Hypervirulent *Klebsiella pneumoniae* Mediated Hepatic Infarction Septic Shock After Rectal Cancer Surgery: A Case Report

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Abstract: The liver receives blood from both the hepatic artery and portal vein. Hepatic infarction is rare in clinical practice as both the hepatic artery and portal vein can supply blood to the liver. Here, we reported a case of a 75-year-old man who underwent radical laparoscopic surgery for rectal cancer and subsequently developed hepatic infarction. The patient experienced severe infection, as well as circulatory and respiratory failure on the third day after surgery. The patient presented with high fever, chest tightness, shortness of breath, decreased blood oxygen saturation and blood pressure. The leukocyte count decreased from 8.10 × 10⁹/L to 1.75 × 10⁹/L. Procalcitonin (PCT) levels increased from 1.02 ng/mL to 67.14 ng/mL, and eventually reaching levels over 200 ng/mL. Enhanced abdominal computed tomography (CT) confirmed the presence of hepatic infarction, but no thrombosis was observed in the hepatic artery or portal vein. Metagenomic next-generation sequencing (mNGS) identified hypervirulent *Klebsiella pneumoniae* (hvKp) in the patient’s blood and ascites, one day earlier than the detection results using traditional culture methods. The patient was diagnosed with hepatic infarction combined with septic shock caused by hvKp. This case emphasizes that in the high-risk group of thrombosis, infection can trigger exacerbated hepatic infarction events, particularly in cases after surgical procedures. For severely ill patients with infectious diseases who are admitted to the ICU with worsening symptoms, it is important to collect appropriate samples and send them for pathogen detection using mNGS in a timely manner. This may aid in early intervention and improve clinical outcomes.

Keywords: hepatic infarction, mNGS, hypervirulent *Klebsiella pneumoniae*, septic shock

**Introduction**

Hepatic infarction is a medical condition characterized by the necrosis of liver tissue resulting from blood flow occlusion. This occlusion can result from various factors, including arterial thrombosis, arterial embolism, vascular compression occlusion, and arterial spasm. The development of hepatic infarction also depends on whether an effective collateral circulation to compensate for the blood flow occlusion can be established. Certain medical techniques and procedures such as transjugular portosystemic shunt,¹,² pancreaticobiliary surgery,³ liver transplantation, and hepatic artery chemoembolization,⁴ have been associated with the occurrence of hepatic infarction. Additionally, blood hypercoagulability and blunt liver injury can increase the risk of hepatic infarction.

Hepatic infarction is rare in clinical practice and is characterized by a lack of specific symptoms. Simple occlusion of the hepatic artery or portal vein does not lead to hepatic infarction. Initial symptoms, as evidenced by prior studies,²,⁵,⁶ may manifest as chest or abdominal pain, accompanied by fever, nausea or vomiting. However, clinical diagnosis
remains challenging due to the limited diagnostic value of laboratory examination and blood biomarkers.\textsuperscript{7,8} Circulatory shock, sepsis, anesthesia, or biliary disease have been proposed as potential contributing factors to hepatic infarction.\textsuperscript{5,6}

Hypervirulent \textit{Klebsiella pneumoniae} (hvKp) has emerged as a global pathogen of concern due to its high toxicity compared to classical \textit{K. pneumoniae} (cKp). HvKp colonizes in the gastrointestinal tract, which facilitates its transmission in both community and medical settings. HvKp can spread to other parts of the body, including the eyes, lungs, and central nervous system (CNS). It is a leading cause of pyogenic liver abscesses, which are associated with primary extrahepatic infections such as hyper viscous bacteremia, pneumonia, soft tissue infections,\textsuperscript{9} and high rates of vascular thrombotic complications.\textsuperscript{10} HvKp infections are particularly prevalent in parts of Asia, including Taiwan, China, Hong Kong, Singapore, and South Korea, and have also been reported in Europe, the United States, South America, the Middle East, and Australia.\textsuperscript{11,12}

Nosocomial infections of \textit{K. pneumoniae} often begin with the colonization of the patient’s gastrointestinal (GI) tract, and the bacterial density of colonized strains can influence progression.\textsuperscript{13} Certain risk factors, such as cancer, diabetes, and alcoholism, have been associated with \textit{K. pneumoniae} infections.\textsuperscript{14–16} \textit{K. pneumoniae} bloodstream infections (BSIs) are prevalent worldwide and associated with significant mortality rates. Drug resistance and virulence are two main factors contributing to \textit{K. pneumoniae} pathogenicity.\textsuperscript{17} The timely and precise identification of pathogens is essential for patients with infections, as it enables physicians to prescribe the most appropriate treatment.

Currently, etiological diagnosis using culture is still the gold standard for the diagnosis of infectious diseases. However, culture methods can take from 24 hours to 1 month to detect pathogens such as fastidious bacteria, anaerobes, viruses, and have a low detection rate in highly suspected infected cases.\textsuperscript{18} In contrast, metagenomic next-generation sequencing (mNGS) has many advantages over traditional detection methods, including faster detection times, higher sensitivity, and broader pathogen spectrum. mNGS is also less affected by previous antibiotic exposure.\textsuperscript{19} Here, we reported a 75-year-old man who developed severe infection, as well as circulatory and respiratory failure on the third day after radical laparoscopic surgery for rectal cancer. Enhanced abdominal computed tomography (CT) confirmed the presence of hepatic infarction and mNGS identified hvKp in the patient’s blood and ascites on the 3 days after hospitalization. The patient was diagnosed with hepatic infarction resulting from septic shock mediated by hvKp eventually.

**Case Report**

A 75-year-old man was admitted to hospital with a complaint of blood in his stool that had persisted for 1 month (Figure 1). The patient had a medical history of coronary heart disease, hypertension, and a long-term smoking for more than 20 years. He was currently being treated with aspirin and clopidogrel. On admission, the patients D-dimer level was 0.0 \( \mu \text{g/mL} \). Electrocardiogram showed sinus rhythm and T wave changes in the anterior lateral wall. After admission, the patient underwent a colonoscopy and tissue biopsy, which confirmed the diagnosis of rectal cancer (Figure 2A). On 20 October 2022, the patient underwent laparoscopic radical resection of rectal cancer. Postoperative rectal pathological results revealed moderately differentiated adenocarcinoma with strong carcinoembryonic antigen (CEA) positive

![Figure 1 The timeline of this patient.](https://doi.org/10.2147/IDR.S452705)
The following night, the patient developed a fever with a maximum temperature of 38.9°C. To prevent infection, the patient was treated with a combination of fosfomycin and ornidazole. Two days after the surgery, the patient’s fever had resolved. During a lower extremity color Doppler ultrasound examination, thrombosis was found in the right peroneal vein and left posterior tibial vein, as well as bilateral calf intermuscular venous thrombosis. Consequently, nadroparin was given to prevent further clotting.

On the morning of October 23 (the third day after surgery), the patient presented high fever, chest tightness, shortness of breath, and decreased oxygen saturation and blood pressure. Enhanced chest and abdominal CT scans reveal no pulmonary embolism (Figure 3). However, multiple irregularly shaped intrahepatic lesions with decreased liver parenchyma density and no obvious space-occupying effect were observed, raising suspicion for focal hepatic fatty...
deposition, hepatic abscess, or hepatic infarction (Figure 4). The lumen of the liver blood supply system (hepatic artery, hepatic vein, and portal vein) appeared thinner and narrower with poor filling after enhanced CT, leading to the diagnosis of hepatic infarction (Figure 5). Due to respiratory failure and septic shock, the patient was transferred to ICU. The patient’s condition deteriorated rapidly during his stay in the ICU, characterized by persistent fever and a significant decrease in leukocyte count from $8.10 \times 10^9$/L to $1.75 \times 10^9$/L. Procalcitonin (PCT) levels increased from 1.02 ng/mL to 67.14 ng/mL, and up to > 200 ng/mL on October 24th. The patient’s electrocardiogram showed T wave changes in the lateral, anterior, and inferior walls of sinus tachycardia. Cardiac troponin was 0.049 ng/mL, myocardial enzyme spectrum showed lactate dehydrogenase was 217 U/L, phosphocreatine kinase was 357 U/L, creatine kinase isoenzyme was 22 U/L and myoglobin was 1522 μg/L. The brain natriuretic peptide was 119 pg/mL, and the presence of non-ST-segment elevation myocardial infarction was not considered. The patient’s SOFA score was 13, APECHE II score was 35, and expected mortality odds was 85.97%. Patients received empirical antimicrobial therapy with intravenous fluid resuscitation, including the administration of imipenem, within the first 3 hours of ICU admission. Although the patient’s liver function was normal when transferred to the ICU, alanine aminotransferase (ALT) levels increased sharply to 1780 U/L.

Figure 4 Plain scan shows multiple irregular low-density shadows of different sizes in the liver. The larger ones are located under the right lobe capsule with clear boundaries. The blue arrow points to the liver infarction lesion observed on CT plain scan.

Figure 5 The lesion density on enhanced scan showed no obvious enhancement, and the density was significantly lower than that of normal liver parenchyma, with no obvious space-occupying effect. Small blood vessels could be seen in the lesion, and no capsule could be seen (Left figure). Coronal view showing wedge-shaped lesions in the liver (fan-shaped changes) (Right figure). The left blue arrow indicates the liver infarction lesion seen on the axial enhanced CT, while the right blue arrow indicates the liver infarction lesion seen on the coronal view.
and aspartate aminotransferase (AST) to 3480 U/L on October 24th. Due to respiratory distress, the patient required tracheal intubation for invasive ventilation, continuous bedside blood purification (CRRT) was initiated, and femoral artery catheter was used for pulse indication continuous cardiac output monitoring (PICCO).

Bedside ultrasound was utilized to assess the liquid dark areas in the splenic and renal recesses, and a diagnostic puncture was performed to extract dark red turbidous liquid for further testing. Bacterial culture, fungal culture and mNGS were performed on the liquid sample, as well as on the patient’s blood sample (WillingMed Technology (Beijing) Co., Ltd). Despite various efforts to rescue the patient, the patient ultimately died at 18:05 on 24 October 2022.

On 25 October 2022, mNGS identified *K. pneumoniae*, *Enterococcus avium*, *Escherichia coli*, *Morganella morganii*, and *Bacteroides plebeius* in both ascites and blood (Table 1). Highly virulent genes associated with *K. pneumoniae* such as galF, fimH, gnd, iucD, iucC, iutA and iroC were identified by ascites mNGS. By contrast, on 26 October 2022, his blood culture was negative, and the culture results of ascites were *K. pneumoniae* and *Morganella morganii*. The culturable *K. pneumoniae* was susceptible to all routinely tested antibiotics except amoxicillin (Table 2).

<table>
<thead>
<tr>
<th>Species Name</th>
<th>Ascites</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sequence Number (RPTM)</td>
<td>Relative Abundance</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>46,847</td>
<td>10.8%</td>
</tr>
<tr>
<td><em>Streptococcus anginosus</em></td>
<td>39,034</td>
<td>9.0%</td>
</tr>
<tr>
<td><em>Enterococcus avium</em></td>
<td>18,059</td>
<td>4.2%</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>15,790</td>
<td>3.7%</td>
</tr>
<tr>
<td><em>Morganella morganii</em></td>
<td>6521</td>
<td>1.5%</td>
</tr>
<tr>
<td><em>Bacteroides plebeius</em></td>
<td>1661</td>
<td>0.38%</td>
</tr>
</tbody>
</table>

**Notes**: RPTM (reads per ten million) refers to number of pathogen sequences per ten million.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th><em>Klebsiella pneumoniae</em></th>
<th><em>Morganella morganii</em></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC (μg/mL)</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>Pipercillin/tazobactam</td>
<td>≤4</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>≤0.12</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Cefperazone/Sulbactam</td>
<td>≤8</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤0.25</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤0.25</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>1</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤1</td>
<td>Sensitive</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>Resistance</td>
<td>Resistance</td>
</tr>
</tbody>
</table>

**Abbreviation**: MIC, minimum inhibitory concentration of the antibiotic.

**Table 1 Test Results of mNGS**

**Table 2 Susceptibility Test Result of the Drainage Fluid Culture Was Obtained on October 28, 2022 (Day 18)**

**Discussion**

Hepatic infarction is a form of liver tissue death caused by blocked blood vessels. It is believed that hepatic infarction is caused by the simultaneous or single occlusion of the hepatic artery and portal vein. Systemic circulatory insufficiency can also reduce intrahepatic blood flow and contribute to the development of hepatic infarction. Hepatic infarction can be caused by iatrogenic injury to the hepatic vessels (mainly the hepatic arteries), liver abscesses, and can be secondary to shock, sepsis, anesthesia, or biliary tract disease. Arteriosclerosis and vascular endothelial damage caused by diabetes and hypertension can also lead to vessel wall thickening and luminal narrowing. The patient in this case had hypertension and coronary atherosclerotic heart disease, indicating poor hepatic vessel conditions and
vulnerability to injury. Additionally, the patient had recently undergone laparoscopic surgery for rectal cancer, exacerbating hepatic ischemia and hypoxia, leading to infarction. Furthermore, in patients with sepsis, the liver is frequently affected by inflammatory dysregulation.\textsuperscript{28,29} Patients with sepsis experience vascular endothelial damage, which can lead to coagulopathy.\textsuperscript{30} In this case, the patient developed septic shock following rectal cancer surgery, which may have caused a reduction in hepatic blood volume and ultimately led to hepatic infarction. In conclusion, several factors contributed to the development of hepatic infarction in this patient, among which septic shock due to infection might a significant factor.

mNGS results of blood and ascites showed \textit{K. pneumoniae}, \textit{Escherichia coli}, \textit{Morganella morganii}, along with the drug resistance gene SHV-71 encoding β-lactamase. Additionally, several \textit{K. pneumoniae} related hypervirulence factors including \textit{galF}, \textit{fimH}, \textit{gnd}, \textit{iucD}, \textit{iucC}, \textit{iutA} and \textit{iroC} were also identified. Although similar results were obtained in culture, the time required for culture detection was longer than that of mNGS, which take 2 days from sampling to report. Research has demonstrated that hvKp can lead to various serious illnesses, such as pneumonia, liver abscesses, urinary tract infections, and bloodstream infections, particularly when the body’s immune function is compromised. In severe cases, hvKp can lead to sepsis and other critical illnesses that are challenging to treat and have a high morbidity and mortality rate.\textsuperscript{31} HvKp can easily enter the liver through direct spread, portal circulation, or by crossing the intestinal barrier, leading to severe \textit{K. pneumoniae} infection in these patients.\textsuperscript{32} Thus, patients with liver and biliary system infections have a higher incidence of hvKp, especially those with malignant tumors complicated by infections. Furthermore, patients with community-acquired infections and underlying conditions such as diabetes, cancer, and hypertension, are more susceptible to HvKp infections.\textsuperscript{33} In this case, the patient had hypertension, malignant tumor, liver abscess, and septic shock, and \textit{K. pneumoniae} had the highest number of reads detected, indicating that HvKp should be the primary pathogen responsible for the infection. Unfortunately, the patient had already passed away at the time of the mNGS report, and the validation of these antibiotic resistance and virulence genes in laboratory tests was not timely. \textit{Morganella morganii} is considered an uncommon opportunistic pathogen that mainly causes sepsis, abscess, postoperative wound, and urinary tract infections. \textit{Morganella morganii} bacteremia often complicates infections of the hepatobiliary system and is associated with a high mortality rate.\textsuperscript{34,35} In a previous study, a patient who underwent pulmonary resection surgery was diagnosed with \textit{Morganella morganii} bacteremia through blood cultures. Unfortunately, the patient had already died before the blood culture report was available.\textsuperscript{35} Therefore, targeted treatment to the greatest extent possible is crucial for the prognosis of patients.

We believe that in this case the transfer of pathogens from the gastrointestinal tract to the bloodstream, leading to further spread of infection and sepsis, induce hepatic infarction. In conclusion, for patients with suspected hvKp infection, mNGS combined with conventional methods should be used as soon as possible to identify his infection status and make a suitable treatment plan.

**Conclusion**

Septic shock can reduce blood flow to the liver, maybe one of the leading reasons for hepatic infarction. Septic shock caused by hypervirulent \textit{K. pneumoniae} is associated with high mortality, necessitating increased vigilance in clinical settings. The utilization of mNGS technology enables rapid pathogen identification and facilitates clinical patient management.

**Data Sharing Statement**

The data presented in the study are deposited in the SRA (\url{https://www.ncbi.nlm.nih.gov/sra/}) repository, accession number PRJNA1037706.

**Ethics Statement**

Since the patient is deceased, written informed consent for publication of her clinical details and clinical images was obtained from the next of kin. This study was approved by the Ethics Review Committee of the Affiliated Changsha Central Hospital, Hengyang Medical School, University of South China (Approve No. KY-2024-004-01).
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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References


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