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CASE REPORT

Invasive Liver Abscess Syndrome Caused by Carbapenem-Resistant Hypervirulent Klebsiella Pneumoniae: a Case Report

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SUMMARY

Background: **Carbapenem-resistant hypervirulent Klebsiella pneumoniae (CR-hvKP) causes fewer infections, and it causes invasive Klebsiella pneumoniae liver abscess syndrome (IKLAS) that can lead to a poor prognosis for patients.**
Methods: **Next-generation sequencing (NGS), sputum culture, drug sensitivity test, and other examination methods can detect the specific situation of pathogens in advance.**
Results: **The patient was determined to have CR-hvKP infection after NGS, sputum culture, and drug sensitivity test, and improved after treatment.**
Conclusions: **When antibiotics are applied in the presence of infection but symptoms do not improve, relevant laboratory or other tests should be performed promptly, and the selection of appropriate antibiotics may improve the survival rate of patients.**
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KEYWORDS

carbapenem-resistant hypervirulent Klebsiella pneumoniae, invasive Klebsiella pneumoniae liver abscess syndrome, next generation sequencing, polymyxin

CASE REPORT

It is not uncommon for Klebsiella pneumoniae to cause infections in daily life as part of the normal flora that colonizes the body. There is a specific type of Klebsiella pneumoniae, i.e., hypervirulent Klebsiella pneumoniae (hvKP), where patients are most likely to develop liver abscesses without biliary tract disease, and if liver abscesses are accompanied by extrahepatic migratory foci of infection such as lung abscess, bacteremia, fasciitis, endophthalmitis, etc., it is called IKLAS [1,2]. Usually, hvKP is pathogenic but sensitive to drugs, but with the massive use of carbapenems in anti-infective therapy, hvKP gradually became resistant to carbapenem antibiotics. It became a type of Klebsiella pneumoniae that is both resistant and highly virulent, posing a new and great challenge to anti-infective therapy worldwide [3,

4]. By reporting this case and analyzing the literature, we aim to remind medical personnel that in clinical work, if they encounter Klebsiella pneumoniae infection, they must consider early whether the strain is both resistant and highly virulent. They need to pay attention to the clinical manifestations and examination test results of the patient, pay attention to the presence of serious migratory infection, give the patient appropriate treatment promptly, reduce the risk of death, and improve the patient's prognosis by providing timely and appropriate treatment to reduce the risk of death and improve the prognosis and quality of life.

A 40-year-old male presented with dyspnea after drinking alcohol and vomiting, with cough, sputum, and intermittent chest pain, which did not improve after he took his medication. On admission, his chest CT suggested inflammatory lesions in both lungs (Figure 1A), and laboratory results suggested normal white blood cell (WBC) count, platelet (PLT) 25 x 10^9/L, procalcitonin (PCT) 34.39 ng/mL, partial pressure of oxygen (PO_2) 84 mmHg, and oxygenation index (PO_2/FIO_2) 289.66 mmHg, with a preliminary diagnosis of severe pneumonia and severe sepsis. We gave the patient a combination therapy of Biapenem (0.3 g, 3/day) combined with Moxifloxacin (0.4 g, 1/day). However, the patient's condition progressed. He was in a hypoxic state with markedly elevated inflammatory indicators. Examination of the chest and abdominal CT suggested unresolved inflammatory lung lesions and the presence of a hepatic cyst was considered in the left lobe of the liver (Figure 2A). He was then transferred to the Department of Critical Care Medicine for tracheal intubation and mechanical ventilation. Alveolar lavage fluid pathogenic microbiological examination suggested Gram-negative bacilli, and NGS results of sputum pathogens suggested Klebsiella pneumoniae. In addition, multiple previous sputum cultures showed Klebsiella pneumoniae and Candida albicans. We added appropriate antifungal therapy, but his condition did not improve significantly and he still had fever and thrombocytopenia. Then he was transferred to Beijing for further treatment. Combined with the results of NGS in our hospital, he was given comprehensive treatment with meropenem (1 g, 3/day) combined with fluconazole (200 mg, 1/day). Relevant laboratory test results: WBC 12.97 x 10^9/L, high sensitivity C-reactive protein (hsCRP) 152.07 mg/L, PCT 2.40 ng/mL; increased lumbar puncture pressure; routine cerebrospinal fluid indicated the increased total number of white blood cells; Klebsiella pneumoniae, only sensitive to polymyxin, tigecycline, co-trimoxazole, minocycline, and amikacin; chest and abdominal CT showed multiple lung abscesses (Figure 1B), left liver lobe low-density shadows are larger than before. Based on the results of the drug sensitivity test, the medication was adjusted to sulfamethoxazole (2 tablets, 2/day), polymyxin B (50 mg, 2/day), and amikacin (0.4 g, 2/day). About 10 days after treatment, chest CT showed that the lung lesion was better than before, and liver ultrasound showed that liver abscess was not excluded, and brain MRI (Figure 3A) suggested that brain abscess was not excluded. The patient was then referred to our hospital again, where he still had coughing and sputum, occasional dyspnea, and markedly darkened skin. CT of the chest and abdomen and MRI of the brain showed better lesions in both lungs than before (Figure 1C), an enlarged liver abscess (Figure 2B), and no significant change in the brain abscess compared with the previous MRI findings (Figure 3B). We gave the patient a combination of tigecycline (50 mg, 2/day), etimicin (100 mL, 2/day), and cotrimoxazole (0.8 g, 2/day) based on the results of the drug sensitivity test at the Beijing hospital. After 15 days of treatment, a repeat chest and abdominal CT showed that the lung lesions continued to improve and the liver abscess was reduced compared to the previous one (Figure 2C). He was discharged after a total of 46 days of hospitalization. A repeat chest CT half a month after his discharge showed that the inflammatory lesions in both lungs were better than before and that the lung abscesses had largely resolved (Figure 1D), and his condition had improved significantly.

DISCUSSION

This paper reports a case of a middle-aged male in good health who was diagnosed with CR-hvKP infection resulting in multiple systemic abscesses. However, the initial admission of the patient with a CURB-65 score of 1 for community-acquired pneumonia, with a low risk of death, did not correspond to the patient's actual condition. The CURB-65 scoring criteria specify a score of ≥ 3 as severe pneumonia, and one of the scores has a cutoff point based on age 65 years, which can lead to an underestimation of the patient's true condition in patients < 65 years. Therefore, the accuracy of the assessment of patients can be improved by combining other scores or inflammatory indicators. Diabetes and Asian populations have been reported as risk factors for hvKP infection [5]. One study found that patients with poor glycemic control were more likely to develop a metastatic infection with liver abscesses [6]. This patient, with a history of type 2 diabetes and community-acquired severe pneumonia combined with IKLAS, developed multiple abscesses in a short period and was in serious condition with the possibility of losing his life at any time, as described in the above report. Therefore, it is important to pay close attention to the patient's glycemic control when treating diabetic patients with hvKP infection. With the widespread use of carbapenem antibiotics, the number of patients with CRKP infections is on the rise, and studies have pointed out that the mechanisms of CRKP resistance include carbapenemase production, deletion of extracellular membrane pore proteins as well as reduced expression, changes in target site proteins and altered mechanisms of active cellular exocytosis, among which the most important mechanism is carbapenemase production [7]. Previous studies have generally concluded that high drug resistance and high viru-

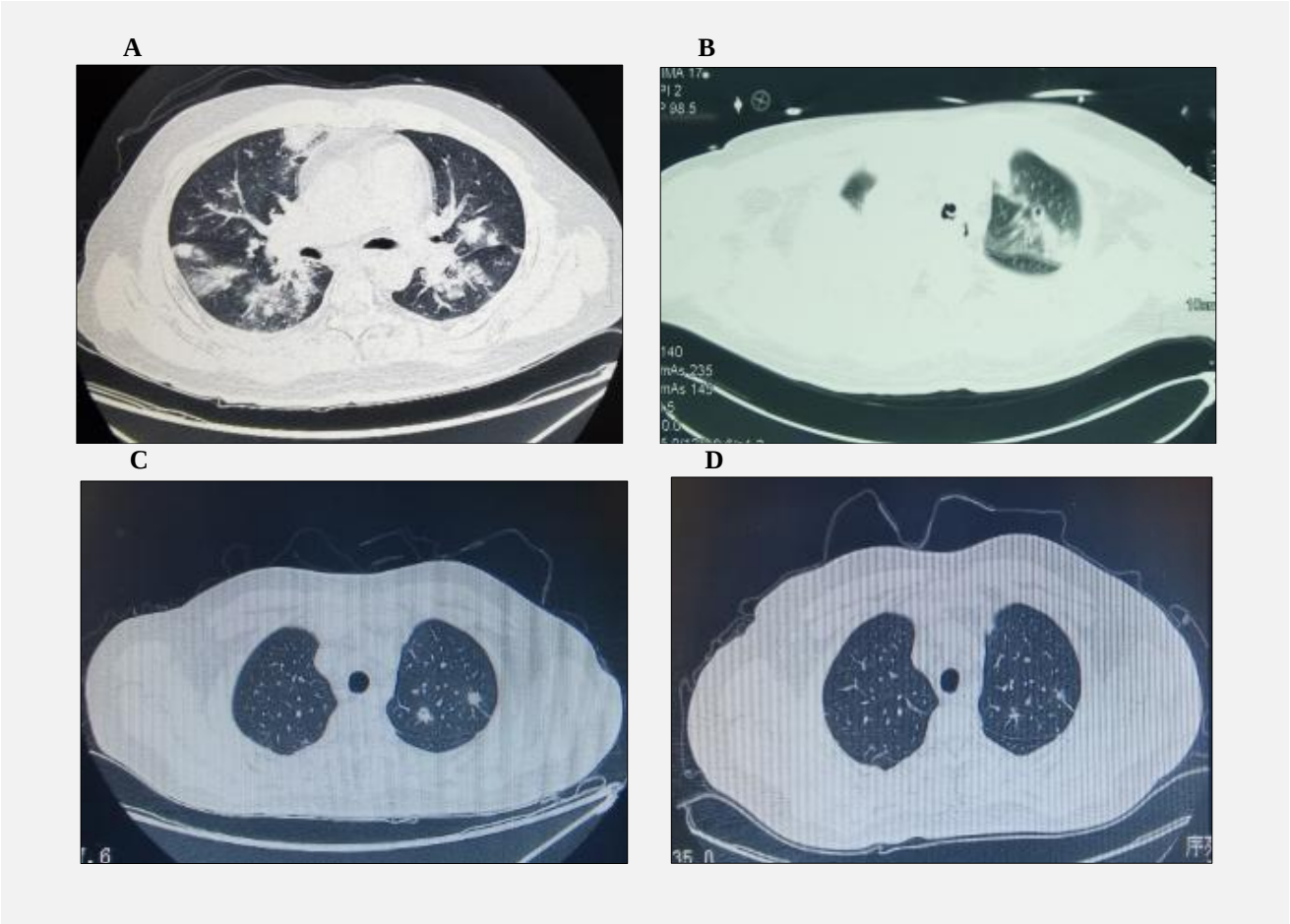

Figure 1. Figure A showed multiple patchy, hyperdense shadows and nodular hyperdense shadows in both lungs at admission. Figure B showed multiple irregular thick-walled cavities and patchy consolidation in bilateral lung fields with aggravation. Figure C showed that the irregular thick-walled cavities were smaller than before after treatment. Figure D was the re-examination image after discharge.

lence of Klebsiella pneumoniae do not coexist. However, due to the continuous evolution of bacteria, CR-hvKP gradually appeared in various reports, and studies suggested that the following pathways may exist for the production of CR-hvKP: 1. CRKP may acquire the virulence gene plasmids carried by hvKP; 2. hvKP may acquire the resistance plasmids carried by CRKP; 3. mutations in the hvKP extracellular membrane pore protein, etc. [8]. Combined with the progression of the patient's disease and IKLAS, etc., this patient was judged to have a CR-hvKP infection. NGS, as a more cutting-edge pathogen detection method, differs from previous traditional tests in that it can directly detect all nucleic acid fragments in extracted specimens (e.g., sputum, blood, alveolar lavage fluid, etc.), thereby obtaining genetic information about the pathogens in the specimens and thus providing rapid, objective, and accurate detection of pathogens [9,10]. We quickly obtained specific pathogenic microorganisms by subjecting the patient's sputum to NGS testing, which in turn guided targeted drug administration. However, this patient was unique in that even though the infection was known to be Klebsiella pneumoniae, the drug resistance of the organism prevented us from administering medication; therefore, NGS alone did not allow us to accurately determine whether the medication was effective in some cases, and further guidance of treatment with drug sensitivity was required. No definitive clinical treatment regimen has been proposed for CR-hvKP infections, and the results of a meta-analysis by Effah CY et al. suggested a higher mortality rate in patients treated with single agents than in those treated with combination therapy for CR-hvKP [11]. Reports indicate that polymyxins, tigecycline, and certain aminoglycosides can be used to treat carbapenem-resistant Enterobacteriaceae, and these antibiotics are considered to be the last line of defense in controlling infections caused by such bacteria [12]. The patient was infected with CR-hvKP which was multi-resistant to clinically used antimicrobial drugs but sensitive to polymyxin, tigecycline, and other

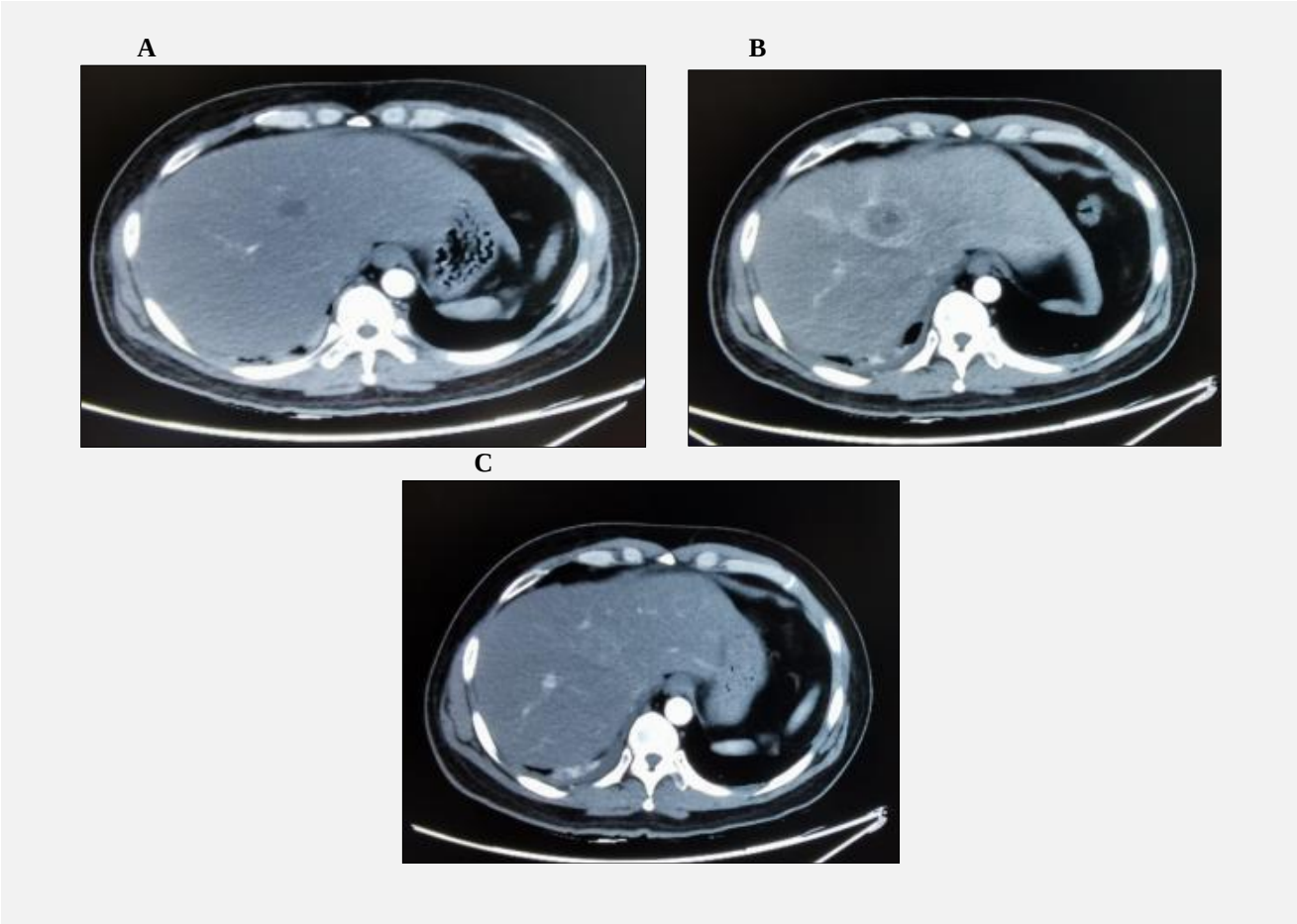

Figure 2. The initial diameter of the liver abscess in Figure A was 1.9 cm, the diameter Figure B was 2.6 cm, and Figure C showed the absorption of the liver abscess after the selection of appropriate antibiotics, with a diameter of 2.2 cm.

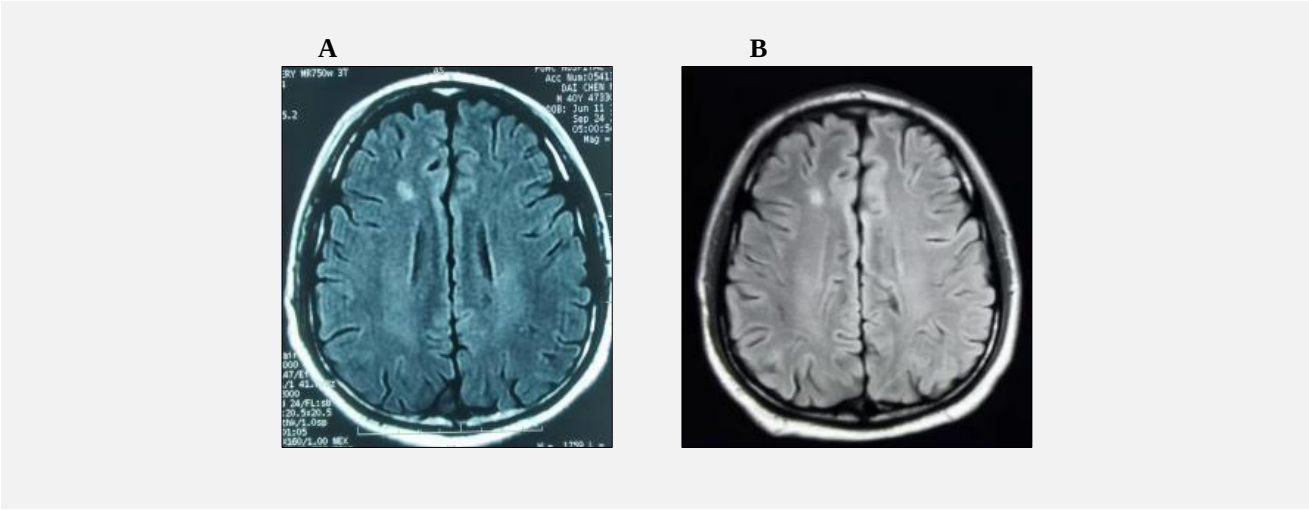

Figure 3. Figure A showed the results of the first MRI of the brain, and Figure B showed the results of the re-examination, with no significant changes compared to Figure A.

drugs, therefore, combined with the results of the drug sensitivity test, we gave the above-mentioned drugs. Polymyxins are mostly used to treat infections with Gram-negative bacteria, but their use was once restricted in the clinic because of nephrotoxicity and neurotoxicity. With the increased detection rate of carbapenem-resistant Gram-negative bacteria, polymyxins have reappeared in our field [13]. While using polymyxin, we should pay close attention to the side effects of polymyxin, of which nephrotoxicity is the most common. Therefore, we need to monitor renal function, especially in the first 5 days of treatment, which can identify patients who may develop nephrotoxicity [14]. It has been reported in the literature that polymyxin B can also cause skin pigmentation, but the patient only showed skin color deepening without other discomfort symptoms; so, there was no need to adjust the drug dosage [15]. In this case, when the patient was transferred to our hospital from Beijing, the skin color was significantly deepened, mainly the face and neck, and the extremities, and the adverse effects of polymyxin B were considered. To prevent acute kidney injury and resistance to polymyxin B, which could affect the patient's prognosis, we adjusted the drug to tigecycline, whose side effects are usually manifested as gastrointestinal reactions [16], but the appearance of pancreatitis has also been reported in some studies [17]. Therefore, during the use of tigecycline, we need to keep an eye on the patient for these symptoms and monitor the pancreatic enzymes to adjust the dose and type of drug promptly. This treatment reminded us to consider whether we could advance the treatment with polymyxin once the patient's condition did not improve with the application of carbapenem antibiotics to control the serious infection and save lives first before changing to other drugs for follow-up treatment. The patient's condition improved after adjusting the medication, which proved that the treatment was effective. Since CR-hvKP is more likely to cause nosocomial infections, hand hygiene is the most effective way to reduce the rate of nosocomial cross-infection, so we should always pay attention to maintaining hand hygiene in our daily work [18].

CONCLUSION

CR-hvKP infections are relatively rare in clinical work, and the IKLAS they cause can easily delay diagnosis and treatment, which may have serious consequences. Sputum culture and drug-sensitivity testing are of great value in the treatment process, and NGS testing can be performed if available to further improve the pathogen detection rate and make adequate preparation for early treatment. This case reminds clinical workers that the emergence of drug-resistant bacteria leads to less controllable symptoms of infection, increased morbidity and mortality, and reduced quality of life of patients. Therefore, we should have a sufficient understanding of the use of antibiotics in our daily work, and use them correctly and regularly to avoid the emergence of more and more drug-resistant bacteria.

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Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

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