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A Case Report: Double Isolation of NDM-1 Producing Enterobacteriaceae in A Military Hospital in Spain

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ABSTRACT

New Delhi metallo-β-lactamase (NDM) is an uncommon type of carbapenemase in our country. Despite this, in recent years the number of isolates of this type of carbapenemase has increased in our country, mainly due to travelers coming from Middle Eastern countries. We report a case of an Iraqi man wounded by an explosive device who arrived at our hospital and who had isolates Staphylococcus aureus which were resistant to ceftobiprole and ceftaroline and NDM-1 producing Klebsiella pneumoniae and Escherichia coli. It must be paid special attention to nationals of countries with a high prevalence of mechanism of resistances, highlighting the importance of an early detection to prevent its spread in our country.

Keywords: *Carbapenemase, Klebsiella Pneumoniae, Escherichia Coli*

Introduction

Resistance to antimicrobial agents of pathogenic bacteria has become a major problem in routine medical practices. Carbapenem resistance has long been increasing during the last years. The production of carbapenem-hydrolysing β-lactamases (carbapenemases), where NDM, KPC, OXA-48, IMP-1 and VIM are the most common mechanisms (Nordmann *et al*., 2011; Bonomo *et al*., 2018). Although it is not the most frequent carbapenemase in our environment, NDM type has becoming a serious problem in nosocomial infections in the last years in some countries around the world (Khan *et al*., 2017). This resistance pattern compromises the efficacy of almost all lactams (except aztreonam), including the last resort carbapenems. Therapeutical options may remain limited mostly to colistin, tigecycline, and fosfomycin.

Presentation of Case

We present a case of a 49 years old male patient, natural from Iraq, wounded by improvised explosive device (IED) explosion. The IED caused shrapnel wounds predominantly in the right facial region, right skull and upper right member.

After a first surgery and several weeks of hospitalization, first in Hasaka, (Syria) and then in Dahuk (Iraq) and several cycles of treatments with wound debridement to the bone plane and antimicrobial therapy with vancomycin and meropenen due to the isolation of a *Staphylococcus aureus,* the patient had a bad evolution. One month later the patient was transferred to our hospital in Madrid (Spain), a cranial CT was performed and showed a right frontal brain abscess which extended from coronal suture to upper cranial base, with bone fragments and intracranial shrapnel. The patient was reintervened and different samples were taken. In bone biopsy of intracranial bone fragments, two different microorganisms were isolated: *methicillin-resistant Staphylococcus aureus* (MRSA), which showed resistance to ceftobiprole and ceftaroline, and a β-lactamase-producing *E. coli*, showing a resistance profile described in table 1. The minimum inhibitory concentration (MIC) was determined by broth microdilution methods (MicroSscan WalkAway, Beackman Coulter) and interpreted according to EUCAST breakpoints (www.eucast.org). After cultures, the patient was treated with linezolid (600mg every 12 hours), fosfomycin (8mg every 8 hours) and tigecycline (100mg every 12 hours).

Ten days later to admission, we also isolated a β-lactamase-producing *K. pneumoniae* from a sputum screening swab, with similar resistance pattern as *E.coli* (Table 1). To improve the knowledge of the resistance pattern, a rapid immunochromatographic diagnostic test (RESIST-5 O.K.N.V. Coris BioConcept) was performed in both isolates, obtaining a positive result for NDM metallo-β-lactamase type. These results were confirmed by Seegene Allplex enteroDR, a novel multiplex real time PCR assay (polymerase chain reaction), which is able to detect eight antibiotic resistant genes: $bla_{\text{OXA-48}}$, bla_{KPC}, bla_{VIM}, bla_{IMP}, bla_{NDM} $bla_{\text{CTX-M}}$, vanA and vanB. Both of our strains were positive for an extended-spectrum β-lactamase type CTX-M as well.

The presence of bla_{NDM} gen type 1 was confirmed in both strains by Multilocus Sequence Typing (MLST) and pulsed-field gel electrophoresis by the National Center for Microbiology "Carlos III" in Madrid (Spain). This find appears to be a possible interspecies plasmid transfer.

Discussion

This type of carbapenemase is rarely isolated in Spain (Mataseje *et al*., 2016). The majority of the patients from North America, Europe and Australia infected with NDM producing bacteria were travellers previously hospitalized in middle eastern countries. The first case reported in an industrialized country was in Sweden in 2009 (Yong *et al*., 2009) and after this, there are sporadic reports from military hospitals Pakistan (Day *et al*., 2013) and Israel (Lerner *et al*., 2016), Syrian refugees (Lerner *et al*., 2016) or travelers returning from India (Oteo *et al*., 2012; Gil-Romero *et al*., 2013) and other European countries, as well as USA (Wilson and Chen, 2012), Canada (Mataseje *et al*., 2016) or Australia (Sidjabat *et al*., 2011) and even cases of nosocomial dissemination (Poirel *et al*., 2014). In this report we described

two different enterobacteriaceae isolated in the same patient with the same resistance pattern suggests a horizontal spread.

Table 1: Sensitivity of *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Escherichia coli*

	K. pneumoniae	*S. aureus*	*E. coli*
Ampiciline	R	R	R
Amoxicilin/Clavulanate	R	R	R
Cefepime	R		R
Cefotaxime	R		R
Ceftazidime	R		R
Cefuroxime	R		R
Ciprofloxacin	R	R	R
Ertapenem	R		R
Meropenem	R		R
Piperaciline/Tazobactam	R		R
Tigeciciline	S	S	S
Tobramycin	R	R	R
Amikacin	R	R	R
Ceftolozane/Tazobactam	R		R
Ceftazidime/Avibactam	R		R
Colistin	S		S
Vancomycin		S	
Erythromycin		R	
Clindamycin		R	
Linezolid		S	
Daptomycin		R	

*R: Resistant

**S: Susceptible

Conclusion

Special attention should be given to patients repatriated from conflict zones, mainly those with accumulating risk factors. The use of rapid molecular methods with multiple targets is essential for an early diagnosis, especially in isolates with resistance patterns that are not so common in low-prevalence countries. Clinicians and microbiologists must focus in detecting these organisms and promoting control measures to prevent nosocomial spread of antimicrobial multirresistance.

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