Report on a transborder spread of carbapenemase-producing bacteria by a patient injured during Euromaidan, Ukraine

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Abstract

Spread of carbapenemase-producing bacteria has been described all over the world. This phenomenon may be accelerated by many factors, including wars and natural disasters. In this report, we described an NDM-1-producing *Klebsiella pneumonia* ST11 recovered from a patient injured during the Maidan revolution in Ukraine. To our knowledge, this is the first report of a carbapenemase-producing *Enterobacteriaceae* in Ukraine and one of several reports describing wound colonization/infection of humans injured during war.

Keywords: Antibiotic resistance, catastrophe, disaster, *Klebsiella pneumoniae*, NDM-1, ST11, war
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Global spread of antibiotic resistance can be accelerated by many factors, including travelling and repatriation of patients. Additionally, antibiotic resistance can be spread by contaminated food as well as wild animals. Few studies describing spread of multiresistant bacteria after natural disasters (e.g. tsunami, earthquake) and repatriation of injured patients (soldiers, civilians) during war have been reported [1–4]. Here we report a case of transmission of NDM-1-producing *Klebsiella pneumoniae* sequence type 11 (ST11) recovered from a Ukrainian patient injured during the Maidan revolution, also known as the Euromaidan (Kiev, Ukraine).

From February until March 2014, 27 Ukrainian patients injured in Maidan Nezalezhnosti square (Independence Square) during Euromaidan have been transferred to Czech hospitals. The patients were admitted to General University Hospital (Prague), Motol University Hospital (Prague) and Central Military Hospital (Prague). On the basis of the Czech National Guidelines for Control of Cases of Colonisation/Infection by Carbapenemase-Producing Enterobacteria (http://www.mzcr.cz/Legislativa/dokumenty/vestnik-c8/2012_6865_2510_11.html), preemptive isolation of the patients and active screening using a rectal swab were performed. *Enterobacteriaceae* isolates recovered from various screening materials (e.g. sputum, blood, swabs) from patients hospitalized in intensive care units were also subjected to susceptibility testing and detection of carbapenemases according to screening cutoffs [5]. All suspected isolates were sent for a confirmation of carbapenemase-production to the National Reference Laboratory of Antibiotics (National Institute of Public Health, Prague, Czech Republic) and Department of Microbiology, Faculty of Medicine, in Plzen (Charles University in Prague, Plzen, Czech Republic). In that period, all of the hospitals also participated on European Survey on Carbapenemase-Producing *Enterobacteriaceae* (EuSCAPE) [6,7].

At Motol University Hospital, a *K. pneumoniae* isolate with reduced susceptibility to carbapenems was recovered from a wound of a 51-year-old Ukrainian man on 24 March 2014. The patient was directly transferred from a hospital in Kiev. Using multilocus sequence typing [8], MALDI-TOF (matrix-assisted laser desorption/ionization time-of-flight mass spectrometry) hydrolysis assay [9] and PCR detection of carbapenemase genes followed by amplicon sequencing [5], the isolate was identified as an NDM-1 producer that was classified into ST11, which belongs to clonal complex 258. Minimum inhibitory concentrations (MICs) of the isolate were determined by the disk diffusion test and by Etest (bioMérieux, Prague, Czech Republic) and interpreted using European Committee on Antimicrobial Susceptibility Testing criteria (http://www.eucast.org). The isolate was nonsusceptible/resistant to ertapenem (MIC 12 mg/L), meropenem (MIC 24 mg/L) and imipenem (MIC 3 mg/L),

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amikacin, amoxicillin/clavulanic acid, ampicillin cefotaxime, ceftazidime, cefepime, ciprofloxacin, gentamicin, piperacillin/tazobactam, tobramycin and trimethoprim/sulfamethoxazole and was susceptible to aztreonam, colistin and tigecycline. No extended-spectrum β-lactamase was detected on the basis of the double-disk synergy test between aztreonam and amoxicillin/clavulanic acid [10].

Simultaneously, a carbapenem-hydrolyzing class D β-lactamase (CHDL)-producing *Acinetobacter baumannii* and a methicillin-resistant *Staphylococcus aureus* were isolated from the same clinical material. No other carbapenemase-producing *Enterobacteriaceae* was isolated from the rest of the 26 patients.

As previously described by other groups, emergence of multidrug-resistant bacteria has been frequently observed among injured soldiers hospitalized in army medical centers [11–13]. Calhoun *et al.* [12] hypothesized that overuse of broad-spectrum antibiotics in military hospitals during war may play an important role in selection and spread of resistant bacteria. Interestingly, *Acinetobacter baumannii* has been recognized as the second most frequent bacterium causing bloodstream infection in U.S. soldiers with extremity wounds during the Vietnam War [14,15]. Spread of *A. baumannii* complex is probably caused by the presence of this bacterium in the hospital environment and hospital-acquired colonization of wounds. Primary colonization of the wound during injury does not probably play an important role [12].

In accordance with the hypotheses described above, isolation of a CHDL-producing isolate from the same clinical material may indicate nosocomial origin of the NDM-1 producer. To our knowledge, neither epidemiologic studies nor case reports describing multiresistant Gram-negative bacteria have been previously reported from Ukraine. However, a previous report from our group described the first NDM-1-producing *K. pneumoniae* (ST11) in the Czech Republic, which was probably imported from Slovakia [15]. Previously, we also reported an isolate of NDM-1-producing *A. baumannii* recovered from a patient repatriated from Egypt [16] and NDM-4-producing *Enterobacter cloacae* isolated from a patient previously hospitalized in Sri Lanka [17]. Such findings may indicate a hidden source of clinically important resistance determinants, such as bla_{NDM-1}, in the specific geographical area. Further studies are needed to uncover the current epidemiologic situation in carbapenemase-producing *Enterobacteriaceae* in Ukraine and surrounding regions.

Conflict of Interest

None declared.

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References

[1] Uckay I, Sax H, Harbarth S, Bernard L, Pittet D. Multi-resistant infections in repatriated patients after natural disasters: lessons learned from the 2004 tsunami for hospital infection control. J Hosp Infect 2007;68:1–8.

[2] Marra AR, Valle Martino MD, Ribas MR, Rodriguez-Taveras C, Pavao Dos Santos OF. Microbiological findings from the Haiti disaster. Travel Med Infect Dis 2012;10:157–61.

[3] Hospenthal DR, Crouch HK, English JF, et al. Multidrug-resistant bacterial colonization of combat-injured personnel at admission to medical centers after evacuation from Afghanistan and Iraq. J Trauma 2011;71(Suppl. 1):S52–7.

[4] Rafei R, Dabboussi F, Hamze M, et al. First report of blaNDM-1-producing *Acinetobacter baumannii* isolated in Lebanon from civilians wounded during the Syrian war. Int J Infect Dis 2014;21:21–3.

[5] Hrabák J, Papagiannitsis CC, Chudáčková E. Detection of carbapenemases in *Enterobacteriaceae*: a challenge for diagnostic microbiological laboratories. Clin Microbiol Infect 2014;20:839–53.

[6] Glasner C, Albiger B, Buist G, et al. European Survey on Carbapenemase-Producing (EuSCAPE) Working Group. Carbapenemase-producing *Enterobacteriaceae* in Europe: a survey among national experts from 39 countries, February 2013. Eurosurveillance 2013;18:20525.

[7] Hrabák J, Študentová V, Jakubů V, et al. Prevalence study on carbapenemase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolates in Czech hospitals—results from Czech part of European Survey on Carbapenemase-Producing *Enterobacteriaceae* (EuSCAPE). Epidemiol Mikrobiol Imunol 2015;64:87–91.

[8] Diancourt L, Passet V, Verhoef J, Grimont PA, Brisse S. Multilocus sequence typing of *Klebsiella pneumoniae* nosocomial isolates. J Clin Microbiol 2005;43:178–82.

[9] Studentova V, Papagiannitsis CC, Izdebski R, et al. Detection of OXA-48-type carbapenemase-producing *Enterobacteriaceae* in diagnostic laboratories can be enhanced by addition of bicarbonates to cultivation media or reaction buffers. Folia Microbiol 2014;20:839–53.

[10] Drieux L, Brossier F, Sougakoff W, Jarlier V. Phenotypic detection of extended-spectrum β-lactamase production in *Enterobacteriaceae*: review and bench guide. Clin Microbiol Infect 2008;14(Suppl. 1):90–103.

[11] Zapor MJ, Erwin D, Erowele G, Wortmann G. Emergence of multidrug resistance in bacteria and impact on antibiotic expenditure at a major army medical center caring for soldiers wounded in Iraq and Afghanistan. Infect Control Hosp Epidemiol 2008;29:661–3.

[12] Calhoun JH, Murray CK, Manring MM. Multidrug-resistant organisms in military wounds from Iraq and Afghanistan. Clin Orthop Relat Res 2008;466:1356–62.

[13] Davis KA, Moran KA, McAllister CK, Gray PJ. Multidrug-resistant *Acinetobacter* extremity infections in soldiers. Emerg Infect Dis 2005;11:1218–24.

[14] Tong MJ. Septic complications of war wounds. JAMA 1972;219:1044–7.

[15] Studentova V, Dobiasova H, Heldova D, Dolejska M, Papagiannitsis CC, Hrabak J. Complete nucleotide sequences of two NDM-1-encoding plasmids from the same sequence type 11 *Klebsiella pneumoniae* strain. Antimicrob Agents Chemother 2015;59:1325–8.

[16] Hrabák J, Štolbová M, Študentová V, Fridrichová M, Chudáčková E, Zemlickova H. NDM-1 producing *Acinetobacter baumannii* isolated from a patient repatriated to the Czech Republic from Egypt, July 2011. Eurosurveillance 2012;17:20085.

[17] Papagiannitsis CC, Studentova V, Chudackova E, et al. Identification of a New Delhi metallo-β-lactamase-4 (NDM-4)-producing *Enterobacter cloacae* from a Czech patient previously hospitalized in Sri Lanka. Folia Microbiol 2013;58:547–9.