Case Report
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# The first report of infection with *Klebsiella pneumoniae* carrying the $bla_{kpc}$ gene in State of Mato Grosso do Sul, Brazil

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**ABSTRACT**

The increased frequency and dissemination of enterobacteria resistant to various antimicrobials is currently worldwide concern. In January 2010, a 94-year-old patient with chronic lymphocytic leukemia was admitted to the University Hospital. This patient died 21 days after hospitalization due to the clinical worsening. *Klebsiella pneumoniae* producing of extended-spectrum β-lactamases (ESBLs) was isolated of urine culture. This bacterium demonstrated resistance to ceftazidime, ciprofloxacin, levofloxacin, ertapenem and imipenem. Susceptibility to cefoxitin, cefepime, meropenem, colistin and tigecycline. This study reports the first case of infection by *Klebsiella pneumoniae* carrying the $bla_{kpc}$ gene in the State of Mato Grosso do Sul, Brazil.

**Keywords:** Carbapenemase. *Klebsiella pneumoniae.* Multidrug- resistant.

## INTRODUCTION

The emergence of β-lactamases producing enterobacteria has been considered one of the major challenges faced by hospitals in recent decades. Recent reports have shown an increasing prevalence of these enterobacteria, especially *Klebsiella pneumoniae* strains resistant to carpabenens, antibiotics indicated for the treatment of patients who are infected with bacteria producing extended-spectrum β-lactamases (ESBLs)[1].

The *Klebsiella pneumoniae* carbapenemase (KPC-KPN) was first described in 1996 in North Carolina, USA[2]. In Brazil, the first reports of KPC-KPN infection among Northeastern patients were described in 2006[3]. However, there is also evidence that the carpabenem-resistant genotype was described in 2005 in São Paulo[4]. Since then, this microorganism has been disseminate to several hospitals in different Brazilian states[5-7].

## CASE REPORT

In January 2010, a 94-year-old female patient who had been diagnosed with chronic lymphocytic leukemia was hospitalized in a teaching hospital with 256 beds in Campo Grande, State of Mato Grosso do Sul, Midwest Brazil. This patient presented with the following symptoms: a cough with sputum production, hoarseness, sibilance, dyspnea and a fever of 39ºC. The patients' blood pressure and glycemia were normal. Antibiotic therapy, consisting of ceftriaxone 1g twice daily, and clindamycin 600mg three times a day for 10 days. During the period of hospitalization, she developed a urinary tract infection, and there was a concomitant worsening of her laboratorial results and clinical condition. The antimicrobial therapy was first switched to ciprofloxacin and piperacilin/tazobactam and was subsequently included vancomycin and fluconazole (yeast in the urine) due to the patient's persistent clinical worsening. However, the patient died 21 days after hospitalization.

The patient had used a central venous catheter for 17 days, and a three-way catheter was used for vesical catheterization over the course of 19 days, with three removals. The urine samples collected at 12 and 15 days post-hospitalization resulted in positive cultures containing greater than $10^5$ UFC/mL (colony forming units/mL) *Klebsiella pneumoniae* was isolated, and the result of the Modified Hodge Test was positive. Moreover, the results produced by the VITEK 2 automated system (bioMérieux, Marcy l'Etoile, France) revealed that the patothogen was producing ESBLs and demonstrated resistance to ceftazidime, the fluoroquinolones ciprofloxacin and levofloxacin, and the carbapenemic ertapenem and imipenem and susceptibility to cefoxitin, cefepime, meropenem, colistin and tigecycline (**Table 1**).

The first positive urine culture sample was sent to the *Laboratório Especial de Microbiologia Clínica da Universidade Federal de São Paulo*, where $bla_{kpc-2}$ gene was detected by polymerase chain reaction analysis followed by deoxyribonucleic acid (DNA) sequencing[3]. The study was approved by the Research Ethics Committee of *Universidade Federal de Mato Grosso do Sul* (UFMS).

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***TABLE 1 - Antimicrobial susceptibility profile of the* Klebsiella pneumoniae *strain isolated from the patient's urine culture.***

| Antimicrobials | Minimum inhibitory concentration (µg/mL) | Interpretation* |
|---|---|---|
| Cefoxitin | 8 | susceptible |
| Ceftazidime | ≥ 64 | resistant |
| Cefepime | 8 | susceptible |
| Meropenem | 1 | susceptible |
| Ertapenem | 4 | resistant |
| Ciprofloxacin | 4 | resistant |
| Levofloxacin | ≥ 8 | resistant |

*Clinical and Laboratory Standards Institute, 2011.

## DISCUSSION

The clonal dissemination of KPC-KPN strains across hospitals throughout the world has been documented[7,8]. Since the first description in 2009, which was made by Monteiro et al.[3], sporadic cases and outbreaks have been reported in Brazil[5,9]. The case presented here represents the first report of infection with *Klebsiella pneumoniaeb*carrying the *bla*$_{kpc}$ gene in the State of Mato Grosso do Sul, Midwest Brazil.

Between 2009 and 2010, an increased number of notifications were made to the *Agência Nacional de Vigilância Sanitária* (ANVISA) concerning outbreaks in different regions of the country, which generated a national response. Faced with this situation, ANVISA published a technical standard in an attempt to control the dissemination of these multidrug-resistant microrganisms[10]. The dissemination of resistant strains mainly results from the lack or failure of proper therapeutic treatments, and the results of such dissemination can be catastrophic if effective control measures are not undertaken.

Infections caused by multidrug-resistant enterobacteriaceae tend to be more frequent among elderly patients with impaired immune systems. This is especially true for those who have other comorbidities[5], such as the patient described here, who was elderly and also had chronic lymphocytic leukemia. Moreover, these types of infections are usually associated with high lethality[5,8].

According to the literature, invasive procedures, such as the use of central venous catheters or urinary catheters, are significant routes of infection resulting from healthcare interventions[11]. In the cases reported by Beirão et al.[5], all of the patients diagnosed with KPC-KPN infections, which had been isolated from the urine, had been given urinary catheters.

It is important to note that the minimum inhibitory concentration (CIM) for meropenem from the sample of KPC-KPN was characterized as susceptible according to the Clinical and Laboratory Standards Institute (CLSI) criteria[12], which indicates a risk of therapeutic failure for cases of infection treated with this antimicrobial.

Health surveillance studies and molecular analyses aimed at identifying antibiotic resistance genes are required for optimal detection of the emergence and occurrence of future KPC-KPN outbreaks. Moreover, such analyses and studies may also identify the likelihood of further dissemination of these genes in Brazil.

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