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Research article

Adaptive resistance to cefiderocol in carbapenem-resistant *Acinetobacter baumannii* (CRAB): Microbiological and clinical issues

Anissa Desmoulin [a,*], Loïk Sababadichetty [b], Laure Kamus [a,b], Marion Daniel [b], Lucie Feletti [a], Nicolas Allou [c], Anaïs Potron [d], Anne-Gaëlle Leroy [e], Marie-Christine Jaffar-Bandjee [a], Olivier Belmonte [a], Thomas Garrigos [a,b,f], Guillaume Miltgen [a,b,f]

[a] *Laboratoire de Bactériologie, CHU Félix Guyon, Saint-Denis, La Réunion, France*
[b] *UMR PIMIT, Processus Infectieux en Milieu Insulaire Tropical, CNRS 9192, INSERM U1187, IRD 249, Université de La Réunion, Sainte-Clotilde, La Réunion, France*
[c] *Service de Réanimation Polyvalente, CHU Félix Guyon, Saint-Denis, La Réunion, France*
[d] *Centre National de La Résistance Aux Antibiotiques, Laboratoire Associé Pseudomonas et Acinetobacter, CHU Jean Minjoz, Besançon, France*
[e] *Laboratoire de Bactériologie, Groupe Hospitalier Sud Réunion, Saint-Pierre, La Réunion, France*
[f] *Centre Régional en Antibiothérapie de La Réunion, Saint-Denis, La Réunion, France*

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ABSTRACT

Objectives: Determining the best available therapy for carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections is a challenge. Cefiderocol is an attractive alternative drug effective against many resistance mechanisms in Gram-negative bacteria. However, its place in the treatment of *Acinetobacter baumannii* infections remains unclear and much debated, with contradictory results.

Methods: We describe here the case of a 37-year-old man with ventilator-associated bacteraemic CRAB pneumonia in an intensive care unit. He was initially treated with a combination of colistin and tigecycline, and was then switched onto colistin and cefiderocol. We then used a new accessible protocol to test 30 CRAB isolates (OXA-23/OXA-24/OXA-58/NDM-1) for adaptive resistance to cefiderocol (ARC) after exposure to this drug.

Results: After clinical failure with the initial combination, we noted a significant clinical improvement in the patient on the second combination, leading to clinical cure. No ARC was detected in the two OXA-23 case-CRAB isolates. All NDM-1 CRAB isolates were resistant to cefiderocol in standard tests; the OXA-23, OXA-24 and OXA-58 CRAB isolates presented 84.2 %, 50 % and 0 % ARC, respectively.

Conclusions: ARC is not routinely assessed for CRAB isolates despite frequently being reported in susceptible isolates (69.2 %). Subpopulations displaying ARC may account for treatment failure, but this hypothesis should be treated with caution in the absence of robust clinical data. The two main findings of this work are that *(i)* cefiderocol monotherapy should probably not be recommended for OXA-23/24 CRAB infections and *(ii)* the characterisation of carbapenemases in CRAB strains may be informative for clinical decision-making.

* Corresponding author. Laboratoire de Bactériologie, CHU Félix Guyon, Saint-Denis, 97400, La Réunion, France.
E-mail address: anissa.desmoulin@chu-reunion.fr (A. Desmoulin).

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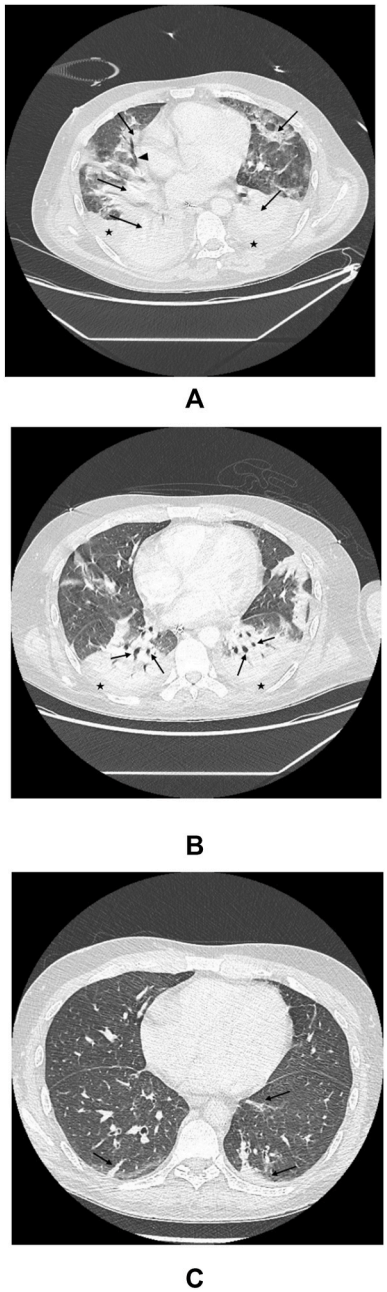

Fig. 1. Progression of lung involvement on CT scans
A. Contrast-enhanced computed tomography (CECT) of the chest, showing bilateral multifocal areas of consolidation (arrows) with a rare air bronchogram in the right middle lobe (arrowhead) and no sign of necrosis or cavitation. Bilateral pleural effusion (★).
B. CECT of the chest, showing a partial regression of consolidation and additional air bronchograms in the upper segments of the lower lobes (arrows). Partial regression of bilateral pleural effusion (★).
C. Non-enhanced computed tomography (NECT) of the chest, showing small residual consolidations in the upper segments of the lower lobes (arrows). No pleural effusion.

1. Introduction

Multidrug- (MDR) and extensively drug-resistant (XDR) Gram-negative bacteria are increasingly emerging worldwide. The burden of these infections is considerable and was estimated at 192 000 years lost to disability and more than 1.27 million attributable deaths in the world in 2019 [1]. The development of new antibiotics is, thus, a global priority for the World Health Organisation (WHO) [2]. Cefiderocol, a siderophore cephalosporin, has emerged as a safe new alternative effective against bacteria displaying a large range of beta-lactam resistance mechanisms: β-lactamases (especially AmpC cephalosporinase; *Klebsiella pneumoniae* carbapenemase KPC, New Delhi Metallo-β-lactamase NDM and Oxacillinase OXA carbapenemases), porin mutations and efflux pumps [3]. However, its value for the clinical treatment of *Acinetobacter baumannii* infections remains unclear and a matter for debate. Cefiderocol has been shown to be effective for treating nosocomial pneumonia [4], but recent studies have reported higher mortality rates for patients on this drug, particularly in cases of bacteraemia and nosocomial pneumonia due to carbapenem-resistant *A. baumannii* (CRAB) [5–8]. One possible reason for this discrepancy is the presence of bacterial subpopulations displaying hetero- or adaptive resistance, unmasked by the use of cefiderocol [9,10]. We report a case of nosocomial CRAB bacteraemia and pneumonia successfully treated with cefiderocol and colistin, which led us to use an accessible new protocol to explore adaptive resistance to cefiderocol (ARC) in our collection of CRAB isolates as a function of carbapenemase type (OXA/NDM).

2. Case description

A 37-year-old man was admitted to the intensive care unit (ICU) in April 2022 for acute respiratory failure and shock. He had a history of asthma since childhood, Biermer's disease, diagnosed in 2021, and chronic alcoholism. His treatments included monthly vitamin B12 supplements and the use of β-2 mimetics as required. He was initially admitted to the hepatogastroenterology unit on April 9th, 2022, for acute necrotic-haemorrhagic pancreatitis. The next day, he was transferred to the ICU for respiratory failure requiring oxygen supplementation at a rate of 15 L/min and low blood pressure (76/33 mmHg). Biological tests revealed an inflammatory syndrome with 20.6 x 10^9 leukocytes/L, a C-reactive protein concentration of 252 mg/L and acute renal failure, with a creatinaemia of 113 μmol/L and a lactate concentration of 2.5 mmol/L. Chest X ray showed a bilateral pulmonary infiltrate. *Trans*-thoracic ultrasound revealed no signs of heart failure. The patient was treated with oxygen therapy and intravenous fluid therapy. The patient's respiratory condition declined, rendering oro-tracheal intubation with one ventral decubitus session necessary on April 12th. A computed tomography scanner showed bibasal pleuropneumonia, probably related to inhalation. All respiratory samples were sterile. Empiric treatment with 2 g cefotaxime and 500 mg metronidazole every 8 h for seven days was initiated. On April 18th, the patient's respiratory condition declined again and ventilator-acquired CRAB and Extended-Spectrum-β-Lactamase (ESBL)-producing *Enterobacter cloacae* pneumonia was documented (Fig. 1A and Table S1). Antimicrobial susceptibility testing for *A. baumannii* revealed resistance to all antibiotics tested (cefiderocol was not initially tested) except colistin and tygecycline. Treatment was resumed with 9 MIU colistin, followed by 4.2 MIU every 12 h, and 200 mg tygecycline followed by 100 mg every 12 h for nine days. On May 6th, the patient's condition worsened, with the development of bacteraemic CRAB pleuropneumonia (Fig. 1B and Table S1). The patient was then switched onto colistin plus 2 g cefiderocol every 6 h until May 24, after standard determination of the susceptibility of the CRAB isolate to cefiderocol (disk diffusion method, European Committee on Antimicrobial Susceptibility Testing, EUCAST 2021 note, MIC assessment not available, The European Committee on Antimicrobial Susceptibility Testing. Breakpoint for cefiderocol from EUCAST. Addendum (May 2020) to EUCAST breakpoint v. 10.0. Breakpoints to be included EUCAST breakpoint tables v 11.0, January 2021Version 10.0, 2024. https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Addenda/Cefiderocol_addendum_20200501.pdf). A significant improvement in the patient's respiratory condition was noted after 10 days of bitherapy, and the patient was weaned off of the ventilator on May 22nd. The patient was transferred to the medical unit on May 23rd, and was discharged home on June 8th, with a favourable clinical outcome (Fig. 1C).

3. Methods

3.1. Microbiological analyses

Thirty carbapenem-resistant *Acinetobacter* sp. isolates from the biobank of Reunion Island University Hospital (UHRI) were used and specifically tested for ARC, according to carbapenemase status (NDM/OXA). We also included the two isolates from the patient studied here (A3a and A3b). For each isolate, susceptibility to cefiderocol was determined by the disk diffusion and microdilution methods (EUCAST recommendations). We used a new method, as described below, to investigate ARC in non-NDM-1 isolates.

3.2. Molecular characterisation of resistance

The two CRAB isolates from the patient with ventilator-associated pneumonia and bacteraemia were screened for the presence of OXA-23-like, OXA-24/58-like and NDM carbapenemases with a lateral flow assay (Coris RESIST Acineto, Coris bioConcept, Gembloux, Belgium). The two isolates were then sent to the French National Centre for Antimicrobial Resistance (FNCAR) for confirmation of their molecular resistance profiles by PCR or whole-genome sequencing.

3.3. Standard antimicrobial susceptibility testing (AST)

We assessed the susceptibility of each isolate to cefiderocol by the disk diffusion and broth microdilution methods, in accordance with the EUCAST 2020 recommendations. Breakpoint for cefiderocol from EUCAST. Addendum (May 2020) to EUCAST breakpoint v. 10.0. Breakpoints to be included EUCAST breakpoint tables v 11.0, January 2021Version 10.0, 2024. https://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/Addenda/Cefiderocol_addendum_20200501.pdf). We used a disk containing 30 μg cefiderocol (Liofilchem Diagnostics, Roseto degli Abruzzi, Italia) on Mueller Hinton agar plates (MHE, bioMérieux, Marcy l'Étoile, France), with a cut-off of 17 mm. Note that the 2022 EUCAST warning does not apply to this combination of reagents. The minimum inhibitory concentration (MIC) of cefiderocol was determined with UMIC®Cefiderocol (Bruker daltonics, Bremen, Germany) on ID-CA-MHB (iron-depleted cation-adjusted Muller Hinton broth) according to EUCAST recommendations. An isolate was considered susceptible to cefiderocol if its MIC was $\leq$2 mg/L. The diameter of inhibition was measured and photographed, and the results were read twice, independently, by two different operators.

3.4. Adaptive resistance to cefiderocol

We investigated the ARC of the isolates with a new protocol adapted from that described by Choby et al. [10]: a single colony of carbapenem-resistant *A. baumannii* from a frozen streak was used to inoculate 1.5 mL ID-CA-MHB (Bruker daltonics). The overnight culture was incubated at 37 °C for 16 h, with shaking at 20 rpm. We then added 1.5 μL of this overnight culture of *Acinetobacter* sp. to 1.5 ml ID-CA-MHB containing 0 or 16 μg/ml cefiderocol (Fetcroja, Shionogi & Co.) and incubated the resulting suspension for 48 h at 37 °C with shaking at 20 rpm. The disk diffusion and microdilution assays were performed as described above, with a reading time of 18–24 h and 48 h for inhibition diameters and 18–24 h for MIC (Fig. 2). For the calculation of resistance percentages, the two isolates obtained from the case described here were considered as a single isolate (A3) among a total of 30 isolates tested (see Table 1).

4. Results

4.1. Two case isolates

Molecular investigation by sequencing revealed an overproduction of AmpC, the production of OXA-23 and TEMoneira (TEM) leading to β-lactam resistance, and an ArmA-type 16sRNA methylase responsible for resistance to aminoglycosides.

In standard AST, the two isolates from the studied case, obtained from lung and blood cultures, were classified as susceptible to cefiderocol in disk diffusion ($\geq$21 mm) and broth microdilution (MIC = 2 mg/L) assays. No ARC was detected in the two isolates from the case, with an MIC = 2 mg/L before and after 48 h of exposure to cefiderocol (see Table 1).

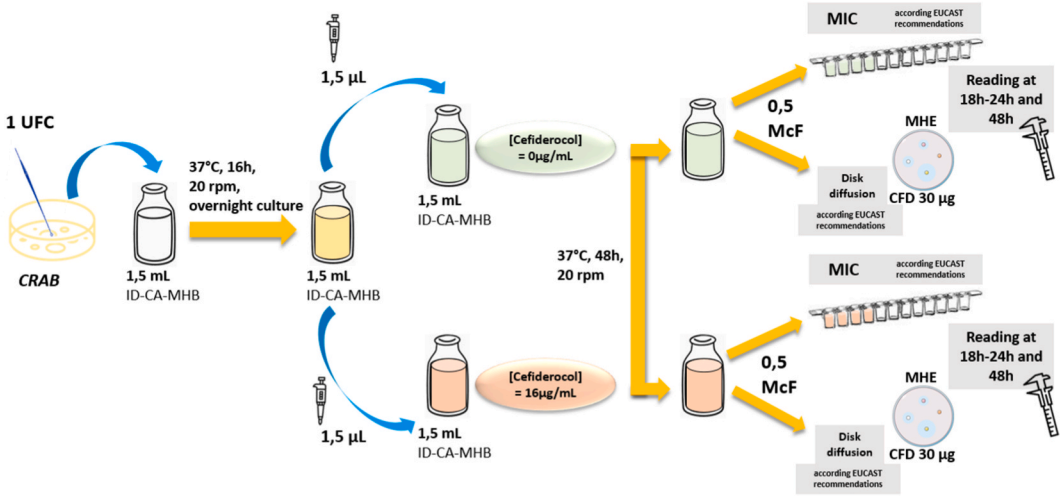

Fig. 2. Procedure used to measure adaptive resistance to cefiderocol by the disk diffusion and minimum inhibitory concentration methods, for each sample (blood culture and lower respiratory tract).
Overnight cultures of carbapenem-resistant *A. baumannii* isolates were prepared by using a single colony from a frozen streak to inoculate 1.5 mL iron-depleted cation-adjusted Mueller Hinton Broth (ID-CA-MHB, Bruker Daltonics). The cultures were incubated at 37 °C for 16 h with shaking at 20 rpm. We then added 1.5 μL of the overnight culture of *A. baumannii* to 1.5 mL ID-CA-MHB supplemented with 0 or 16 μg/mL cefiderocol (*Fetcroja*, Shionogi & Co.) and incubated the culture at 37 °C for 48 h, with shaking at 20 rpm. Readings were taken after 18–24 h and 48 h of growth for inhibition diameters and after 18–24 h for MIC determination.
CFD: cefiderocol; ID-CA-MHB: iron-depleted cation-adjusted Mueller-Hinton broth; McF: MacFarland; MHE: Mueller-Hinton E agar; MIC: minimum inhibitory concentration; RPM: rotations per minute; CFU: colony-forming units.

Table 1
Tests for adaptive resistance to cefiderocol performed on 30 carbapenem-resistant *Acinetobacter* spp. isolates with the new protocol adapted from that described by Choby et al. [10].

Isolate	Origin	Species	Carbapenemase	Resistance genes	CFD 0 μg/mL			CFD 16 μg/mL		
					ID (mm)		MIC (mg/L)	ID (mm)		MIC (mg/L)
					18–24 h	48 h	18–24 h	18–24 h	48 h	18–24 h
A1	Madagascar	*A. baumannii*	OXA-24	*AmpC, TEM*	S (22)	S (21)	S (0,5)	R (15)	R (13)	R (32)
A2	Mainland France	*A. baumannii*	OXA-24	*AmpC*	S (24)	S (24)	S (0.25)	R (16)	R (11)	R (16)
A3a	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (22)	S (22)	S (2)	S (18)	S (18)	S (2)
A3b	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (21)	S (20)	S (2)	S (21)	S (19)	S (2)
A4	Mayotte	*A. baumannii*	OXA-23	–	S (23)	S (23)	S (0.25)	R (16)	R (16)	R (8)
A5	Comoros	*A. baumannii*	OXA-58	–	S (27)	S (27)	S (0.06)	S (32)	S (32)	S (0.06)
A6	Ivory Coast	*A. baumannii*	OXA-58	–	S (22)	S (22)	S (0.25)	S (17)	S (17)	S (0,03)
A7	Mainland France	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (19)	S (18)	S (1)	R (11)	R (6)	R (16)
A8	Mayotte	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (24)	S (21)	S (1)	S (20)	R (15)	R (16)
A9	Reunion Island	*A. baumannii*	OXA-72 (OXA-24 type)	–	S (25)	S (24)	S (0.125)	S (25)	S (20)	S (0.5)
A10	Madagascar	*A. baumannii*	OXA-23	*AmpC*	S (20)	S (19)	S (0.25)	R (12)	R (7)	R (16)
A11	Madagascar	*A. baumannii*	OXA-23	*AmpC*	S (20)	S (19)	S (1)	R (13)	R (8)	R (8)
A12	Madagascar	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (22)	S (21)	S (2)	R (6)	R (6)	R (16)
A13	Mauritius	*A. baumannii*	OXA-23	*AmpC*	S (20)	S (19)	S (2)	S (18)	R (14)	R (16)
A14	Reunion Island	*A. baumannii*	OXA-23	*AmpC*	S (21)	S (18)	S (0.5)	S (14)	S (21)	S (0.25)
A15	Reunion Island	*A. baumannii*	OXA-23	*AmpC*	S (23)	S (23)	S (0.5)	S (30)	S (26)	S (0.125)
A16	Reunion Island	*A. baumannii*	OXA-24	*AmpC, TEM*	S (22)	S (20)	S (1)	S (23)	S (21)	S (0.5)
A17	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (20)	S (19)	S (2)	R (16)	R (14)	R (16)
A18	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (26)	S (20)	S (0.25)	R (10)	R (10)	R (16)
A19	Madagascar	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (28)	S (25)	S (1)	R (8)	R (8)	R (8)
A20	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM, ArmA*	S (25)	S (24)	S (0.5)	R (10)	R (12)	R (8)
A21	Mauritius	*A. baumannii*	OXA-23	*ArmA*	S (25)	S (24)	S (0.25)	R (14)	R (14)	R (8)
A22	Madagascar	*A. baumannii*	OXA-23	*PER-7, ArmA*	R (12)	R (12)	R (8)	R (8)	R (8)	R (16)
A23	Mainland France	*A. baumannii*	OXA-23	*ArmA*	S (25)	S (25)	S (0.25)	R (16)	R (14)	R (4)
A24	Mayotte	*A. nosocomialis*	OXA-420 (OXA-58 type)	–	S (21)	S (21)	S (0.5)	S (23)	S (23)	S (1)
A25	Reunion Island	*A. baumannii*	OXA-23	*AmpC, ArmA*	S (21)	S (19)	S (0.5)	R (14)	R (14)	R (8)
A26	Reunion Island	*A. baumannii*	OXA-23	*AmpC, TEM*	S (21)	S (19)	S (0.5)	R (16)	R (16)	R (8)
A27	Madagascar	*A. baumannii*	OXA-23	*AmpC, TEM*	S (22)	S (19)	S (0.5)	R (14)	R (14)	R (32)
A28	Mayotte	*A. ursingii*	NDM-1	–	R (14)	–	R (4)	–	–	–
A29	Reunion Island	*A. baumannii*	NDM-1	–	R (11)	–	R (16)	–	–	–
A30	Mayotte	*A. baumannii*	NDM-1 + OXA-23	-	R (8)	–	R (32)	–	–	–

Resistance to cefiderocol was detected in all NDM-1 (3/3) and OXA-23+PER-7 isolates in standard AST. Adaptive resistance to cefiderocol was detected in 84.2 % (16/19) and 50 % (2/4) of OXA-23 and OXA-24-type isolates, respectively.
MIC: minimum inhibitory concentration; R: resistant; S: susceptible; ID: inhibition diameter.

4.2. ARC in the UHRI collection

In the second phase of our study, we tested a collection of 30 carbapenem-resistant *Acinetobacter* spp. isolates (OXA-23 without NDM-1, $n = 20$; OXA-24 type, $n = 4$; OXA-58 type, $n = 3$; NDM-1, $n = 3$). All NDM-1 isolates ($n = 3$) were categorised resistant to cefiderocol in standard AST (MIC >2 mg/L). One (OXA-23+PER-7) of the 27 isolates with OXA-type carbapenemases was resistant, whereas the other 26 were categorised susceptible in standard AST (MIC ≤2 mg/L). None of the OXA-58 type isolates had adaptive resistance, with no difference observed in the inhibition diameter (≥17 mm with no colonies appearing close to the disk) or MIC (≤2 mg/mL) determinations with and without cefiderocol exposure. We found that 84.2 % (16/19) of OXA-23 isolates and 50 % (2/4) of OXA-24 type isolates (excluding OXA-23+PER-7) displayed a significant decrease in inhibition diameter (<17 mm, 6–16 mm) and an increase in MIC (>2 mg/L, 4–32 mg/L) after 48 h of exposure to cefiderocol; these isolates were considered to display adaptive resistance to cefiderocol (see Table 1 and Fig. S1). For two isolates, only a reading of inhibition diameter after 48 h was able to distinguish a subpopulation with a reduced inhibition diameter (<17 mm; see supplementary data, Fig. S1). Finally, 69.2 % of the isolates initially categorised as susceptible to cefiderocol in standard AST ($n = 26$) were found to display ARC. All these isolates harboured OXA-23 or OXA-24 class D carbapenemases.

5. Discussion

A. baumannii infections are associated with significant mortality, particularly in vulnerable ICU patients. Discordant results between the APEKS-NP and CREDIBLE-CR [5] studies and other case series [4,6] have led to a reluctance to use cefiderocol to treat *A. baumannii* complex infections. In two correspondences, Choby et al., 2021 [9,10] suggested that these discrepancies might be due to cefiderocol-heteroresistant subpopulations not detected by standard AST. This hypothesis seems to be invalidated by the latest results from the CREDIBLE-CR study presented by Longshaw et al. [11]. However, the apparently high rate of clinical or microbiological failure in some case series cannot be ignored, although other factors, such as clinical severity (septic shock) or strong immunosuppression, may influence these poor patient outcomes [6,12]. Recently, the rapid development of adaptive resistance to this molecule *in vitro* was well documented by Stracquadanio et al. [13]. As mentioned in two recent reviews [14,15], the clinical relevance of heteroresistance in the context of treatment failure has not been demonstrated with a sufficient level of evidence (retrospective studies, case reports) for any species other than *Staphylococcus aureus* (meta-analyses). We prefer the term "adaptive resistance" over heteroresistance, as it is deliberately less precise (heteroresistance being defined as a subpopulation with a frequency $\leq 10^{-6}$ [15]). Indeed, we wished to highlight the intrinsic capacity of this bacterial genus to adapt rapidly to this new drug. Moreover, we used a technique simpler using commercial reagents and more accessible than the current reference methods (Population analysis profile, PAPs, [10]), which cannot quantify the fraction of the subpopulation displaying ARC. We focused on the presence/absence of ARC in the isolates tested, to simulate as closely as possible the situation encountered *in vivo* and to orient potential use by clinicians.

We observed a clear clinical improvement in the patient studied here following combination therapy with cefiderocol and colistin. It should be noted that, despite the susceptibility of the isolate to cefiderocol in the standard AST performed at the time of diagnosis (four days after diagnosis), the ICU clinician did not select this treatment option, even though the microbiologist advised the use of a β-lactam, because of the results for the *Acinetobacter* subgroup obtained in the CREDIBLE-CR study. The two key points to note in this case are that *(i)* the isolate responsible for the infection did not develop ARC *in vitro* and *(ii)* the patient was treated with combination therapy, in this case with colistin, rather than monotherapy.

Our microbiological analyses with this new protocol (adapted from that described by Weiss et al.) yielded very similar results to recent studies based on the reference technique (PAPs): 84.2 % of the OXA-23 carbapenemase-producing CRAB isolates initially categorised as susceptible, 80 % if we include the OXA-23+PER-7 isolate initially categorised as resistant, developed ARC (80 % in the study by Stracqadanio et al.) [13]. For OXA-24-producing CRAB, it is difficult to draw any firm conclusions due to the very small number of isolates. ARC developed in 69.2 % of the isolates initially classified as susceptible in standard AST, considered together. Isolates producing another class D carbapenemase, OXA-58, did not develop ARC. All the isolates producing the NDM-1 metallo-β-lactamase or PER extended-spectrum β-lactamase were initially categorised as resistant to cefiderocol in standard AST, as previously described [16]. Thus, the type of carbapenemase type can potentially guide the choice of treatment, with a presumptive prediction of microbiological category (NDM-1: R, OXA-23/24: HR, OXA-58: S). Greater understanding of the genetic determinants (single-nucleotide polymorphisms) involved in this adaptive resistance needs to be explored. New-generation sequencing (NGS) of iron transport genes seems to be a promising way, as highlighted by of Stracquadanio S et al., [13]. The presence/absence of non-synonymous mutations at variable frequencies in OXA-23, OXA-24 or OXA-58 genes, could be a potential pathway for the discrepancies observed. These preliminary results, of course, require confirmation in studies on larger numbers of isolates, but to our knowledge, this is the first study to establish a link between adaptive resistance and OXA-type carbapenemases. Nevertheless, this finding remains highly relevant in the context of the development of new rapid and accessible lateral flow assays (Coris bioConcept, NG biotech) allowing the rapid characterisation of the carbapenemase type in an *Acinetobacter* spp. isolate. With effective clinical-biological dialogue, these rapid tests can provide clinicians indications within a few minutes.

Heteroresistance is not a new phenomenon in microbiology, but its clinical implications remain unclear (except for *S. aureus*). It has been described for many antibiotics and combination treatments are generally used to prevent it; this would be an interesting to confirm in the context of CRAB infections [17]. Moreover, the toned to simulate iron depletion *in vitro,* as such depletion is thought to occur *in vivo*, should lead to caution in the interpretation of these microbiological results and the *in vitro/in vivo* correlation. Our findings suggest that cefiderocol should be considered as an alternative treatment for CRAB infections if the isolate is classified as susceptible to this antibiotic in standard AST and no other β-lactam is available. However, it should be used in combinations (colistin,

tigecycline or rifampicin) to prevent the development of adaptive resistance phenomena [12,13]. Finally, it may be useful to advise microbiologists to repeat standard AST (MIC) on *Acinetobacter* spp. isolates after 48 or 72 h of exposure *in vivo* to cefiderocol in cases of infection, to check that the strain remains susceptible.

The chief limitations of this study are that we were unable to test other strains exposed to cefiderocol *in vivo* and we did not compare our technique to the reference technique (PAPs).

However, the protocol proposed here offers the benefit of accessibility, although it remains time-consuming (five days). To date, the clinical impact of heteroresistance remains uncertain and has been the subject of scientific world debate since 2021 [4–6,9,10,12,13,18]. Understanding the genetic determinants in the emergence of resistance to cefiderocol, whether adaptive or not, will both require the use of standardised methods and large-scale, ideally prospective, studies [14]. Our study adds to knowledge of this phenomenon by linking the clinical course of the infection and microbiological investigations. We have three main conclusions: *(i)* for cefiderocol, EUCAST susceptibility testing is unable to detect adaptive resistance in *Acinetobacter* spp., *(ii)* knowledge of the carbapenemase produced by the CRAB isolate is useful, to guide the use of this drug, and *(iii)* the use of cefiderocol in monotherapy for OXA-23/24-producing CRAB should probably not be recommended, or should be considered only after an assessment of ARC. These last two conclusions could gain further value if more data can be generated from both work on a wider collection of strains to see if difference between OXA-58 and others may be confirmed understanding their genetic support and on more clinical isolates after cefiderocol treatment. According to the WHO, research in this field is a matter of priority, to provide clinicians with guidance in the management of CRAB infections.

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Ethics approval and consent to participate

Informed consent was obtained from the patient for the publication of this case report and the corresponding images.

Consent for publication

All authors have seen and approved the final manuscript. All authors consent to publication.

Data availability statement

All the data are available from the manuscript text, tables, the figures and the supplementary materials.

CRediT authorship contribution statement

Anissa Desmoulin: Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Loïk Sababadichetty:** Investigation. **Laure Kamus:** Writing – review & editing, Writing – original draft. **Marion Daniel:** Investigation, Formal analysis. **Lucie Feletti:** Writing – review & editing, Investigation, Formal analysis. **Nicolas Allou:** Writing – review & editing, Supervision, Investigation, Formal analysis, Conceptualization. **Anaïs Potron:** Writing – review & editing, Formal analysis. **Anne-Gaëlle Leroy:** Writing – review & editing, Formal analysis. **Marie-Christine Jaffar-Bandjee:** Writing – review & editing, Supervision. **Olivier Belmonte:** Writing – review & editing, Supervision. **Thomas Garrigos:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Guillaume Miltgen:** Writing – review & editing, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e30365.

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