² A recent study of patients who suffer from viral infection pneumonia shows that risk factors for invasive Candidiasis are inevitably present in critically ill patients admitted to the ICU, including mechanical ventilation, indwelling devices, broad-spectrum antibiotic therapy, and glucocorticoid use.¹⁴ In this patient presented, he received antibiotic therapy and corticosteroid. They are considered risk factors associated with fungal infection, despite the patient's multi comorbidities (hypertension, polyneuropathy, rosacea and right iliac artery occlusive disease). The number of antibiotics patients have been exposed to before plays a role in this case.

Candidiasis can be treated with antifungals that belong to different drugs and target different cellular processes, thereby inhibiting (fungistatic) or killing (fungicidal) the growth of this pathogenic yeast. These cellular processes include the biosynthesis of the cell wall, cell membrane, and RNA biosynthesis. Each of these biosynthesis processes involves a series of enzymes.¹⁵ Azoles are the most common antifungal drug class used for treating and preventing *Candida* infections.¹⁵ Fluconazole is grouped as Azole antifungal agent. It gives fungicidal effect by inhibiting the lanosterol 14 α -demethylase, blocking the synthesis of ergosterol and resulting in impaired membrane stability and the accumulation of precursors.¹¹ Ergosterol is the major sterol component of fungal cell membranes, including the plasma and mitochondrial membranes. Ergosterol's biosynthesis pathway constitutes an ideal drug target because ergosterol is a very important lipid for fungi.¹⁵

Lastly, the aging process includes changes in various physiological functions, making older patients more prone to infections, including fungal pathogens. *Candida* was rarely the cause of pneumonia except in immunocompromised patients.

A fungal test is considered to be done in a susceptible case of an elderly patient.

The rapid diagnosis followed with prompt initiation of appropriate antibiotic and antifungal therapy is urgently required. The challenge of modern medicine is to promote the prolongation of life in good health while reducing morbidity and disabilities.

CONCLUSION

Increasing case of antimicrobial resistance in elderly patients is a challenge for the clinician. Culture and sensitivity tests performed before starting antimicrobial treatment in hospitalized geriatric patients can reduce unnecessary and inappropriate antimicrobial use. Fungal tests are considered to be done in a susceptible case of the elderly patient. The rapid diagnosis followed with prompt initiation of appropriate antibiotic and antifungal therapy is urgently required.

CONFLICT OF INTEREST

All authors declared that there is no conflict of interest regarding this article

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ETHICS CONSIDERATION

This study has been ethically approved and the informed consent from the patient was also had been obtained.

AUTHOR CONTRIBUTION

All authors contributed equally in the writing process of this article

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