Nosocomial Liver Abscess Caused by Extended-Spectrum Beta-Lactamase producing *Klebsiella pneumoniae*: A Case Report

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Running Title: ESBL-producing *K. pneumoniae* liver abscess

Key words: *K. pneumoniae*, Liver abscess, ESBL

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Abstract

Nosocomial pyogenic liver abscess caused by extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* presented in a man with adenocarcinoma of the stomach. *K. pneumoniae* strain isolated from blood and liver aspirate culture after antibiotic therapy for recurrent bacteremia, was resistant to all extended-spectrum beta-lactams except imipenem, and differed from *K. pneumoniae* strains causing community-acquired liver abscess.
Case report

A 48-year-old man with adenocarcinoma of the stomach received radical gastrectomy in 2003 and then 11 courses of intensive chemotherapy with fluorouracil, calcium folinate, and oxaliplatin for tumor metastasis to liver and peritoneum. In July 2005, he was admitted to our hospital for treatment of oral candidiasis associated with shaking chills, spiking fever, and abdominal fullness. Initially, intravenous ampicillin/sulbactam and oral fluconazole were given. *Escherichia coli*, *Bacteroides fragilis*, and *Fusobacterium varium* were isolated from two sets of blood cultures. *E. coli* was susceptible to all cephalosporins, but resistant to ampicillin and trimethoprim/sulfamethoxazole. Cefpirome and metronidazole were administered 5 days later, but the patient’s intermittent spiking fever persisted. A blood culture disclosed *Enterococcus faecium* and *Bacteroides thetaiotaomicron*. Gentamicin was added. On day 14, he developed spiking fever again with pain over the right upper quadrant of his abdomen. Computed tomography of the abdomen showed a 4-cm hypodense lesion over segment 6 of the liver (fig. 1). Percutaneous drainage was performed and pus was aspirated. The liver biopsy revealed a massive necrosis with inflammatory cells in liver tissue. Extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae* detected by double disk screening and confirmatory tests based on CLSI recommendations was isolated from cultures of
blood and pus aspirated from the liver. *K. pneumoniae* was resistant to all cephalosporins and aminoglycosides, but it was sensitive to imipenem. The MICs of antimicrobial agents were determined by Etest using interpretive standards based on CLSI recommendations. The results of MICs of ceftazidime 256 μg/ml, ceftriaxone 256 μg/ml, cefepime 128 μg/ml, cefoxitin 128 μg/ml, gentamicin 96 μg/ml, ciprofloxacin 32 μg/ml, and imipenem 0.75 μg/ml were demonstrated (6). Detection of plasmid-mediated AmpC beta-lactamases with AmpC disk test was negative (figure was not shown) (1). The capsular serotype was non-K1/K2 by countercurrent immuno-electrophoresis and the phenotype was non-mucoid (9,10). PCR for *magA* gene was negative (7). In this case, the same antibiogram and Pulsed field gel electrophoresis (PFGE) demonstrated for isolates from blood and pus aspirated from the liver (data not shown). PFGE demonstrated completely different patterns for strains from community-acquired liver abscess and nosocomial ESBL-producing *K. pneumoniae* bacteremia (fig. 2A, 2B) (20). Though his clinical symptoms and signs improved after treatment with imipenem for 6 weeks, he died of progressive carcinomatosis with multiple organ failure 2 months later.
Discussion

This is the first report on nosocomial liver abscess caused by ESBL-producing *K. pneumoniae* after intensive chemotherapy for carcinoma of the stomach and prolonged antibiotic treatment for recurrent bacteremia. *K. pneumoniae* has been emerging as the leading cause of community-acquired pyogenic liver abscess in Taiwan and the United States (2,3,8,11,14). Different clonal populations of *K. pneumoniae* cause community-acquired pyogenic liver abscess (4,5). Serotype K1/K2 accounts for 78% of isolates, and non-K1/K2 for 22% (9). ESBL-producing *K. pneumoniae* is one of the most frequent causes of nosocomial pneumonia, intra-abdominal infection, urinary tract infection, and primary bacteremia (13). The prevalence of ESBL-producing *K. pneumoniae* as a nosocomial pathogen is increasing worldwide (13,15,19). Information regarding *K. pneumoniae* associated infection is summarized in Table 1 (3,9,12-14,17). The newly emerged community-acquired *K. pneumoniae* strains causing liver abscess have been associated with more septic metastatic complications and low mortality rate, whereas nosocomial *K. pneumoniae* strains including non-ESBL and ESBL-producing strains have been associated with less septic metastatic complications and high mortality. These community-acquired and nosocomial infections have very different presentations.
Extended-spectrum cephalosporins have facilitated treatment of severe infections caused by Gram-negative bacteria. However, increasing use of these agents has been associated with the emergence of resistant bacterial strains, such as those producing different SHV- or TEM-derived ESBLs (12,16).

A well-known virulence factor of *K. pneumoniae* associated with liver abscess is the capsular polysaccharide serotype (such as K1 and K2) (9). However, the ESBL-producing *K. pneumoniae* strain in our case was *magA*⁻ and non-K1/K2. The PFGE pattern of genomic DNA from the 8 *K. pneumoniae* strains isolated from community-acquired liver abscesses (serotype K1, n= 4), nosocomial bacteremias (K1 and non-K1/K2 [i.e., K54 and K55]), and the present case were different, and the genetic dendrogram showed low similarity. Further study is needed to determine whether other virulence factors such as the strain of ESBL-producing *K pneumoniae* are important.

Intensive chemotherapy and prolonged use of antibiotics puts patients with intestinal tract tumors, hepato-biliary tract tumors, or intra-abdominal carcinomatosis at risk for infection by opportunistic pathogens and recurrent bacteremia (18). However, selective antibiotic pressure may play a role for the selection of ESBL-producing strains (13). In our case, nosocomial liver abscess caused by ESBL-producing *K. pneumoniae* was selected by prolonged broad-spectrum antibiotic treatment.
In conclusion, the strain of ESBL-producing *K. pneumoniae* causing nosocomial liver abscess in our case differed from strains causing community-acquired liver abscess with respect to capsular serotype, antibiogram pattern, and PFGE pattern. More judicious use of antibiotics is recommended to decrease resistance and slow the emergence of resistant bacteria.
Acknowledge

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Table 1. Summary of *Klebsiella pneumoniae* infection

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean age (SD or range)</th>
<th>S/S</th>
<th>serotype</th>
<th>Hepatobiliary-GI tract abnormal</th>
<th>N/A</th>
<th>Metastatic complication</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community-acquired <em>K. pneumoniae</em> bacteremia(^a)</td>
<td>61.2 (± 15.7)</td>
<td>Fever</td>
<td>K1: 30%</td>
<td>K2: 6%</td>
<td>13%</td>
<td>Not found except combined with liver abscess</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>K2: 6%</td>
<td>Non-K1/K2: 64%</td>
<td></td>
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</tr>
<tr>
<td>Community-acquired <em>K. pneumoniae</em> Liver abscess-Taiwan(^b)</td>
<td>56.4 (34-78)</td>
<td>Fever</td>
<td>K1: 64%</td>
<td>K2: 14%</td>
<td>8.2%</td>
<td>Endophthalmitis:</td>
<td>10.4%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RUQ pain</td>
<td>Non-K1/K2: 22%</td>
<td></td>
<td>78%</td>
<td>Other site metastasis:</td>
<td>6%</td>
</tr>
<tr>
<td>Community-acquired <em>K. pneumoniae</em> Liver abscess-USA(^c)</td>
<td>56.4 (25-90)</td>
<td>Fever</td>
<td>N/A</td>
<td></td>
<td>43%</td>
<td>Not found</td>
<td>2.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RUQ pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nosocomial-acquired <em>K. pneumoniae</em> bacteremia(^a)</td>
<td>59.2 (± 20.7)</td>
<td>Fever</td>
<td>K1: 14%</td>
<td>K2: 3%</td>
<td>2%</td>
<td>Not found</td>
<td>36%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Jaundice</td>
<td>Non-K1/K2: 83%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nosocomial-acquired ESBL-<em>K. pneumoniae</em> bacteremia(^d)</td>
<td>58 (17-90)</td>
<td>Septic shock</td>
<td>N/A</td>
<td></td>
<td>13.1%</td>
<td>Not found</td>
<td>23.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pneumonia</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Nosocomial-acquired ESBL-<em>K. pneumoniae</em> Liver abscess</td>
<td>48</td>
<td>Fever</td>
<td>Non-K1/K2</td>
<td>Yes</td>
<td>15%</td>
<td>Not found</td>
<td>Expired</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RUQ pain</td>
<td></td>
<td>no</td>
<td></td>
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</tr>
</tbody>
</table>

Abbreviation: DM, diabetes mellitus; UTI, urinary tract infection; S/S, symptoms and signs; RUQ, right upper quadrant; GI tract, gastro-intestinal tract; and N/A, not assayed

\(^a\) Reference 17
\(^b\) Reference 9
\(^c\) Reference 14
\(^d\) Reference 12, 13
**Figures Legends**

Fig. 1. Computed tomography of the abdomen showed a hypodense lesion about 4 cm in size over the right lobe of the liver.

Fig. 2A. Dendrogram based on the PFGE results of 8 clinical isolates of *K. pneumoniae*. Strains were clustered by the unweighted-pair group method using arithmetic averages (Nos. 1, 3, 13, and 23: isolated from community-acquired liver abscess, serotype K1; Nos. 33, 37, and 38: isolated from nosocomial bloodstream infections of ESBL-producing non-K1/K2; I: the present strain).

Fig. 2B. PFGE. Image shows the different molecular clones of *K. pneumoniae* strains isolated from community-acquired liver abscess and nosocomial bloodstream infection, and the presented strain.
Fig. 2B.
Positive control CMY2 carrying *E. coli*

Present strain

*E. coli* ATCC 25922