Hypervirulent and multidrug resistant Klebsiella in China

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Sources:

Abstract

Background
Hypervirulent Klebsiella pneumoniae strains often cause life-threatening community-acquired infections in young and healthy hosts, but are usually sensitive to antibiotics. In this study, we investigated a fatal outbreak of ventilator-associated pneumonia caused by a new emerging hypervirulent K. pneumoniae strain.

Methods
The outbreak occurred in the integrated intensive care unit of a new branch of the Second Affiliated Hospital of Zhejiang University (Hangzhou, China). We collected 21 carbapenem-resistant K. pneumoniae strains from five patients and characterised these strains for their antimicrobial susceptibility, multilocus sequence types and genetic relatedness using the VITEK-2 compact system, multilocus sequence typing and whole genome sequencing. We selected one representative isolate from each patient to establish the virulence potential using a human neutrophil assay and the Galleria mellonella model to establish the genetic basis of their hypervirulence phenotype.

Findings
All five patients had undergone surgery for multiple trauma and subsequently received mechanical ventilation. The patients were aged 53–73 years and were admitted to the intensive care unit between late February and April 2016. They all had severe pneumonia, carbapenem-resistant K. pneumoniae infections, and poor responses to antibiotic treatment. They died due to severe lung infection, multiorgan failure, or septic shock. All five representative carbapenem-resistant K. pneumoniae strains belonged to the ST11 type, which is the most prevalent carbapenem-resistant K. pneumoniae type in China, and originated from the same clone. The strains were positive on the string test, had a survival of about 80% after 1 h incubation in human neutrophils, and killed 100% of wax moth larvae (G. mellonella) inoculated with 1 × 10^6 colony-forming units of the specimens within 24 h, suggesting they were hypervirulent. Genomic analyses showed that the emergence of these ST11 carbapenem-resistant hypervirulent K. pneumoniae strains was due to the acquisition of a roughly 170 kbp pLVPK-like virulence plasmid by classic ST11 carbapenem-resistant K. pneumoniae strains. We also detected these strains in specimens collected in other regions of China.

Interpretation
The ST11 carbapenem-resistant hypervirulent K. pneumoniae strains pose a substantial threat to human health because they are simultaneously hypervirulent, multidrug resistant (MDR) and highly transmissible. Control measures should be implemented to prevent further dissemination of such organisms in the hospital setting and the community.
Comment
Carbapenemase-producing hypervirulent *K. pneumoniae*: when multidrug resistance meets virulence.

The increasing trend of resistance traits that may accumulate in Gram-negative rods, and particularly in *K. pneumoniae* clinical isolates, is currently observed. This accumulation, that is likely resulting from an overtime consecutive acquisition of resistance plasmids and possibly additional chromosomally-encoded permeability defects, often leads to multidrug resistance. Examples of producers of the carbapenemase genes *bla*<sub>NDM-1</sub> and *bla*KPC are unfortunately quite notorious, being increasingly reported worldwide and responsible for life-threatening infections almost impossible to eradicate.

Fortunately, MDR does not mean increased virulence. Indeed, a vast majority of MDR isolates are classical pathogens that do not exhibit any additional virulence markers that would make them true monsters. In addition, co-location of (at least obvious) virulence determinants onto resistance plasmids is almost never observed, which makes the threat less serious then what could be expected. As one is used to say: “it might be worse!”.

The identification of an outbreak of infections caused by a KPC-2-producing MDR and additionally hypervirulent *K. pneumoniae* strain in a Chinese hospital by Gu et al. therefore represents the worse scenario that could have been expected.
Indeed, the nosocomial pathogen described here, accumulated the capacity to resist almost all antibiotics (with tigecycline and colistin being the only drugs left) and to cause fatal infections due to its hypervirulent feature.

This unfortunate event was however predictable, considering that China has faced a wide spread of MDR strains for many years, and particularly KPC-producing *K. pneumoniae* and the increasing occurrence of hypervirulent *K. pneumoniae* strains in China. The resulting superimposition was therefore likely to happen, and create the phenomenon that we are now witnessing.

What shall be done now?
In the short term, reinforcement of screening strategies and infection control measures seem the best available weapons by far. Rapid and accurate detection of MDR bacteria by using modern and effective diagnostic techniques is mandatory, as it facilitates subsequent control measures. Even if new therapeutic alternatives might be available and save lives (such as the ceftazidime/avibactam drug combination), antagonizing the spread of those “superbugs” remains a priority.

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