Official journal of the Spanish Society of Chemotherapy

ISSN: 0214-3429 / ©The Author 2023. Published by Sociedad Española de Quimioterapia. This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0)(https://creativecommons.org/licenses/by-nc/4.0/).

Letter to the Editor

Revista Española de Quimioterapia
doi:10.37201/req/012.2023

María Martínez Pérez[1]
Alberto Vázquez Blanquiño[2]
Rocío Morón[1]
Lucía Pérez Rodríguez[2]
Natalia Chueca Porcuna[2]

Multidrug-resistant *Acinetobacter baumannii*: A therapeutic challenge

[1]Servicio Farmacia Hospitalaria, Hospital Universitario Clínico San Cecilio, Granada, España
[2]Servicio de Microbiología Clínica, Hospital Universitario Clínico San Cecilio, Granada, España

Article history
Received: 25 January 2023; Revision Requested: 9 April 2023; Revision Received: 9 May 2023; Accepted: 1 June 2023; Published: 21 July 2023

Sir,

The World Health Organization (WHO) has classified carbapenem-resistant *Acinetobacter baumannii* (AB) as a priority pathogen whose epidemiological evolution toward multidrug resistance or pan-resistance is a critical threat to global welfare [1]. We present the clinical case of a 49-year-old man with a history of inflammatory bowel disease and human immunodeficiency virus (HIV) infection diagnosed in the 7 months before to admission. He attended the emergency department with acute paraparesis 0/5 in muscle balance and was admitted to neurosurgery where a D7-D10 laminectomy was performed where samples were taken for pathological anatomy. Following the results, a diagnosis of Burkitt's lymphoma was made, and the treatment was started on an inpatient basis in accordance with the BURKIMAB protocol. After 5 days of intensive treatment, the patient was stable and blood cultures (BC) were repeatedly negative; however, he presented occasional febrile peaks that were well tolerated. Given the oscillating clinical manifestations with recurrent signs of infection, and after new BC and catheter cultures pending results, treatment with meropenem was prescribed empirically, adding daptomycin after 48 hours as the tendency to worsen persisted.

Twelve hours after starting daptomycin, the patient developed a rash and it was decided to replace it with teicoplanin. Due to the patient's clinical situation (HIV infection with CD4/CD8 T-cell inversion (29/41), elevated hepatobiliary profile with symptoms suggestive of acute viral/toxic/ischaemic hepatitis and signs of septic shock without a definite primary focus of infection (high fever, tachycardia and a tendency to hypotension), the immunosuppressed state and the high susceptibility to infection by opportunistic pathogens led to admission to the Intensive Care Unit (ICU) under empirical treatment with imipenem, vancomycin, tigecycline, acyclovir and cotrimoxazole. AB producing carbapenemase type IMP and OXA-48, with restricted susceptibility to colistin and cefiderocol, was isolated in the BC. A complete study of antibiotic synergies was carried out according to the evidence, and all combinations were negative. Previous antibiotherapy was replaced by colistin at a loading dose of 9 million international units (MUI) and maintenance dose of 4.5 MUI/12h together with cefiderocol at 2 mg/8h administered over 3 hours, both for 8 days. Despite the vital compromise that our patient had who required close multidisciplinary management and the use of noradrenaline at a dose of 1-1.5 mcg/kg/min; 48 hours after the start of the referred treatment, hemodynamic stability was achieved, with a decrease in procalcitonin and other inflammation parameters, and he could be transferred back to Hematology for the management of his Burkitt's lymphoma.

The choice of a correct empirical treatment is of vital importance to reduce death in patients with sepsis or septic shock, where even with an adequate therapeutic line, mortality can reach 40% if the patient is immunocompromised [2]. We find ourselves in a complex era in which the emergence of multidrug-resistant (MDR) bacteria in nosocomial spaces has increased in recent years, where the therapeutic options available against these pathogens are more limited. This is even more worrying in the case of oncology and HIV+ patients.

Focusing on AB, we know that it is a non-fermenting Gram-negative coccobacillus that mainly affects hospitalized and immunocompromised patients producing nosocomial and opportunistic infections, such as ventilator-associated pneumonias, urinary tract infections, meningitis or sepsis. The main world health authorities, such as ECDC, have warned of the development of resistances that pose a therapeutic challenge and compromise the lives of our patients [3, 4].

In our case we were faced with a AB-MDR resistant to the first lines of treatment (carbapenems, glycylcyclines, aminoglycosides and rifampicin) [4] with an antibiogram that re-

Correspondence:
Rocío Morón Romero.
Servicio Farmacia Hospitalaria, Hospital Universitario Clínico San Cecilio, Granada, Spain
E-mail: rmoronr@gmail.com

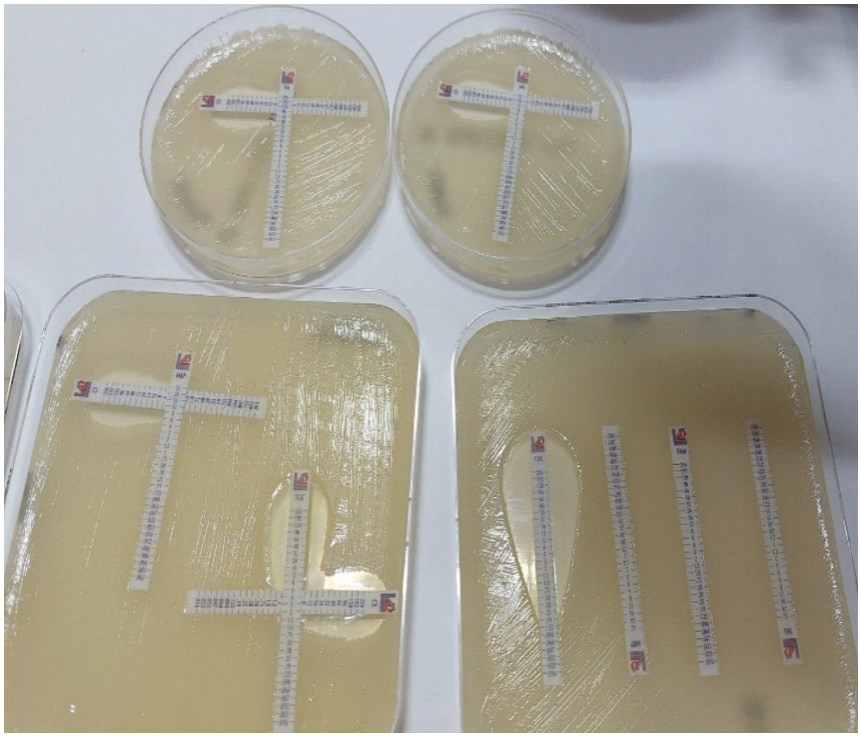

Figure 1 | **Synergy study of multidrug-resistant *Acinetobacter baumannii*.**

flected susceptibility only to colistin with a MIC ≤ 0.5 mg/L and to cefiderocol with MIC ≤ 0.125 mg/L. Hernández-Torres et al. demonstrated in their study that the use of therapeutic combinations such as colistin + tigecycline, colistin + meropenem, colistin + vancomycin or colistin + rifampicin, constituted a positive interaction in which significantly greater activity was obtained than expected in monotherapy in severe infections. Despite this scientific evidence, it was not possible to apply this therapeutic combination, because after its study, it was concluded that our pathogen did not present synergies (Figure 1). Finally, based on the patient's clinical situation and the data obtained, it was decided to prescribe colistin + cefiderocol bitherapy, despite the fact that the clinical practice guidelines of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) [5] and Infectious Diseases Society of America (IDSA) [6] advise against the use of cefiderocol in AB infections due to the results of the phase III CREDIBLE-CR clinical trial in which patients with severe AB infections treated with cefiderocol had higher mortality than those treated the best available therapy at the time. However, our patient responded favorably. In short, cefiderocol is a new siderophore cephalosporin, which differs from the mechanisms of action usually known, making it one of the best therapeutic alternatives in patients with severe AB-MDR infections despite its limited evidence [7].

FUNDING

None to declare

CONFLICTS OF INTEREST

The authors declare no conflicts of interest

REFERENCES

1. Reina R, León-Moya C, Garnacho-Montero J. Treatment of *Acinetobacter baumannii* severe infections. Med Intensiva. 2022;700-710. doi: 10.1016/j.medine.2022.08.007
2. Maseda E, Suárez de la Risa A. The role of cefiderocol in clinical practice. Rev Esp Quimioter. 2022;35(SUPPL.2):39-44. doi: 10.37201/req/s02.06.2022
3. JianMea-Phelim H, Yong-Eng VC, Wong H. An overview of *Acinetobacter baumannii* pathogenesis: Mortility, adherence and biofil formation. Microbiol Res. 2021(247);126722. doi: 10.1016/j.micres.2021.126722
4. Martínez JA. Approach to directed therapy after knowledge of the isolate:carbapenemase-producing Enterobacteriaceae, multidrug-resistant *Pseudomonas aeruginosa* and carbaapenem-resistant *Acinetobacter baumannii*. Rev Esp Quimioter. 2016;29(Supple1):31-34.

5. Paul M, Carrara E, Retamar P, Tängdén T, et al. European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European society of intensive care medicine). Clin Microbiol Infect. 2022 Apr;28(4):521-547. doi: 10.1016/j.cmi.2021.11.025.
6. Tamma PD, Aitken SL, Bonomo RA, et al. Infectious Diseases Society of America Guidance on the Treatment of AmpC β-Lactamase-Producing *Enterobacterales*, Carbapenem-Resistant *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia* Infections. Clin Infect Dis. 2022 Jul 6;74(12):2089-2114. doi: 10.1093/cid/ciab1013.
7. Soriano A, Mensa J. Mechanism of action of cefiderocol. Rev Esp Quimioter. 2022;35(Supple2):16-19. doi: 10.37201/req/s02.02.2022