Case Reports

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A case report of pyogenic liver abscess caused by hypervirulent *Klebsiella pneumoniae* diagnosed by metagenomic next-generation sequencing

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Abstract

A 56-year-old woman with a history of diabetes mellitus presented with high fever but no abdominal pain. An abdominal computed tomography scan showed a large liver abscess. Hypervirulent, string test-positive, *rmpA*/*ampA*2-, and *iutA*-positive *Klebsiella pneumoniae* was rapidly identified from drainage fluid of the liver abscess using metagenomic next-generation sequencing (mNGS). After intravenous antibiotic therapy and drainage of the abscess, the patient's condition resolved. This case report highlights the value of mNGS in rapidly and accurately identifying a pathogenic microorganism, which helps reduce the incidence of antimicrobial resistance and enables the targeted use of antibiotics.

Keywords

Pyogenic liver abscess, hypervirulent *Klebsiella pneumoniae*, metagenomic next-generation sequencing, antimicrobial resistance, targeted antibiotic, traditional bacterial culture

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Introduction

In 1986, *Klebsiella pneumoniae* as a cause of abscesses at multiple sites was first reported in Taiwan and defined as hypervirulent *K. pneumoniae* (hvKP).[1] Liver abscesses caused by hvKP infection have become a

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serious threat to public health, especially in Asia.[2–4] Conventional pathogen detection methods do not provide a rapid identification, which may affect the treatment and prognosis of patients. Here, we report the rapid diagnosis of an hvKP liver abscess by metagenomic next-generation sequencing (mNGS).

Case report

The reporting of this study conforms to CARE guidelines.[5]

A 56-year-old woman with a history of diabetes mellitus and hypertension was admitted to our hospital presenting with fever and chest tightness for the past 4 days. She had no gastrointestinal symptoms, such as diarrhea and abdominal pain, or respiratory symptoms such as cough and expectoration. Despite her medical history, she was strong and able to withstand intensive physical labor including farm work. She had not received antimicrobial agents or been hospitalized in the previous 90 days, and had no history of overseas travel. None of her family members had any sign of infection.

Upon admission, her general condition was serious and vital signs indicated sepsis; her body temperature was 39.5°C, heart rate 122 beats per minute, blood pressure 117/64 mmHg with the continuous use of norepinephrine 0.3 μg/kg/minute, respiratory rate 25 breaths/minute, and peripheral oxygen saturation 95% after nasal catheter oxygen inhalation with an oxygen flow rate of 8 L/minute. Meningeal irritation signs and the Babinski sign were negative. Breath sounds in both lungs were thick with a small amount of dry rales, and decreased breath sounds were detected in the right lower lung field. Liver percussion caused pain, although her abdomen was soft with no tenderness and her liver and spleen were not palpable.

Peripheral blood analysis yielded the following results: white blood cell count, 8.65×10^9/L (neutrophils 94.7%); hemoglobin level, 106.1 g/L; and platelet count, 32×10^9/L. C-reactive protein levels were 400.7 mg/L and procalcitonin (PCT) levels were 92.28 ng/mL. Her serum aspartate aminotransferase and alanine aminotransferase levels were elevated (691 IU/L and 571 IU/L, respectively), and her glycosylated hemoglobin A1 (HbA1C) level was 13.2%. Chest and abdominal computed tomography (CT) scanning revealed bilateral pulmonary infection and a right lobe liver abscess (Figure 1). Fiberoptic bronchoscopy showed luminal mucosal edema congestion and erosion without obvious sputum. Quantitative bacterial culture from bronchoalveolar lavage fluid was negative.

Because of the poor general condition of the patient, empirical treatment was given immediately: meropenem (1 g every 8 hours), linezolid (600 mg every 12 hours), and voriconazole (first dose 400 mg every 12 hours, then 200 mg every 12 hours). On the second day after admission, ultrasound-guided puncture of the liver abscess was performed, and drainage fluid was collected for IDseq™ detection (Weiyuan Gene Technology Co., Ltd., Guangzhou, China) and pathogen culture. On the third day after admission, 119,331 specific sequences of *K. pneumoniae*, 90 specific sequences of the drug resistance gene bla_{SHV}, 432 specific sequences of the virulence gene *iutA*, and 86 specific sequences of *rmpA* were detected by DNA sequencing (Table 1). The drug resistance and virulence genes were associated with *K. pneumoniae*, with an association confidence level of >95%, suggesting that *K. pneumoniae* producing extended-spectrum β-lactamases (ESBL) are highly virulent.

Based on a comprehensive analysis of the test results, and considering the presence of an hvKP liver abscess but no

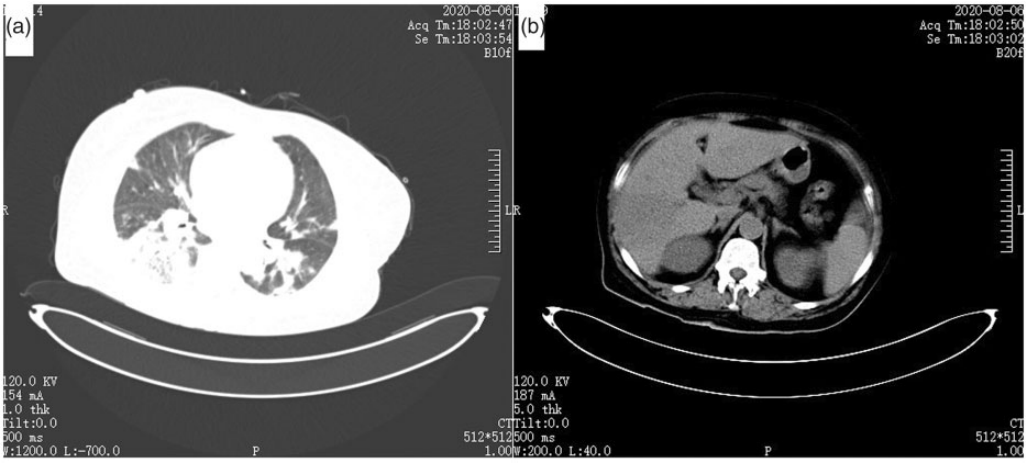

Figure 1. Computed tomography findings of the patient on the first day of admission. CT scan showing bilateral pulmonary infection (a) and a hepatic abscess (b).
CT, computed tomography.

Table 1. hvKP virulence genes identified in this study from *Klebsiella pneumoniae* 119331 in liver abscess drainage fluid.

Gene_id	Map_read	Coverage	Cov_ rate
(iutA)_ferric_aerobactin_receptor_lutA	432	2197/2202	0.9977294
(rmpA)_regulator_of_mucoid_phenotype_ [RmpA_(CVF855)]	56	512/633	0.8088468
(rmpA)_regulator_of_mucoid_phenotype_ RmpA_[RmpA_(VF0570)]	86	630/633	0.9952607
(rmpA2)_regulator_of_mucoid_phenotype_ RmpA2_[RmpA_(VF0570)]	47	274/300	0.9133334
NC_005249.1:55749-56387_Klebsiella_pneumoniae_ CG43_plasmid_pLVPK,_complete_sequence	93	626/639	0.9796557

hvKP, hypervirulent *Klebsiella pneumoniae*.

endophthalmitis or abnormality in cerebrospinal fluid examination by lumbar puncture, meropenem 1.0 g every 8 hours was given and linezolid and voriconazole were discontinued. On the fifth day after admission, the *Klebsiella* culture of the liver drainage solution was confirmed to be positive and the wire drawing test showed positive findings, which confirmed the accuracy of the IDseq^{TM} needle test results. The antibiotic susceptibility test suggested sensitivity to meropenem (Table 2). Combining mNGS and antibiotic susceptibility findings indicated pan-sensitive but hypervirulent *K. pneumoniae*.

To maintain a strong treatment effect, we continued to use meropenem after communicating with the patient's family rather than changing to a cheaper antibiotic. The patient's body temperature, PCT, and liver function all gradually returned to normal. After the clinical indicators had improved

Table 2. Antibiotic susceptibility test results of *Klebsiella pneumoniae* isolated from the liver abscess drainage fluid.

Antibiotic	Antibiotic susceptibility test result
Ticacillin/clavulanate	≤8 S*
Piperacillin/tazobactam	≤4 S
Ceftazidime	0.25 S
Cefepime	≤0.12 S
Aztreonam	≤1 S
Imipenem	≤0.25 S
Meropenem	≤0.25 S
Amikacin	≤2 S
Tobramycin	≤1 S
Levofloxacin	≤0.12 S
Ciprofloxacin	≤0.25 S
Trimethoprim/sulfamethoxazole	≤1/19 S
Minocyline	4 S
Tigecyline	≤0.5 S
Cefuroxime	19 S
Ceftriaxone	24 S
Amoxicillin/clavulanate	19 S
Doxycycline	1 S
Colistin	≤0.5 S
Cefoperazone/sulbactam	≤8 S
Ampicillin/sulbactam	15 S

*S: susceptibility.

on the sixth day post-admission, a repeat CT showed that the liver abscess had also improved (Figure 2). On the seventh day, three sets of blood cultures showed no bacterial growth, suggesting that it was a primary liver abscess.

Discussion

K. pneumoniae is an important pathogen of the Enterobacteriaceae family that causes a variety of infectious diseases, including pneumonia, liver abscesses, urinary tract infections, and bacteremia.[6] *K. pneumoniae* can be categorized according to virulence, with the hvKP infection detected in our patient causing the liver abscess as its main symptom. Such infections can lead to migratory infections in other tissues, including splenic abscesses, lung abscesses, endophthalmitis, and meningitis, mostly in patients with a weak immune system.[7] HvKP can also infect previously healthy and young individuals, typically more men than women (male:female ratio between 1.5:1 to 2.5:1).[8] Diabetes mellitus is the most common underlying disease of liver abscesses caused by hvKP,[9] and the proportion of these abscesses complicated with diabetes mellitus can be as high as 76.3%.[10] The most recognized explanation for this is that higher blood glucose levels not only reduce the function of neutrophils, including adhesion, chemotaxis, phagocytosis, and bactericidal activity, but also selectively impair neutrophil phagocytosis of serotypes K1/K2 in patients with diabetes.[11,12] Our patient also had diabetes and poor blood glucose control, so her infection may have been closely related to diabetes.

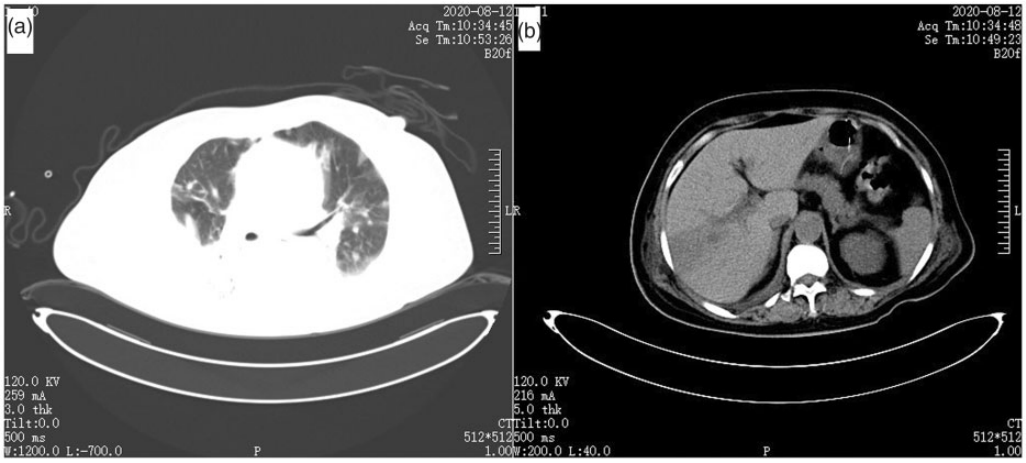

Figure 2. Computed tomography findings of the patient on the sixth day of admission. CT scan showing the improving lung infection (a) and hepatic abscess (b).
CT, computed tomography.

Hsu et al. reported that fever and abdominal pain were present in most pyogenic liver abscess patients, with about one-third of patients presenting with right upper abdominal pain and cough.[13] However, our patient had no obvious abdominal pain and her symptoms were not typical.

Liver abscesses caused by hvKP have the characteristics of acute onset, rapid progress, and a high mortality rate. Therefore, a timely assessment of the disease and its prognosis is particularly important. Traditional detection methods of pathogenic microorganisms, such as morphological detection, culture separation, biochemical detection, immunology, and nucleic acid detection, are limited in their sensitivity, specificity, and amount of information provided, as well as the speed of identification in the case of rare pathogenic microorganisms. mNGS does not rely on traditional microbial culture, instead directly carrying out high-throughput sequencing of nucleic acids in clinical samples, and comparing sequence findings with the database. It quickly and objectively detects many different pathogenic microorganisms (including viruses, bacteria, and fungi) in clinical samples without the need for specific amplification.[14,15] It is therefore especially suited to the diagnosis of acute and critical cases and difficult infections. mNGS can also associate drug resistance/virulence genes with drug-resistant bacteria to assess the source of the genes with a confidence interval. The benefits of identifying hvKP at an early stage enable a search for metastatic infection to be made, such as an early ophthalmology examination to rule out endophthalmitis; the consideration of aggressive source control, such as using larger gauge aspirates or more aggressive procedures because of the viscosity of the organism; and allowing a longer duration of antibiotic treatment to reduce the likelihood of recurrence.

Our patient was admitted in a critical condition so there was an urgent need to identify her infection to develop a suitable treatment plan. We used mNGS to quickly diagnose the type and virulence of the pathogen, including the drug resistance genes. However, our bacterial culture results, rather than mNGS, suggested infection

with pan-sensitive, not ESBL-producing *K. pneumoniae*. mNGS would have been challenging if the available sequence of the drug resistance gene had been too short; if the identified genes did not encode the corresponding protein, so no ESBL enzyme was produced; and if bacterial culture findings showed mostly dominant bacteria. Additionally, we emphasize that mNGS cannot completely replace bacterial culture as a diagnostic tool. The advantage of mNGS lies in its rapid identification of pathogens and clear guidance for the treatment of severe infections. However, in clinical practice, the use of a new diagnostic method and broad-spectrum antibiotics is generally avoided, thus limiting the ability to select appropriate antibiotics to findings from basic culture and susceptibility tests.

For patients with liver abscesses caused by hvKP, which are not easily diagnosed clinically, mNGS can rapidly identify the pathogen and analyze drug resistance/virulence genes within the range of accessibility. This aids the timely adjustment of treatment, curbs bacterial drug resistance, realizes the rational use of antibiotics, and reduces the economic and social burden of infectious diseases.

Ethics approval and consent to participate

The study has been approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University. Written informed consent was obtained from the patient and her family for the publication of this case report and accompanying images.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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