

## Case Report

# Transfer between an Algerian and a French hospital of four multi-drug resistant bacterial strains together via a single patient

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**Abstract:** A 5 years-old girl, seriously burnt with fire, was first hospitalized during four days in an hospital at Alger, and then transferred to our hospital at Paris. Admitted in our intensive care burns unit, she was third degree burnt on 78% of total body surface area, already treated with imipenem and vancomycin at her arrival. Clinical aggravation was rapidly observed and death occurred within 24 hours. Cultures of blood and multiple wound swabs yielded 3 multi-drug resistant bacterial strains: *Acinetobacter baumannii* with carbapenemase OXA-23, *Pseudomonas aeruginosa* serotype O11 with metallo- $\beta$ -lactamase VIM-4 and *Klebsiella pneumoniae* with CTX-M-15 extended-spectrum  $\beta$ -lactamase. Culture of a rectal swab showed colonization by *Enterococcus faecium* with *vanA* glycopeptides resistance. Patients colonized with one or two multi-drug-resistant strains were not rare in our burns unit, especially those transferred from Algeria, but this case of a single patient harboring four multi-drug-resistant strains is exceptional.

**Keywords:** Third degree burns, carbapenemase, metallo- $\beta$ -lactamase, extended-spectrum  $\beta$ -lactamase, glycopeptides resistance, four multi-drug-resistant strains

### Case report

A 5 years-old girl, seriously burnt after a fire accident of her clothes on 2<sup>nd</sup> June 2012, was first hospitalized in an hospital at Alger. Four days later, she was transferred into the intensive care burns unit (ICBU) of Trousseau hospital, at Paris. The child was third degree burnt on 78% of total body surface area, already treated with imipenem and vancomycin without any available bacteriological data at the admission. In our ICBU, the following treatment was established: vascular filling perfusion with Ringer solution 2/3 and glucose 5% 1/3, removal of dressings and washing under anesthesia, analgesia with intravenous morphine, local disinfection with chlorhexidine spray every 2 hours. The antibiotic treatment was switched to piperacil-

lin-tazobactam combined with amikacin by femoral peripheral administration. Clinical aggravation with tachycardia, blood pressure fall, polypnea, desaturation and anuria was rapidly observed, requiring naso-tracheal intubation and assisted ventilation, establishment of a left subclavian catheter under anesthesia. On 7<sup>th</sup> June 2012, after a brutal cardiovascular failure, the child died, 24 h after her admission.

Cultures of 23 different wounds swabs yielded *Acinetobacter baumannii* while 7 swabs yielded *Pseudomonas aeruginosa* serotype O11. *Klebsiella pneumoniae* was found on a single swab. Two blood cultures set up on 6 June 2012 (at 3 hours AM, temperature 38.2°C and at 9 hours AM, temperature 38.9°C), using the BacT/Alert system (bioMérieux, Marcy-l'Etoile,

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France), were positive in less than 10 hours, yielding *A. baumannii* and *P. aeruginosa* serotype O11. The three Gram-negative species were identified with Gram-negative Vitek card (bioMérieux). Post mortem culture of catheter yielded  $4.10^2$  UFC/ml of *P. aeruginosa* serotype O11.

At the admission, routine screening of Multi-Drug Resistant (MDR) bacteria colonization with a rectal swab was performed by culture onto a chromogenic cefpodoxime-containing medium (chromID® ESBL, bioMérieux) and a chromogenic vancomycin-containing medium (chromID® VRE, bioMérieux): the only positive result was a vancomycin-resistant *Enterococcus faecium* strain identified with Gram-positive Vitek card (bioMérieux). Susceptibility testing was performed by the disk diffusion method according to the Comité de l'Antibiogramme, Société Française de Microbiologie (<http://sfm.asso.fr/>). *A. baumannii* strain showed a MDR pattern (ticarcillin, ceftazidime and imipenem resistance associated with aminoglycosides resistance, except amikacin). The *K. pneumoniae* strain showed the well-known synergy between cefotaxime and amoxicillin-clavulanate and the following pattern: resistance to cefotaxime and ceftazidime but susceptibility to imipenem, combined with aminoglycosides resistance, except amikacin. The *P. aeruginosa* strain also showed a MDR pattern (ticarcillin, ceftazidime and imipenem resistance, combined with all aminoglycosides resistance). Gene sequencing with consensus primers targeting the  $bla_{OXA}$ ,  $bla_{VIM}$  and  $bla_{CTX-M}$  allowed to characterize an oxacillinase (carbapenemase) OXA-23 in *A. baumannii*, a metallo- $\beta$ -lactamase (MBL) VIM-4 (here associated to the restricted-spectrum oxacillinase OXA-10) in *P. aeruginosa*, and a CTX-M-15 extended-spectrum  $\beta$ -lactamase (ESBL) in *K. pneumoniae* [1-3]. Amikacin was active against the *A. baumannii* and *K. pneumoniae* strains, ciprofloxacin was active against the *A. baumannii* and *P. aeruginosa* strains, but finally, only ciprofloxacin remained active against the 3 gram-negative strains. The resistant *E. faecium* rectal strain was characterized as *vanA*.

Most of the organisms commonly isolated from infected patients in burn intensive care units are members of the ESKAPE (*Enterococcus faecium*, *Acinetobacter baumannii*, *Pseudo-*

*monas aeruginosa*, and *Enterobacter* species) group of pathogens recognized by the Infectious Disease Society of America as the most challenging bacteria facing clinicians today [4]. These organisms are of particular concern because they are responsible for a majority of hospital infections and often "escape" the effects of traditional antimicrobials through broad-spectrum resistance. Over time these organisms have developed resistance to several classes of antibiotics and the term "multi-drug-resistant" is commonly used in the biomedical literature to describe antimicrobial resistance levels among bacteria. Whether both *A. baumannii* and *P. aeruginosa* are frequently gram negative species isolated in burns wards [5], resistant strains with MBL were only occasionally founded since these last 10 years [6-8]. As reported by Keen III et al., *A. baumannii* isolates recovered from patients with burns greater than 30% of total body surface area were more likely to be MDR (61%) with no significant difference for *P. aeruginosa* and *K. pneumoniae* [5]. OXA-23 is the most frequently carbapenemase found in *A. baumannii* strains, almost a specific marker of *A. baumannii* species with worldwide spread observed even before the use of carbapenems [9]. Clonal outbreaks of carbapenem-resistant and OXA-23-producing *A. baumannii* have been reported in many countries [10-15]. In 2014, Gap et al. observed that airborne *A. baumannii* in the burn wards had multidrug resistance and complex molecular diversity, and OXA-23 and OXA-51 were dominant mechanisms for resisting carbapenems [16]. The *P. aeruginosa* strain produced VIM-4 and surprisingly not VIM-2 MBL, which is the most strongly prevalent in France ([http://www.hcsp.fr/docs/pdf/avis-rapports/hcspr20101116\\_bmrimport.pdf](http://www.hcsp.fr/docs/pdf/avis-rapports/hcspr20101116_bmrimport.pdf)). An outbreak involving 47 VIM-producing *P. aeruginosa* isolates was reported from the University Hospital of Thessaly, Greece, in 2001 to 2002, involving the  $bla_{VIM-4}$  gene, which was originally identified [17]. In 2014, Anvarinejad et al. noted that metallo-beta-lactamase producing *Pseudomonas aeruginosa* in the burn patients is a leading cause of morbidity and mortality and remains a serious health concern among the clinicians [18].

The *K. pneumoniae* strain produced an ESBL belonging to the CTX-M group, which is the most frequent ESBL in enterobacteria [19]. The

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CTX-M ESBL diffusion was rapidly worldwide since the middle of the 1990s and explosion of the worldwide diffusion was observed in the last 15 years, hence the term "CTX-M  $\beta$ -lactamase pandemic" [19].

Moreover, *vanA* gene was found in the colonizing glycopeptides-resistant *Enterococcus* (GRE) strain, *E. faecium*. In 2007, an investigation carried out by l'Observatoire National de l'Epidémiologie de la Résistance Bactérienne aux Antibiotiques (<http://www.onerba.org/>) in France showed that GRE carriage is infrequent in France: GRE carriers were found in 11% of hospitals and represented 0.3% of screened patients, who were mostly colonized with *E. faecium* harboring *vanA* gene.

The risk of MDR bacterial carriage in transferred patients after abroad hospitalization is serious. On July 2013, the French Haut Conseil de la Santé Publique edited recommendations for control of diffusion of multi-drug resistant commensal bacteria imported in France during the support of repatriated patients or having history of abroad hospitalization (<http://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefs=372>). These recommendations are supporting the prevention of infections related to the carbapenemases producing enterobacteria and the glycopeptides-resistant enterococci and imply the digestive screening with rectal swab or stool specimen and complementary «contact» measures at the patient admission, according to the last recommendations of the Société française d'hygiène hospitalière (<http://www.sfhf.net/>).

From 2006 to 2009, in France, the Institut de Veille Sanitaire recorded 42 nosocomial infections in patients coming from abroad of which 29% of infections with several MDR bacteria. Among these cases, 42% were due to *A. baumannii* of which 80% were imipenem resistant, 22% due to *E. faecium* with 100% glycopeptides resistance, 20% due to *K. pneumoniae* with 58% producing ESBL, while only 7% were due to *P. aeruginosa* of which 50% producing ESBL and 50% with imipenem resistance (<http://www.invs.sante.fr/raisin/>).

In our burns unit, infections with MDR bacteria were previously observed in several children coming from Maghreb but the detection of 4 multi-drug-resistant strains together from a

single patient is exceptional. While patient's severe infected wound zones support a high risk of MDR strains spread, the strict technical and geographic isolation measures immediately applied at the admission, as well as the unfortunate child's short stay, allowed to avoid any secondary case during the following weeks.

### Disclosure of conflict of interest

None.

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