Case Report

**Klebsiella pneumoniae** K2 producer of pyogenic liver abscess associated with biliary communication

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**Abstract**

Introduction: Hypervirulent strains of **Klebsiella pneumoniae** have gained clinical and epidemiological interest because of their capacity to cause severe and life-threatening infections.

Methodology: We report a case involving infection with a hypervirulent **K. pneumoniae** K2 strain that caused liver abscess in a young woman with type 1 diabetes in Mexico.

Results: The infection was found to be associated with biliary tract communication. The virulence factors and capsular serotypes were identified by polymerase chain reaction analysis. After guided drainage and directed antibiotic treatment, the infection resolved and the patient recovered.

Colonization of the gastrointestinal tract by hypervirulent **K. pneumoniae** strains, together with the presence of comorbidity, such as diabetes are important factors that contribute to the development of liver abscess.

Conclusions: The identification of virulent clones is important to understand the pathogenicity and improve control of infections in the patients.

**Key words:** infection; colonization; **Klebsiella**; abscess; virulence; K2.

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Introduction

The worldwide human nosocomial pathogen **Klebsiella pneumoniae** is a Gram-negative bacillus belonging to the Enterobacteriaceae family. This bacterium is one of the principal pathogens causing nosocomial infections and are responsible for respiratory, urinary, and gastrointestinal tract infections [1]. **K. pneumoniae** liver abscess (KLA) is an emerging infection worldwide that can cause **K. pneumoniae** invasive syndrome characterized by liver abscesses, bacteremia, and metastatic infections of the eyes and central nervous system [2].

Pyogenic liver abscesses in people with diabetes without a biliary tract disorder can be caused by the hypervirulent **K. pneumoniae** (hvKpn) pathotype and was first described in Asia in the 1980s. Lin *et al.* [3] suggested colonization of the gastrointestinal tract by **K. pneumoniae** via the portal vein as the primary cause of liver abscess after isolating this bacterium in feces from a healthy Chinese person. The major risk factors for the development of KLA caused by hvKpn are diabetes, cholelithiasis, and the dietary composition. Diabetic patients with poor glycemic control may have impaired neutrophil phagocytosis. KLA infection in people with diabetes, especially if poorly controlled, increases the risk of hepatic vein thrombophlebitis and gas production caused by changes in the local microenvironment that favor bacterial growth [4,5].

Cases of KLA caused by hvKpn have also been reported from North America and Europe, but there are few reports from Latin America. The hvKpn has been described with serotypes K1, K5, and K19 in Brazil, K1 in Argentina, and K2 in Mexico [6–8]. The reason for higher prevalence in Asia is unclear, but it may be related to the ethnicity and differences in the virulence of the bacterium itself.

The hvKpn strains present more frequently as the capsular serotypes K1 and K2, which are associated with the phenotype of hypermucoviscosity (hmv). The hvKpn phenotype is mediated by the presence of virulence genes such as the regulators of the mucoid phenotype (*rmpA* and *rmpA2*) and of siderophore biosynthesis such as *iroB* (salmochelin), *entB* (enterobactin), *ybtQ* (yersiniabactin), and *iucA*.
(aerobactin); the latter is considered to be the most important [9]. A putative transporter (peg-344) is considered to be a biomarker for the hvKpn strain, and it has been suggested that this gene can be used to differentiate between hypervirulent and typical *K. pneumoniae* [10].

The hyperproduction of capsule in hvKpn strains increases its resistance to humoral defenses, killing by complement, and phagocytosis by macrophages and neutrophils. Thus, hvKp has a potential invasive phenotype and could produce liver abscesses [11]. Most hvKpn isolates with serotype K1 from clonal group (CG) 23 have been described in Taiwan, Singapore, and China. CG23 includes the sequence type (ST) 23, ST26, ST57, and ST1633. This CG was originally associated with the lack of acquired antimicrobial resistance, although this has changed recently, and the resistance to cephalosporins and carbapenems is increasing [12].

**Case presentation**

A 30-year-old woman was admitted to the intensive care unit of Medica Sur Hospital, Mexico City, Mexico, in September 2019. The patient’s comorbidities included type 1 diabetes without intra-abdominal or biliary tract infection. She was previously hospitalized for diabetic ketoacidosis and by the time of this hospital admission she was on insulin glargine (20 units per day) and insulin lispro (15 units’ pre-meal). The patient reported consumption of *Ganoderma lucidum* mushroom powder in tea several times during the month before the onset of her symptoms. There was no history of travel to Asia.

On admission, the patient was alert but exhibited fatigue, generalized jaundice, nausea, and oral intolerance. On physical exam, her vital signs were blood pressure 80/50 mmHg, heart rate 115 beats/min, and body temperature 39.3 °C. She had abdominal pain in the right upper quadrant. Laboratory data showed white blood cell count $41 \times 10^3/µL$ (neutrophils $36.9 \times 10^3/µL$, lymphocytes $1.6 \times 10^3/µL$), hemoglobin level 8.3 g/dL, platelet count $327 \times 10^3/µL$, C-reactive protein level 162 mg/L, creatinine level 1.55 mg/dL, and HbA1c (glycated hemoglobin) level 10.1%. Serum aspartate aminotransferase and alanine aminotransferase levels were 287 U/L and 33 U/L, respectively. Serum direct and indirect bilirubin were 11.39 mg/dL and 12.22 mg/dL, respectively. A bedside hepatic ultrasound revealed three heterogenic images...

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**Figure 1.** Computed tomography images showing multiple liver abscesses before drainage (a–c, dotted circle). After drainage, the abscesses have resolved (d, arrow).
related to hepatic abscesses, the biggest was localized on segment VI with 70 mm × 57 mm × 55 mm; the remaining two abscesses were localized on segments VII with 55 mm × 31 mm × 17 mm, and 47 mm × 40 mm × 39 mm respectively (Figure 1). The patient underwent surgical drainage of the largest abscess where approximately 300 ml of purulent content was reported. An initial antimicrobial scheme was based on intravenous ceftriaxone plus metronidazole.

Purulent samples were cultured and pan-susceptible *K. pneumoniae* was isolated. The antibiotic therapy was adjusted to ertapenem. The *Entamoeba* IgG antibody test was negative (1.37 U, cutoff value 0–8.99 U), and the stool culture was also negative.

Days later a computed tomography (CT) scan of the abdomen revealed images compatible with the presence of residual liver abscesses; the most representative were two abscesses in segment VII measuring 45 × 43 mm and 58 × 43 mm and another across segment VI that was in close contact with the ipsilateral kidney (Figure 1). Liver cysts and cholelithiasis were not seen in the abdominal CT images. Those latter abscesses were drainage by percutaneous aspiration and placement of a catheter with the same microbiology results as the samples.

Several days later the clinical and laboratory parameters improved, a new CT scan of the abdomen revealed reduction of more than 90% of the abscesses. The patient was discharged with a prescription for ertapenem for 14 more days as an outpatient antimicrobial therapy.

**Bacterial isolates and antimicrobial susceptibility**

Drainage samples were collected aseptically from the patient with liver abscesses. The bacteria isolated from the abscesses were cultivated and subjected to MALDI-TOF-MS (Becton-Dickinson, Heidelberg, Germany) analysis, and identified as *K. pneumoniae*. Antimicrobial susceptibility was identified using a BD Phoenix™ automated system (Becton-Dickinson, Maryland, USA), and the results were interpreted using CLSI M100 breakpoints [14].

**Determination of the hvKpn phenotype**

The *K. pneumoniae* 3322874 isolate was plated in blood agar using a bacteriology loop and grown in a MacConkey plate for 18 h at 37 °C. The formation of a viscous string > 10 mm was defined as string test positive [13]. The phenotype of the isolate spread by the bacteriology loop did not necessarily equate to the hvKpn phenotype [8].

**Detection of virulence factors**

The **peg-344**, **iroB**, **iucA**, **entB**, **rmpA**, and **rmpA2** virulence factors and capsular serotypes (K1, K2, K5, K20, K54, and K57) were identified by polymerase chain reaction (PCR), and the primer sets are described in Table 1.

<table>
<thead>
<tr>
<th>Gene and serotype</th>
<th>Sequence (5’–3’)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>rmpA</td>
<td>rmpA-F: ACTGGGCTACCTCTGCTTCA</td>
<td>[15]</td>
</tr>
<tr>
<td></td>
<td>rmpA-R: CTTGCATGAGCCATCTTTCIA</td>
<td></td>
</tr>
<tr>
<td>rmpA2</td>
<td>rmpA2-F: CTTTATGTCATAAAAGGTGT</td>
<td>[15]</td>
</tr>
<tr>
<td></td>
<td>rmpA2-R: CCTCTCTGAGAGTAAGCATTT</td>
<td></td>
</tr>
<tr>
<td>entB</td>
<td>entB-F: GATGAAAGCACTACCGTC</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td>entB-R: ACCGAAATGGAGACCAGTGC</td>
<td></td>
</tr>
<tr>
<td>iroB</td>
<td>iroB-F: ATCTCATCCTCTACCGTGC</td>
<td>[16]</td>
</tr>
<tr>
<td></td>
<td>iroB-R: GGTGCGGCTGTTTCAA</td>
<td></td>
</tr>
<tr>
<td>iucA</td>
<td>iucA-F: AATCAATGGCTAATCCCGGTG</td>
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<tr>
<td></td>
<td>iucA-R: CGCTTCACTTTCCTGACAGG</td>
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</tr>
<tr>
<td>peg-344</td>
<td>F1: CCTGAAAATCTCCACTGTC</td>
<td>[17]</td>
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<tr>
<td></td>
<td>R1: CCAGGAAAGAAATACCCCA</td>
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<tr>
<td>wzy_K1</td>
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<tr>
<td></td>
<td>wzyK1-R: GCAATGCCCTTGGCATAG</td>
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</tr>
<tr>
<td>wzy_K2</td>
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<td>wzyK20-R: TCCACTTCCTTTCCCTCC</td>
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<td>wzyK57-F: CTCAGGGCTGAGATGTGTCAT</td>
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<tr>
<td></td>
<td>wzyK57-R: CACTAACCAGAGAGCTGAG</td>
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</tbody>
</table>
**Table 2. Phenotypic and genotype characteristic of hypervirulent *K. pneumoniae* clinical isolate**

<table>
<thead>
<tr>
<th>Strain</th>
<th>Origin of sample</th>
<th>String test</th>
<th>Capsular genotype</th>
<th><em>rmpA</em>/rmpA2</th>
<th>iucA/iroB/entB</th>
<th>peg-344</th>
<th>MLST</th>
<th>LD&lt;sub&gt;50&lt;/sub&gt; (CFU/mL)</th>
<th>Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>3322874</td>
<td>Liver abscess</td>
<td>-</td>
<td>K2</td>
<td>+/-</td>
<td>+/+/+</td>
<td>+</td>
<td>ST380</td>
<td>100</td>
<td>Hypervirulent</td>
</tr>
</tbody>
</table>

MLST: MultiLocus Sequence Typing; CFU: colony-forming unit.
Despite the fact that there is no evidence that K. pneumoniae is a digestive tract commensal, we consider that the presence of hypervirulent strains coupled with the uncontrolled diabetes are factors that lead to the production of liver abscesses in young patients. In addition, we considered that the patient’s consumption of G. lucidum may have been responsible for the hepatotoxicity, because the liver chemistry can mimic acute cholangitis after consumption of G. lucidum [36]. However, no cases of infections related to the consumption of this dry preparation of fungus have been reported. Finally, studying the phenotypic and genotypic characteristics of bacteria can be useful for identifying other pathologies, such as the association between K. pneumoniae strains and fatty liver disease, which involves successive complications such as inflammation, fibrosis, steatohepatitis, cirrhosis, and hepatocellular carcinoma [37,38].

Conclusions
Thus, hypervirulent K. pneumoniae is a highly virulent strain related to hepatic abscess in particular in diabetic patients. In Mexico, hvKpn K. pneumoniae is susceptible to antibiotics. However, with the increase in cases of drug-resistant Enterobacteriaceae, the evolution of the susceptibility pattern should be monitored to prevent hypervirulent K. pneumoniae from becoming an epidemiological threat.

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References

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