Treating a patient with pan-resistant Acinetobacter: a case study

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Abstract

Acinetobacter has emerged as a highly important organism in global healthcare, owing to its propensity to develop pan-resistance. This resistant pathogen poses a significant challenge to healthcare professionals because it not only restricts patient care through ineffective treatment modalities but also leads to high mortality and morbidity rates. The case of a 22-year-old young man reporting to the Emergency department (ER) of Pakistan Institute of Medical Sciences (PIMS), Islamabad, on 6th June, 2023 is presented. He complained of fever accompanied with seizures which gave a suspicion of autoimmune encephalitis or viral haemorrhagic fever. Despite initial therapeutic interventions, the patient's condition worsened, prompting further investigations. Culture and sensitivity testing of tracheal secretions revealed pan-resistance, and subsequent treatment with a combination of antibiotics including Tigecycline and Colistin, yielded a favourable response. The aim for reporting this case, is to highlight the challenges inherent in diagnosing and managing patients with pan-resistant Acinetobacter, as antimicrobial resistance continues to evolve. Furthermore, research endeavours should focus on identifying safe and effective antibiotic combinations, exploring novel treatment approaches, and improving patient outcomes.

Keywords: Acinetobacter, multi-drug resistance, pan resistant, encephalitis, colistin, tigecycline.

DOI: https://doi.org/10.47391/JPMA.10688

Introduction

Acinetobacter has emerged as a significant nosocomial pathogen, causing infectious outbreaks in critically ill patients, leading to high mortality and morbidity rates.[1] Acinetobacter is a Gram-negative bacterium. The most frequently reported strains are Acinetobacter rufi, Acinetobacter calcoaceticus and Acinetobacter baumannii. Among these, Acinetobacter baumannii possesses the greatest clinical significance, owing to its ability to accumulate multiple drug resistance genes, resulting in multidrug resistance (MDR).[2] Moreover, pan-resistance to therapeutically prescribed antibiotics has also been reported.[3] Consequently, Acinetobacter baumannii has become a formidable pathogen in global healthcare, with a surge in nosocomial infections and community-acquired epidemics. It is now recognized as a highly resistant pathogen in the hospitals of Pakistan also.[4]

Numerous studies have demonstrated a correlation between multidrug-resistant Acinetobacter and mortality. The crude mortality (at any age) for Acinetobacter spp. is reported to range from 23 - 73%.[1] Despite the lack of an established therapy regimen, treating pan-drug resistant (PDR) Acinetobacter baumannii strains is becoming increasingly significant due to their high mortality rates.[5]

This case report thus intends to emphasize the clinical characteristics, challenges encountered and management techniques for a patient with pan-resistant Acinetobacter associated with encephalitis.

Case Report

This case concerns a 22-year-old unmarried male, with no known comorbidities, who presented at the Emergency department (ER) of Pakistan Institute of Medical Sciences (PIMS), Islamabad on 6th of June, 2023. His Glasgow Coma Scale (GCS) 6 was 8/15 and he complained of fever, nasal congestion and a sore throat. The patient had been ambulant when he suddenly developed a high grade, continuous fever, unresponsive to antipyretics. Subsequently, after an interval of 1 day, the patient experienced a generalized tonic-clonic seizure lasting for one minute, unaccompanied by headache, photophobia, vomiting, or altered bowel habits. Shortness of breath was noted, with no chest pain or bleeding from any site. Mild ataxia and dysarthria had been present for 4 years, with no history of substance addiction or drug allergy.

Following the patient's condition, admission to the

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Submission complete: 20-09-2023 **Review began:** 22-11-2023
Acceptance: 01-06-2024 **Review end:** 08-05-2024

Table: Tracheal culture and sensitivity report

Antibiotics	Acinetobacter SPP. (XDR)	E.coli (MDR)
Amikacin AK	R	S
Amoxi/clavul.acid AMC	-	R
CEFTAZIDIME-AVIBACTAM CZA	R	-
Cefipime FEP	R	R
Ceftazidime CAZ	R	R
Ceftriaxone CRO	R	R
Chloramphenicol C	R	-
Ciprofloxacin CIP	R	R
Co-Trimoxazole SXT	R	R
Colistin CT	I	I
ERTAPENEM	-	S
FOSFOMYCIN IV	-	S
Gentamicin CN	R	R
Imipenem IPM	R	S
Levofloxacin LEV	R	R
Meropenem MEM	R	S
Minocycline	R	R
Pip-Tazobactam TZP	R	R

(R= Resistance, S= Sensitive, I= Intermediate Resistance)

Medical Intensive Care Unit (MICU) of PIMS ensued, with an established provisional diagnosis of Autoimmune Encephalitis or Viral Haemorrhagic Fever. Due to his critical condition, he required intubation, which was maintained for 11 days. Subsequently, he was successfully extubated and transferred to the medical ward for treatment under the protocols of autoimmune encephalitis. Lab investigations for renal function tests (RFTs) and liver function tests (LFTs), revealed inconclusive results except for an elevated alanine transaminase (ALT) level, potentially attributed to sepsis. The patient's erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were raised probably due to shortness of breath with associated hospital-acquired pneumonia (HAP) or community-acquired pneumonia (CAP). A serum ceruloplasmin level test to rule out Wilson's Disease yielded unremarkable results. Serum electrolytes test reported hyponatraemia, common in various brain diseases. In this regard, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) scans were performed, yielding inconclusive results. Electroencephalography (EEG) was conducted multiple times, revealing diffuse slowing, suggestive of diffuse encephalopathy. However, cerebrospinal fluid routine examination (CSF-RE) revealed no abnormal findings. In the workup for autoimmune encephalitis, all the antibodies, including anti-nDNA antibodies were negative. There was no bleeding tendency or purpura, petechiae and bruises anywhere on the body. Prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR) were within the normal ranges, excluding viral haemorrhagic fever from the differential diagnosis.

Besides all workup, tracheal secretions culture and sensitivity (C/S) test was advised. (Table 1) Which revealed pan-resistant, Gram-negative Acinetobacter baumannii infection. Treatment with high-potency antibiotics, specifically tigecycline and colistin was initiated, which resulted in an improved CRP. Despite this improvement in CRP during the short hospital stay, the patient's GCS exhibited a persistent declining trend, presumably due to the encephalitis. Regrettably, on the 8th day, the patient succumbed to respiratory failure.

Discussion

Pan-resistant Acinetobacter baumannii poses a significant concern within global healthcare settings. Acinetobacter baumannii infections are rare and typically affect organ systems with high fluid content, such as the urinary tract, peritoneal cavity, respiratory tract, and cerebrospinal fluid (CSF). Nosocomial pneumonia is the most common clinical manifestation of these infections. The risk factors associated with nosocomial infections stemming from this bacterium include mechanical ventilation, prolonged hospitalisation, intensive care unit admission, recent surgical procedures, and central venous catheter usage.[3]

In this case study, the patient presented with fever, neurological symptoms (including seizures, ataxia, and dysarthria), and dyspnoea. The initial diagnosis suggested autoimmune encephalitis or viral haemorrhagic fever. However, the patient's condition failed to improve with conventional treatment, and the fever persisted. Subsequent investigations revealed the presence of pan-resistant Acinetobacter baumannii in the tracheal culture, as confirmed by sensitivity testing. Multidrug-resistant Acinetobacter (MDRA) is defined as resistance to more than two of the five classes of drugs: cephalosporins, carbapenems, ampicillin-sulbactam, fluoroquinolones and aminoglycosides.[3] However, pan-resistant Acinetobacter (PRA) is defined as resistance to all five classes of the aforementioned drugs.[7]

The significance of pan-resistant Acinetobacter baumannii is associated with high mortality and limited therapeutic options. Research studies have reported the crude morality rate of Acinetobacter infections to range from 23 - 73%.[1] Therefore, a combination of antibiotics is used in the treatment regimen of pan-resistance Acinetobacter. The most studied combinations are polymyxin-based combinations including sulbactam, carbapenems and vancomycin, rifampicin, and fosfomycin.[8] These combinations of antibiotics have

demonstrated a synergistic action against PDR A. baumannii.[9] In this case, the patient responded positively to a regimen comprising high-potency antibiotics, tigecycline, and colistin. Research findings suggest that tigecycline-colistin combination are more synergistic than the tigecycline-rifampicin and colistin–rifampicin combinations.[5] For the first-line treatment, the carbapenem meropenem is the most recommended empirical treatment. However, its efficacy is compromised by a resistance rate exceeding 40% in carbapenem-resistant strains.[2] In the case of carbapenem resistant gram-negative bacterium (CRGM), double combination antibiotics are used, especially when treating bacteraemia, pneumonia and central nervous system infections. The most common combination involves a polymyxin paired with a carbapenem.[10] Since polymyxins have a poor blood-brain barrier; a combination of intravenous and intrathecal administration is often employed.[5] Notably, a case study from Karachi, Pakistan has also reported successful treatment with Intravenous (IV) and Intrathecal (IT) polymyxins in paediatric patients with Acinetobacter meningitis.[7]

Conclusion

This case study underscores the challenges inherent in diagnosing and treating very rare infections caused by the pan-resistant Acinetobacter baumannii. Preceding literature has elucidated the critical importance of this highly resilient pathogen. Thus, pan-resistant Acinetobacter baumannii poses a grave threat that necessitates continuous surveillance and effective management. Furthermore, there exists a compelling need for augmented research endeavours aimed at refining and validating the existing antibiotic combinations. This pursuit is crucial to the development of a treatment regimen that is both safe and efficacious against pan-resistant Acinetobacter baumannii.

Consent: Written consent was obtained from the patient's attendant for publishing his case.

Disclaimer: None.

Conflict of Interest: None.

Funding disclosure: None.

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Authors' Contribution:
MN: Concept, data interpretation, drafting, writing, proofreading, final approval and responsible for all aspects of this work.
NA: Concept, data collection, proofreading, final approval and responsible for all aspects of this work.
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