BJMS BATNA JOURNAL OF MEDICAL SCIENCES
www.batnajms.net

BATNA JOURNAL OF MEDICAL SCIENCES
2024, VOL. 11, NO. 4, 510–512
DOI: 10.48087/BJMScr.2024.11418

ORIGINAL ARTICLE

OPEN ACCESS

Isolation of VIM-producing multidrug-resistant *Pseudomonas aeruginosa* in pediatric haematology ward

Siham AZROU, Djamila TOUATI, Fazia DJENNANE

Mother-Child Medical Biology Laboratory, Béni Messous University Hospital , Microbiology Laboratory, Faculty of Pharmacy of Algiers.

ABSTRACT

The Gram-negative bacillus *Pseudomonas aeruginosa* is renowned for its extensive natural antibiotic resistance and opportunistic behaviour. With the exception of ertapenem, carbapenems represent the optimal pharmacological intervention for the treatment of infections caused by Pseudomonas species resistant to ceftazidime. Nevertheless, the presence of a Pseudomonas strain that produces carbapenemase renders this therapeutic approach ineffective. In this report, we describe the isolation of a multidrug-resistant VIM-producing strain of *Pseudomonas aeruginosa* from a patient in a paediatric haematology ward. A 13-year-old patient was admitted to the paediatric ward for the purpose of undergoing treatment for acute myeloblastic leukaemia. The patient presented with a fever of 40°C, accompanied by abdominal discomfort and diarrhoea. An abdominal ultrasound scan revealed the presence of colitis, exhibiting both inflammatory and infectious characteristics. The results of the stool analysis indicated the presence of *Pseudomonas aeruginosa*. Antibiotic susceptibility testing was conducted using the Gram-negative NMIC/ID 94 panel. The results of the antibiotic susceptibility testing indicated resistance to amikacin, cefepime, ceftazidime, ciprofloxacin, gentamicin, imipenem, levofloxacin, meropenem and piperacillin-tazobactam. The resistance mechanisms of carbapenem were confirmed by a positive EDTA test. The carbapenemase were detected using a chromogenic test . The isolated Pseudomonas strain was found to produce VIM. This discovery offers an opportunity to enhance the national database on the profile and resistance mechanisms of *Pseudomonas aeruginosa* strains. However, a molecular study of the strain is essential for precise typing of the VIM variant.

ARTICLE HISTORY

Received 06 Mai 2024
Accepted 28 Jun 2024

KEYWORDS

Pseudomonas, carbapenemase, leukaemia, colitis, Algeria.

CORRESPONDING AUTHOR

Siham AZROU
s.azrou@univ-alger.dz

1. INTRODUCTION

Pseudomonas aeruginosa is an opportunistic pathogen that primarily affects vulnerable and immunocompromised individuals(1,2). This bacterium is renowned for its intrinsic resistance to antibiotics and disinfectants(3). It poses a significant public health concern due to the emergence of multidrug-resistant strains, particularly those resistant to carbapenems, which are typically effective against multidrug-resistant Gram-negative bacteria(4,5).

Pseudomonas exhibits resistance to carbapenems through both non-enzymatic mechanisms, such as efflux pump hyperexpression and D2 porin modification, and enzymatic mechanisms, including the production of carbapenemases, predominantly metallo-beta-lactamases (MBL)(6). These carbapenemases belong to Ambler's class B, comprising primarily imipenemase (IMP), Verona integron-mediated metallo-beta-lactamase (VIM), Sao Paulo MBL (SPM), Saul imipenemase (SIM), Australian imipenemase (AIM), German imipenemase (GIM),

To cite the article: Azrou S et al. Isolation of VIM-producing multidrug-resistant *Pseudomonas aeruginosa* in pediatric haematology ward Batna J Med Sci 2024; 11(4): 510-512

Dutch imipenemase (DIM), and New Delhi metallo-beta-lactamase (NDM)(7,8). MBL-producing strains are frequently linked to resistance against other antibiotics. They can rapidly disseminate within healthcare facilities, leading to challenging-to-treat infections that escalate morbidity, mortality, and treatment expenses(9,10). We present the isolation of a VIM-producing multidrug-resistant strain of *P. aeruginosa*.

2. CASE REPORT

As part of an infectious disease assessment following post-chemotherapy febrile aplasia (temperature of 39°C, white blood cell count of 0.63x103/µl), a 13-year-old patient admitted to the pediatric ward of Beni-Messous university hospital center for acute myeloblastic leukaemia management had their blood culture sent to the laboratory for bacteriological analysis. Initially, triple antibiotic therapy comprising cefotaxime, amikacin, and vancomycin was administered. On the second day of febrile aplasia, blood culture results revealed the isolation of Klebsiella pneumoniae resistant to third-generation cephalosporins, prompting discontinuation of cefotaxime and mevancomycin and initiation of imipenem therapy.

By the fourth day of febrile aplasia, the patient experienced a fever spike of 40°C accompanied by abdominal pain and diarrhoea episodes. Abdominal ultrasound detected colitis with inflammatory or infectious features. Stool analysis revealed rare leukocytes on microscopic examination and lactose-negative colonies growth in stool culture in Hektoen medium (Dimed, Algeria).

The bacterial strain and antibiotic susceptibility testing were identified using the Gram-negative NMIC/ID 94 panel (Phoenix, BD) . Antibiotic sensitivity tests were conducted and interpreted in accordance with the Clinical Laboratory Standards Institute (CLSI M100, 2022). Antibiotic susceptibility test reports resistance to amikacin, cefepime, ceftazidime, ciprofloxacin, gentamicin, imipenèm, levofloxacinem, meropem and piperacilline-tazobactam .The strain is sensitive to aztreonam (Table 1).

Further investigations of the isolated strain were conducted to detect and confirm resistance mechanisms to third-generation cephalosporins and carbapenems, including a negative synergy test and a positive EDTA test (11) . MBL detection was conducted using a chromogenic test (Coris, Bio Concept) to characterize MBLs: IMP, VIM, NDM, KPC, and OXA-48. The isolated Pseudomonas strain was found to produce VIM.

3. DISCUSSION

A multidrug-resistant strain of *P. aeruginosa* was isolated from an oncohematologicpediatric centre. This strain resisted to carbapenems due to MBL production. This report holds significant importance as carbapenem-resistant *P. aeruginosa* has been categorized as a priority bacterium on the WHO priority list of antibiotic-resistant bacteria (12).*P. aeruginosa* is a particularly significant pathogen in patients with haematological malignancies(13). The number of antimicrobial molecules that are active against this bacterium is limited and include β-lactams (piperacillin and ticarcillin, with or without an inhibitor, ceftazidime, cefepime, aztreonam, imipenem, meropenem, doripenem), fluoroquinolones (ciprofloxacin, levofloxacin), aminoglycosides (except kanamycin), fosfomycin and colimycin (14).

Tableau 1. Antibiotic susceptibility test results

Antibiotics	MIC (ug/ml)	SIR
Amikacin	> 32	R
Aztreonam	8	S
Cefepime	16	R
Ceftazidime	16	R
Ciprofloxacin	2	R
Colistin	1	X
Gentamicin	8	R
Imipenem	8	R
Levofloxacine	4	R
Meropenem	8	R
Piperacilline-Tazobactam	64/4	I

S: Susceptible, I: intermediate, R: resistant, X: not interpretable.

Bacteria have gradually adapted to β-lactam class antibiotics by various mechanisms, including the production of enzymes called β-lactamases, which are capable of hydrolysing the β-lactam ring that is required for their antibacterial activity. Moreover, the progressive emergence of multi-resistant strains producing extended-spectrum β-lactamases and carbapenemases has also been documented. Carbapenemases are β-lactamases with the capacity to degrade carbapenems (imipenem, meropenem and/or doripenem) (15). The most prevalent and impactful carbapenemases in Pseudomonas aeruginosa are MBL (Ambler class B) who confer resistance to all antibiotics, with the exception of aztreonam, including ceftolozane-tazobactam and ceftazidime-avibactam. In contrast, cefiderocol is not affected (16). Among the MBLs produced by *P. aeruginosa*, NDM, VIM, and IMP are the most commonly encountered (17,18), with VIM showing a clear predominance (19). This enzyme has been detected in various regions of Algeria (20–22).These enzymes are encoded on mobile genetic elements carrying genes to resist other antibiotics, facilitating horizontal transfer to other bacterial genera and species. When associated with carbapenem resistance genes, this phenomenon contributes to the emergence of multidrug-resistant strains diminishing the

To cite the article: Azrou S et al. Isolation of VIM-producing multidrug-resistant *Pseudomonas aeruginosa* in pediatric haematology ward Batna J Med Sci 2024; 11(4): 510-512

effectiveness of available treatments and sometimes rendering them ineffective (23,24).

4. CONCLUSION

Our discovery provides an opportunity to enhance the national database concerning the profile and resistance mechanisms of *P. aeruginosa* strains. However, conducting a molecular study of the strain is imperative for precisely typing the VIM variant.

Competing interests: The authors declare that they have no competing interest.

REFERENCES

1. Er H, Altındiş M, Aşık G, Demir C. [Molecular epidemiology of beta-lactamases in ceftazidime-resistant Pseudomonas aeruginosa isolates]. MikrobiyolBul. avr 2015;49(2):156-65.
2. Tissot F, Blanc DS, Basset P, Zanetti G, Berger MM, Que YA, et al. New genotyping method discovers sustained nosocomial Pseudomonas aeruginosa outbreak in an intensive care burn unit. J Hosp Infect. 1 sept 2016;94(1):2-7.
3. Stover CK, Pham XQ, Erwin AL, Mizoguchi SD, Warrener P, Hickey MJ, et al. Complete genome sequence of Pseudomonas aeruginosa PAO1, an opportunistic pathogen. Nature. 31 août 2000;406(6799):959-64.
4. Simner PJ, Opene BNA, Chambers KK, Naumann ME, Carroll KC, Tamma PD. Carbapenemase Detection among Carbapenem-Resistant Glucose-Nonfermenting Gram-Negative Bacilli. J ClinMicrobiol. sept 2017;55(9):2858-64.
5. Zahran W, Hindawi G, Labeeb A, Galal R. Prevalence of Multidrug-Resistant Pseudomonas aeruginosa in Patients with Nosocomial Infections at a University Hospital in Egypt, with Special Reference to Typing Methods. J VirolMicrobiol. 6 mars 2013;2013:1-13.
6. Rodríguez-Martínez JM, Poirel L, Nordmann P. Molecular Epidemiology and Mechanisms of Carbapenem Resistance in Pseudomonas aeruginosa. Antimicrob Agents Chemother. nov 2009;53(11):4783-8.
7. Cornaglia G, Giamarellou H, Rossolini GM. Metallo-β-lactamases: a last frontier for β-lactams? Lancet Infect Dis. mai 2011;11(5):381-93.
8. Jovcic B, Lepsanovic Z, Suljagic V, Rackov G, Begovic J, Topisirovic L, et al. Emergence of NDM-1 Metallo-β-Lactamase in Pseudomonas aeruginosa Clinical Isolates from Serbia ▿. Antimicrob Agents Chemother. août 2011;55(8):3929-31.
9. Walters MS, Grass JE, Bulens SN, Hancock EB, Phipps EC, Muleta D, et al. Carbapenem-Resistant Pseudomonas aeruginosa at US Emerging Infections Program Sites, 2015. Emerg Infect Dis. juill 2019;25(7):1281-8.
10. Cantón R, Akóva M, Carmeli Y, Giske CG, Glupczynski Y, Gniadkowski M, et al. Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe. ClinMicrobiol Infect Off PublEurSocClinMicrobiol Infect Dis. mai 2012;18(5):413-31.
11. Algerian Network for Monitoring the Resistance of Bacteria to Antibiotic. Standardisation of the Antibiotic at the National Scale (Human and Veterinary Medicine). 6th Edition. 2011.
12. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. Discovery, research, and development of new antibiotics: the WHO priority list of antibiotic-resistant bacteria and tuberculosis. Lancet Infect Dis. mars 2018;18(3):318-27.
13. Reynolds, D.; Kollef, M. The Epidemiology and Pathogenesis and Treatment of Pseudomonas aeruginosa Infections: An Update. Drugs 2021, 81, 2117–2131.]
14. Clinical and Laboratory Standards Institute. Performance and Standards for Antimicrobial Susceptibility Testing. Available online: https://www.nih.org.pk/wp-content/uploads/2021/02/CLSI-2020.pdf (accessed on 10 January 2023)
15. Audrey Mérensa, Hervé Delacoura , Patrick Plésiatb, Jean-Didier Cavalloc , Katy Jeannotb. Pseudomonas aeruginosa et résistance aux antibiotiques. REVUE FRANCOPHONE DES LABORATOIRES - SEPTEMBRE-OCTOBRE 2011 - N°435
16. Glen, K.A.; Lamont, I.L. β-lactam Resistance in Pseudomonas aeruginosa: Current Status, Future Prospects. Pathogens 2021, 10, 1638. [CrossRef]
17. Watanabe M, Iyobe S, Inoue M, Mitsuhashi S. Transferable imipenem resistance in Pseudomonas aeruginosa. Antimicrob Agents Chemother. janv 1991;35(1):147-51.
18. Shanthi M, Sekar U, Kamalanathan A, Sekar B. Detection of New Delhi metallo beta lactamase-1 (NDM-1) carbapenemase in Pseudomonas aeruginosa in a single centre in southern India. Indian J Med Res. oct 2014;140(4):546-50.
19. Diene SM, Rolain JM. Carbapenemase genes and genetic platforms in Gram-negative bacilli: Enterobacteriaceae, Pseudomonas and Acinetobacter species. ClinMicrobiol Infect Off PublEurSocClinMicrobiol Infect Dis. sept 2014;20(9):831-8.
20. Sefraoui I, Berrazeg M, Drissi M, Rolain JM. Molecular epidemiology of carbapenem-resistant Pseudomonas aeruginosa clinical strains isolated from western Algeria between 2009 and 2012. Microb Drug Resist Larchmt N. avr 2014;20(2):156-61.
21. Touati M, Diene SM, Dekhil M, Djahoudi A, Racherache A, Rolain JM. Dissemination of a class I integron carrying VIM-2 carbapenemase in Pseudomonas aeruginosa clinical isolates from a hospital intensive care unit in Annaba, Algeria. Antimicrob Agents Chemother. mai 2013;57(5):2426-7.
22. Mellouk FZ, Bakour S, Meradji S, Al-Bayssari C, Bentakouk MC, Zouyed F, et al. First Detection of VIM-4-Producing Pseudomonas aeruginosa and OXA-48-Producing Klebsiella pneumoniae in Northeastern (Annaba, Skikda) Algeria. Microb Drug Resist Larchmt N. avr 2017;23(3):335-44.
23. Jacoby GA, Munoz-Price LS. The new beta-lactamases. N Engl J Med. 27 janv 2005;352(4):380-91.
24. Queenan AM, Bush K. Carbapenemases: the versatile beta-lactamases. Clin MicrobiolRev. juill 2007;20(3):440-58, table of contents.