Case Report

Vancomycin-Allergy and Linezolid-Resistance in Patient with Methicillin-Resistance *Staphylococcus aureus* and Multi-Drug Resistance *Acinetobacter baumannii* Infection

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Submitted: January 9th, 2023
Accepted: April 14th, 2023
Published: June 28th, 2023

Respir Sci. 2023; 3(3): 208-17
https://doi.org/10.36497/respirsci.v3i3.82

Abstract

Background: Hospital Acquired Pneumonia (HAP) has been burdening the healthcare system, especially when bacteria such as *Acinetobacter baumannii* and methicillin-resistance *Staphylococcus aureus* (MRSA) are involved. They created a dilemma regarding the appropriate antibiotic therapy utilized against them, especially when the patient is allergic/intolerant to their drug of choice.

Case: A 71-year-old man developed HAP while he was admitted for an ischaemic stroke. His bronchoalveolar lavage (BAL) culture showed MRSA and *Acinetobacter baumannii* infection with multiple drug resistance including one of the drugs for MRSA infection, linezolid. Amikacin and vancomycin were given, but he developed an allergy to vancomycin. Due to the difficulty in treating him, we opted to administer only amikacin. His clinical condition showed daily improvement. During the last day of hospitalization, his sputum culture showed only normal flora. He no longer needed oxygen therapy and there was no longer any indication for him to be hospitalized.

Conclusion: Individuals with multiple comorbidities, recent antibiotic use within the past 90 days, and immune-deficient conditions are at a higher risk of developing infections, including the possibility of dual infections. In this case, we found that the patient was unable to tolerate first-line drugs for MRSA like linezolid and vancomycin, which makes it difficult to decide upon effective treatments.

Keywords: *Acinetobacter baumannii*, MDR, MRSA, pneumonia, vancomycin allergic

INTRODUCTION

The emergence of multidrug resistance among gram-negative and gram-positive bacteria has caused difficulties in treatment. Bacteria such as *Acinetobacter baumannii* and methicillin-resistance *Staphylococcus aureus* (MRSA) are difficult to treat and can survive for a long time in hospital environments, increasing the risk of transmission between patients.[1]

Acinetobacter spp. is a significant cause of hospital-associated infections and

can persist on inanimate surfaces.[2] A study in a division of infectious disease and department of infection control in St. John's Mercy Medical Center, St. Louis, Missouri showed *A. baumannii* was isolated from environmental surfaces of hospital rooms that had been thoroughly cleaned and disinfected after being occupied by patients with multidrug-resistance *Acinetobacter baumannii complex* (MDRABC).[3] MRSA can also persist in the hospital environment[4] and its risk factors for infection or colonization often overlap those of MDRABC,[5] so its isolation from room surfaces was also studied.

MRSA and *A. baumannii* are serious nosocomial pathogens because of their environmental resilience, antimicrobial resistance, and potential to cause outbreaks.[3,6] Surface contamination has been linked to the transmission of these organisms,[7] and previous room occupancy by patients with MRSA or *A. baumannii* infection or colonization is an independent risk factor for the acquisition of these pathogens by subsequently admitted patients.[8]

According to a descriptive study by Dent et al, it was found that MDR *A. baumannii* infection was significantly associated with a higher mortality rate. A different case-control study indicates that the crude mortality rate linked to pan-drug resistance *A. baumannii* could be much higher compared to infection with a more antibiotic-sensitive strain of *A. baumannii*. In this study, it was found that 80% of patients with extremely drug-resistance *A. baumannii* died, in contrast to 14% of those infected with a sensitive strain of *A. baumannii*.[2]

Studies of multidrug-resistance (MDR) bacterial isolates like *A. baumannii* and MRSA are crucial not only for the proper management of infections caused by them, but also for the prevention of dissemination of such strains in the community and in hospitals.

In this paper, we review a case about vancomycin allergy and linezolid resistance of MRSA and MDR *Acinetobacter baumannii* isolates in clinical samples from patients of lower respiratory tract infections (LRTIs).

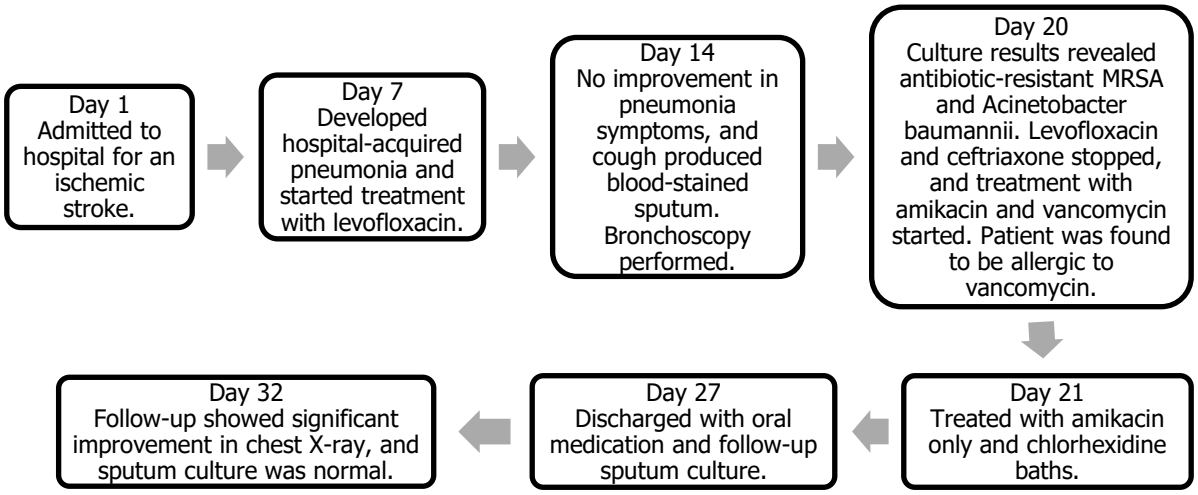

Figure 1. Patient's course of the disease from day one he was hospitalized with an ischemic stroke, on day 7 Hospital Acquired Pneumonia developed and discharged on day 27

CASE

A 71-year-old man, complained of dyspnea when he was on the 7th day of hospital stay for an ischemic stroke. Furthermore, he presented with a fever and a cough that was at times accompanied by bloody sputum.

He showed no sign of infection before coming to the hospital. On examination, the patient was febrile (38ºC) with decreased oxygen saturation from 95% to 90% measured by pulse oximetry. The patient had rhonchi on the left side of the lung and the chest X-ray showed more infiltration than before (Figure 2).

Laboratory findings also showed leucocytosis and neutrophilia (Table 1). He was diagnosed with Hospital Acquired Pneumonia and given levofloxacin as the drug of choice.

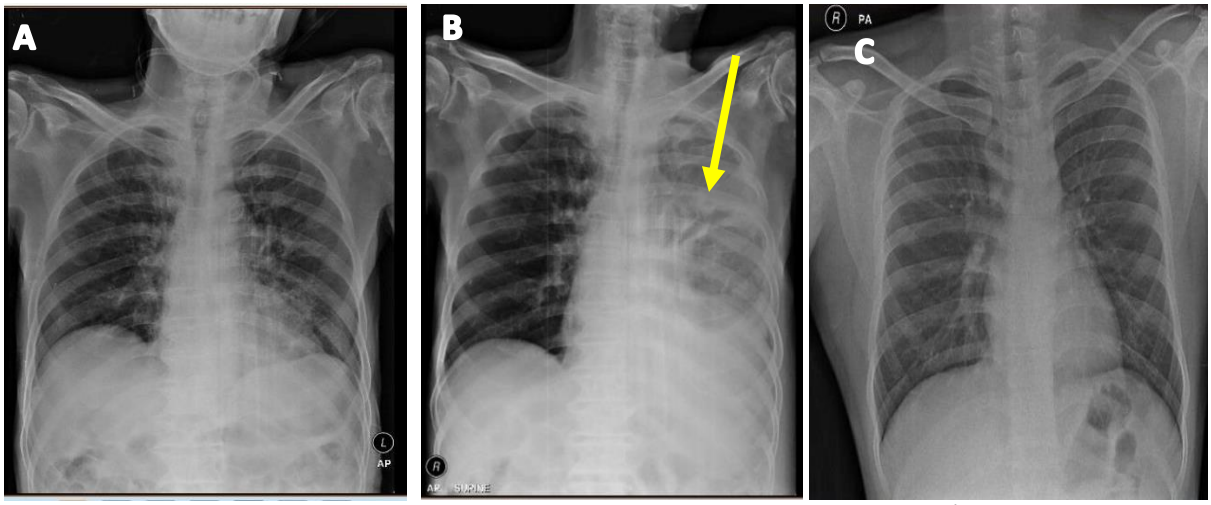

Figure 2. Chest X-ray comparison: (a) Chest X-ray on admission (b) Chest X-Ray on 7th day of hospital stay showing more infiltrate than chest X-ray on admission (yellow arrow) (c) A week after being discharged

Table 1. Laboratory Result: showing leucocytosis on 7th day of hospitalization

Indicators	On admission	On 7th day of hospitalization (when the patient complained of dyspnea)	Last day of admission
Leucocyte (10^3/µL)	11.25	16.60	11.61
Erythrocyte (10^6/µL)	5.7	3.74	3.9
Hemoglobin (g/dL)	17.9	11.5	12
Hematocrit (%)	53.6	34.2	35.7
Thrombocytes (10^3/µL)	212	353	384
Neutrophils (%)	90	84.6	79.9
Lymphocytes (%)	4.8	5.2	8.5
Neutrophils/Lymphocytes Ratio	18.92	16.12	9.37
SGPT (U/L)	41	---	---
Blood Gas Analysis	---	pH=7.47	---
		PCO_2=34	
		PO_2=52	
		HCO_3=25	
		ABE=1	
		SBC=26	
		SO_2=90	

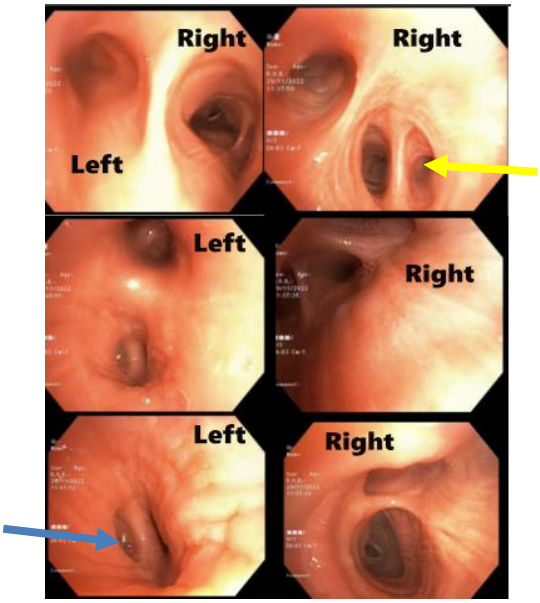

Figure 3. Bronchoscopy imaging. It showed edema and erythema upper and lower left bronchi (blue arrow). There is much sputum with a blood streak on his left bronchi. Right bronchi showed normal on bronchoscopy (yellow arrow)

A bronchoscopy was performed with xylocaine spray and atropine sulfate as premedication. Bronchial washing was performed and a sample of bronchoalveolar lavage (BAL) culture was taken. The bronchoscopy imaging revealed purulent bronchial secretions mixed with phlegm, as well as mucosal swelling and diffuse erythema in the upper lobe of the left main bronchus. Also, there were red purulent bronchial secretions covering the lower lobe lumen of the left main bronchus. The lumen appeared slightly narrowed, the mucosa was swollen, the surface was uneven, and the hyperemic mucosa easily bleeds (Figure 3).

The patient showed no sign of improvement with levofloxacin after being given for a week, while waiting for the BAL culture's result, ceftriaxone was given. The culture showed MRSA and *Acinetobacter baumannii* infection with multiple drug resistance including levofloxacin, meropenem, tetracycline, and one of the MRSA infection drug therapy, linezolid. His BAL culture results also showed that he was sensitive to amikacin and vancomycin (Table 2), so levofloxacin and ceftriaxone were stopped, and amikacin and vancomycin were given.

Table 2. Table of antibiotic list from the patient. The patient was resistant to linezolid and sensitive to Amikacin and Vancomycin.

Antibiotics Resistance	Antibiotics Sensitive
Ciprofloxacin	Gentamycin
Levofloxacin	Trimethoprim/ Sulfamethoxazole
Cefepime	Colistin
Meropenem	Gentamicin
Linezolid	Vancomycin
Tetracycline	Rifampicin
----	Amikacin

On the first day of therapy with vancomycin, the patient was getting harder to breathe and developed wheezing in both lungs and swelling on both palpebrae. He desaturated and vancomycin was quickly stopped. Steroid inhalations, steroid injections, and anti-histamine injections were given to settle his allergic reaction. Besides drugs, the patient was given chlorhexidine 2-4%. He received amikacin as his main treatment and his clinical condition showed better day by day. On the last day of admission, his sputum culture showed only normal flora. He no longer needed oxygen therapy and there was no longer any indication for him to be hospitalized.

DISCUSSION

Lower respiratory tract infections acquired in a healthcare setting, such as

hospital-acquired pneumonia (HAP), are highly common and place a significant burden on healthcare resources. HAP specifically is defined as pneumonia that occurs after a patient has been hospitalized for at least 48 hours and any infections incubating before admission to the hospital have been ruled out.[9]

To improve the accuracy and objectivity of early recognition of pneumonia, various scoring systems have been developed and new surveillance guidelines have been implemented. According to European guidelines, the term 'low probability of HAP' refers to patients with low Clinical Pulmonary Infection Score (CPIS) scores or a clinical presentation that is not highly suggestive of pneumonia at symptom onset and continuing up to 72 hours. In contrast, American guidelines rely on clinical criteria alone, rather than using the CPIS in conjunction with clinical criteria, to decide whether or not to initiate antibiotic therapy and do not use the CPIS to guide the discontinuation of antibiotic therapy.[9]

One key difference between the American and European guidelines for the treatment of pneumonia is their recommendations for the use of single versus combination therapies. While the American guidelines recommend combination therapy mainly for targeted therapy and de-escalation, the European guidelines recommend empirical combination therapy for patients with septic shock. It is worth noting that for patients with a low risk of mortality (defined as a 15% or less chance of dying), both guidelines agree that a 7-day course of antimicrobial therapy is preferred over a longer duration. However, European guidelines suggest that monotherapy may be more effective in these patients with serious infections compared to combination therapy.[9]

Pneumonia is typically characterized by the sudden onset of lower respiratory tract infection symptoms, including fever, cough, pleurisy, shortness of breath, and increased production of sputum with consistent radiographic findings. However, in some patients, the presentation of pneumonia may be atypical and primarily consist of non-respiratory symptoms like malaise, muscle pain, confusion, and diarrhea. Elderly individuals may be more likely to experience this type of atypical presentation, which can lead to delays in treatment and increased mortality.[10]

Pneumonia that occurs in a hospital setting (hospital-acquired pneumonia or HAP) that develops more than 5 days after hospitalization (late-onset) is often caused by certain types of bacteria, such as aerobic gram-negative bacilli (e.g., *Acinetobacter species*) or MRSA.[11] Pneumonia usually gets into lung parenchyma, but when the inflammation gets into the bronchi, the infections are highly contagious like in this patient.

MRSA is a type of bacteria that can cause infections. It is commonly found in hospitals (HA-MRSA) and can also be found in the community (CA-MRSA). Compared to HA-MRSA, CA-MRSA typically has smaller SCCmec cassettes and is less resistant to

antibiotics other than the β-lactams antibiotic group.[12]

Research on MDR bacterial strains, including the *A. baumannii complex* and MRSA, is important for understanding and managing infections caused by these bacteria, as well as for preventing the spread of these strains in hospitals and the community.[1] This patient developed MRSA based on his BAL culture and was allergic to its main treatment, vancomycin, while resistant to another treatment, linezolid. Those were the reasons that he had high mortality and morbidity.

Multidrug-resistance *Acinetobacter baumannii* (MDRAB) is a type of bacteria that is resistant to more than three types of antibiotics. A study looked at a database of *A. baumannii* isolates from patients in a city hospital. The study found that 72% (177 out of 247) of the A*. baumannii* isolates were MDR. Fifty-eight percent of the isolates (143 out of 247) were resistant to imipenem, amikacin, and ampicillin-sulbactam, which is considered to be a high level of resistance. Forty-six percent (113 out of 247) of the isolates were resistant to all commonly used antibiotics, including aminoglycosides, cephalosporins, carbapenems, extended-spectrum penicillins, and quinolones, and were therefore classified as pan-drug-resistance.[13]

Carbapenem resistance is a serious problem because it indicates the emergence of antimicrobial resistance and can make it difficult to treat infections. It is especially challenging to manage because it confers high resistance to many drugs. The major site of *A. baumannii* isolation in this study was the respiratory tract, and 86% of patients who died had a positive *A. baumanni* isolate recovered from the respiratory tract.[13]

Factors associated with MDR included the recovery of *Acinetobacter* from multiple sites, mechanical ventilation, previous antibiotic use, and the presence of co-morbidities, particularly neurologic impairment. MDRAB was also significantly associated with an increased mortality rate.[13] Patients with co-morbidities like this patient who had a stroke increased the chance of developing multiple-drug resistance.

Multidrug-resistance *A. baumannii* is resistance to at least two of the following classes of drugs, which are typically effective against these pathogens: antipseudomonal cephalosporins (e.g., ceftazidime or cefepime), antipseudomonal carbapenems (e.g., imipenem or meropenem), ampicillin/sulbactam, fluoroquinolones (e.g., ciprofloxacin or levofloxacin), and aminoglycosides (e.g., gentamicin, tobramycin, or amikacin).[14]

Acinetobacter spp. are a common cause of hospital-associated infections, and they can survive on inanimate surfaces for long periods. In a study, *A. baumannii* was found on the surfaces of hospital rooms that had been cleaned and disinfected after being occupied by patients with MDRAB infections or colonization. At the same time, the presence of MRSA on these surfaces was also investigated, as MRSA can also survive in the hospital

environment and has similar risk factors for infection or colonization as MDRAB.[3]

A study in Hong Kong reported that there has been an increase in the prevalence of multidrug-resistance organisms (MDROs) among 28 nursing homes in the Hong Kong West District. The study analyzed the epidemiological risk factors for colonization with carbapenem-resistance *Acinetobacter baumannii* (CRAB) and MRSA among nursing home residents. The results of the multivariate analysis showed that being bed-bound, using adult diapers due to incontinence, and having a nasogastric tube were common risk factors for both CRAB and MRSA colonization.[15]

Common criteria for diagnosis of HAP/VAP are based on a combination of new and/or progressive lung infiltrates on chest radiograph plus two or more additional criteria that include fever (>38.5°C) or hypothermia; leucocytosis, purulent tracheobronchial secretions, and reduction of partial pressure of oxygen (PaO_2)/FiO_2 ratio of at least 15% in the last 48 hours.[16] This patient was diagnosed with a clinical condition like fever, progressive lung infiltrates on chest radiograph and leucocytosis in laboratory findings. BAL also showed purulent tracheobronchial secretions.

In contrast to community-acquired pneumonia (CAP) in which the dominant typical pathogens are *Streptococcus pneumoniae*, *Mycoplasma pneumoniae*, and *Haemophilus influenzae*, the etiology of HAP/VAP is quite different and challenging. It is noteworthy that obtaining a microbiological culture from the lower respiratory tract in patients developing VAP is relatively easy through the endotracheal tube. This collection appears more difficult to obtain in patients developing HAP, so microbial aetiologies remain poorly documented. However, microbial aetiologies in HAP and VAP are mostly identical. More generally, gram-negative organisms represented a large part of VAP/HAP etiology, ranging from 61.5% and 76.1% of isolates in the US and Europe respectively.[17]

Bronchoscopy was performed on this patient to take BAL culture and bronchial washing. *Bronchoscopy with bronchoalveolar lavage (BAL)* allows the sampling of the lung segments which are suspected to be affected by pneumonia decreasing the false-negative rate. This patient showed edema and erythema left bronchi both on the upper and lower bronchi. Purulent tracheobronchial secret and secret with a blood streak also showed and bronchial washing was performed to minimize hypoxia in this patient. When the bronchi become edema and erythema, the pathogen of pneumonia infection is highly contagious. BAL culture is a gold standard to diagnose pneumonia and accurately can show an antibiotic list for the pathogens.[18]

Vancomycin and linezolid were recommended for HAP patients with MRSA infection, specifically those with prior intravenous antibiotic use within 90 days and in hospitalization units like ICU.[18] This patient developed allergies to vancomycin and was resistant to linezolid, so he was

evaluated based on clinical response and microbiologic results. Amikacin was given and clinical response was evaluated and it was improved. Duration of antibiotic therapy in most patients with HAP or VAP of 7 days appears to be as effective as longer durations and may limit the emergence of resistant organisms.[19]

However, for patients with a severe illness, bacteremia, slow response to therapy, immunocompromise, and complications such as empyema or lung abscess, a longer duration of therapy is indicated.[19] As microbiological results are available, empirical treatment should be revised and possibly narrowed. Rapid molecular diagnostics could have a key role in early de-escalation due to their ability to get rapid pathogen identification and antimicrobial resistance patterns.

American Thoracic Society recommends that all hospitals regularly generate and disseminate a local antibiogram, ideally one that is tailored to their HAP population, if possible, and also recommends that empiric antibiotic regimens be based upon the local distribution of pathogens associated with HAP and their antimicrobial susceptibilities.[19]

A local antibiogram and empiric antibiotic were given to this patient but showed no better condition. Considerations should include their rate of change, resources, and the amount of data available for analysis. An endorsed strategy for the duration of antibiotic treatment in pneumonia consists in giving the shortest course of therapy that is likely to be effective to reduce risks of antibiotic resistance and adverse events.[16] So we concluded and gave the patient based on his culture and evaluated his condition after giving the antibiotics.

Managing hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) requires an interprofessional team of specialists in infectious diseases, pulmonary diseases, critical care, anesthesiologist, and any clinicians and healthcare providers including nurses and pharmacists caring for hospitalized patients with nosocomial pneumonia. Without proper management the morbidity and mortality from HAP and VAP are high.[18]

CONCLUSION

Contracting infections, including dual infections, which could lead to severe consequences are more likely in individuals with multiple comorbidities, including chronic ailments, recent antibiotic usage within 90 days, and immune-deficiency conditions. Prompt diagnosis and treatment of double infections are particularly crucial in patients with MRSA and MDRAB.

Based on the case, it has been observed that the patient was not responsive to the first-line drugs for MRSA, such as linezolid and vancomycin, which makes it challenging to determine an effective treatment plan. These findings also indicate the possibility of heightened morbidity and mortality, emphasizing the importance of timely and effective

treatment by practitioners. Proper follow-up care, including microbiological, clinical, and radiological monitoring, is crucial for the patient's recovery.

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