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Severe intracranial infection caused by community-acquired hypervirulent *Klebsiella pneumoniae*: A case report

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ABSTRACT

Hypervirulent *Klebsiella pneumoniae* (HvKp) is a dynamic pathotype characterized by heightened mucoviscosity and virulence, typically afflicting individuals within the community, who commonly exhibit good health. We presented a case study of a 65-year-old male with diabetes who developed community acquired pneumonia, septic shock, and intracranial infection. The diagnosis was established through cranial magnetic resonance imaging (MRI), typical clinical presentation, and biological culture. The presence of HvKp infection was confirmed by cerebrospinal fluid (CSF) metagenomic next-generation sequencing (mNGS) and blood culture. Treatment consisted of Amikacin 0.8 g qd in combination with meropenem 2.0 g q8h, based on drug sensitivity testing. The patient experienced symptom relief, with the CSF becoming clear and the elimination of the pathogen, ultimately resulting in a successful recovery. The clinical data, diagnosis, and treatment of the patient were documented, and a review of the literature was conducted to offer clinical guidance regarding the intracranial infection resulting from community-acquired HvKp.

Introduction

Klebsiella pneumoniae, a bacterium belonging to the Enterobacteriaceae family, is characterized as a Gram-negative, non-motile capsulated organism that produces gas [1]. It can be further classified into two distinct types based on virulence characteristics: classical *Klebsiella pneumoniae* (cKP) and Hypervirulent *Klebsiella pneumoniae* (HvKP). cKP primarily affects immunocompromised individuals admitted to the intensive care unit, including those with conditions such as Acquired Immune Deficiency Syndrome (AIDS) or recipients of organ transplants [2]. In contrast to cKP, HvKP possesses the capacity to induce community-acquired infections, including liver abscess, endophthalmitis, and meningitis, in individuals without underlying health conditions [3]. In this report, we present and analyze a case involving a 65-year-old male patient with diabetes who experienced fever, community-acquired pneumonia, septic shock, and severe intracranial infection attributed to HvKP.

Case report

A 65-year-old male residing in Ningbo City, located in the southeastern region of China, with a medical history of diabetes, was admitted to the hospital due to fever (39.1 ℃), headache, dizziness, and cough persisting for a duration of 5 days. The patient has experienced poorly managed diabetes mellitus for over 20 years. Cranial MRI results exhibited the presence of "multiple abnormal signals" in various regions including the bilateral temporal lobes, hippocampus, sylvian cistern, bilateral cerebellum, and fourth ventricle, which were indicative of encephalitis (Fig. 1A and B). Additionally, a chest CT scan revealed the existence of multiple lung inflammations, pleural adhesions, and pleural effusion in both lungs (Fig. 1C and D). The C-reactive protein (CRP) level was measured at 340.0 mg/L, suggesting a severe infection. The patient exhibited symptoms of neck stiffness and was in a deep coma, as indicated by a Glasgow Coma Scale score of 5. Additionally, the patient experienced weakness, nausea, repeated vomiting, and persistent coma, necessitating admission to the intensive care unit (ICU).

On the first day of ICU admission, a lumbar puncture was conducted, and cerebrospinal fluid (CSF) analysis was performed (Fig. 2). The

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cerebrospinal fluid (CSF) exhibited cloudiness and had a white blood cell count of 3437/μL (85 % polymorpholeukocytes), a glucose level of 0.6 mmol/L (with a corresponding blood glucose level of 10.4 mmol/L), and a microprotein level of 164.4 mg/dL (within the normal range of 15.0–45.0 mg/dL). Pan's test yielded a result of (+++), indicating a significant presence of certain substances. Although the pressure was not measured, the fluid was described as forcefully expelled. On the second day in the intensive care unit (ICU), the CSF sample was identified as HvKP through metagenomic next-generation sequencing (mNGS), which revealed the presence of virulence factors including *rmpA, iutA, iucA, iucB, iucC, iucD, iroB, iroC, iroD*, and *fimH*. On the third day in the ICU, the CSF routine, bronchoalveolar lavage fluid (BALF), and two sets of blood cultures all indicated an HvKP infection (Fig. 3). The drug sensitivity analysis revealed resistance to piperacillin, levofloxacin, and other antibiotics, while exhibiting sensitivity to amikacin. The patient was diagnosed with a severe intracranial infection caused by the community-acquired HvKP pathogen.

In addition to the original antibiotic treatment of meropenem 2.0 g q8h, intravenous amikacin (0.8 g qd) was prescribed based on drug sensitivity results from CSF, blood, and BALF specimens. Following the initiation of amikacin therapy, the patient's fever subsided and vital signs stabilized. Throughout this period, close monitoring of the patient's blood sugar levels was conducted, ensuring they remained within the normal range of 6.0–10.0 mmol/L. On the 9th day of ICU admission, a repeat CSF analysis was performed. The cerebrospinal fluid (CSF) exhibited clarity and colorlessness, with no presence of microorganisms observed on the Gram-stained smear or cultivated from routine CSF culture. On the 11th day of intensive care unit (ICU) admission, the patient regained consciousness and the endotracheal tube was

Fig. 2. CSF exhibited cloudiness, with Pan's test showing a strong positive result (+++). Additionally, the glucose level was below the limit of detection, the microprotein level was measured at 164.4 mg/dL (within the normal range of 15.0–45.0 mg/dL), and there were 3437 white blood cells (WBC)/mm3 present, with 85 % of these cells being polymorphonuclear (PMN) cells.

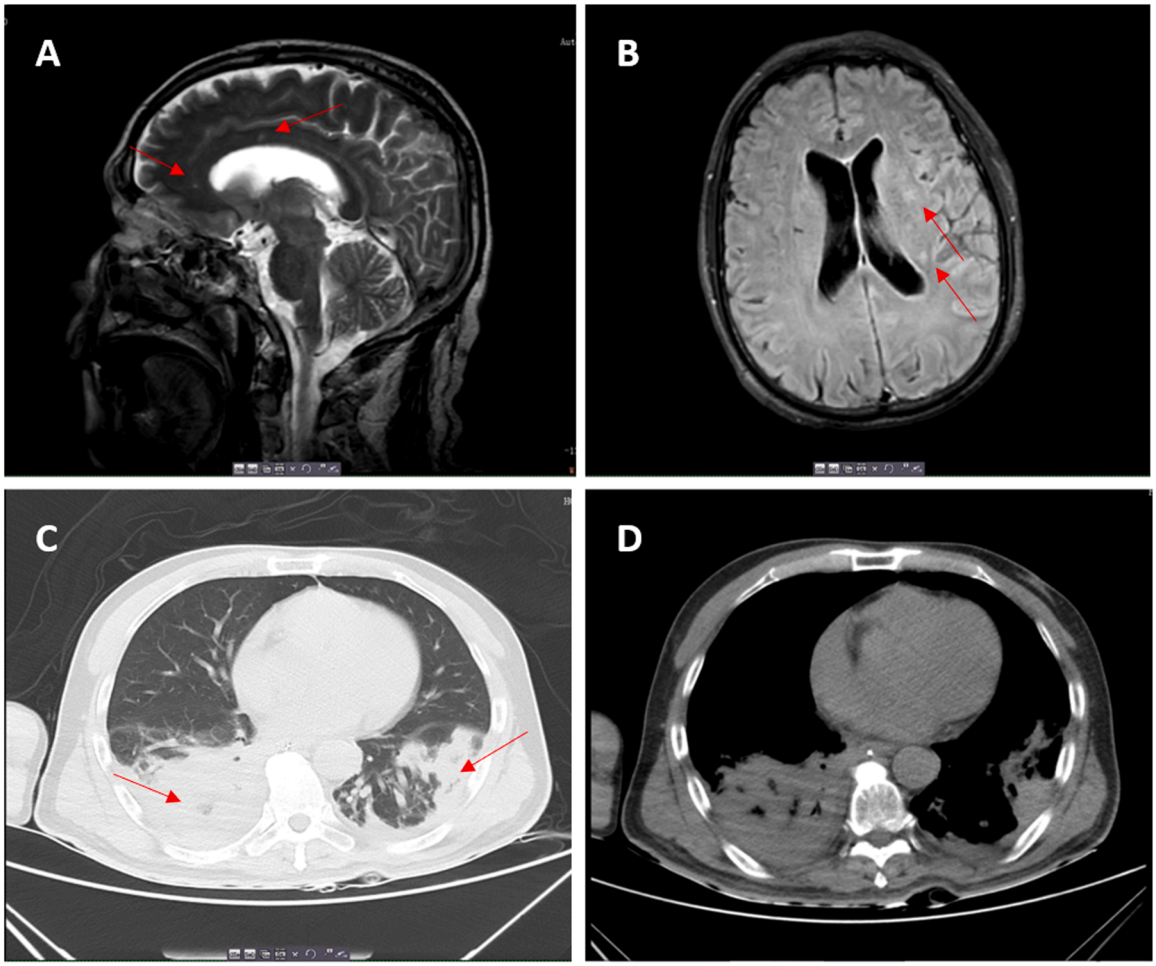

Fig. 1. Cranial MRI revealed the presence of numerous abnormal signals in various regions including the bilateral temporal lobes, hippocampus, sylvian cistern, bilateral cerebellum, and fourth ventricle, indicating a potential case of encephalitis (A and B). Additionally, a chest CT scan exhibited the presence of multiple lung inflammations, pleural adhesions, and pleural effusion (C and D).

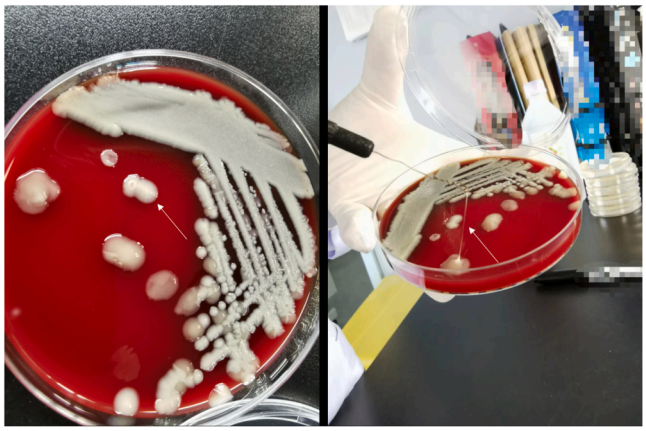

Fig. 3. The presence of HvKP infection was confirmed through blood cultures. The colonies observed were accompanied by a significant amount of mucus, and the wire drawing experiment yielded a preliminary positive result.

subsequently extubated. The duration of antimicrobial treatment for Meropenem was 21 days, while the duration of treatment for Amikacin was 14 days. Ultimately, the patient was discharged without any complications 10 days after extubation.

Discussion

Klebsiella pneumoniae was initially discovered by Friedlander in 1882 and is a Gram-negative bacterium that is widely distributed in terrestrial and aquatic environments. This bacterium falls under the gamma subdivision of the class Proteobacteria and demonstrates considerable genetic similarity to other genera within the Enterobacteriaceae family, which is known to cause pulmonary infections such as lobar pneumonia [1]. HvKP represents a novel variant of *Klebsiella pneumoniae*. In the 1980 s, a distinctive occurrence of liver abscess accompanied by endophthalmitis caused by *Klebsiella pneumoniae* was documented in Taiwan, marking the first report of such a case. This particular strain of *Klebsiella pneumoniae* was subsequently identified as hypervirulent HvKP [4]. Diverging from the classical variant of *Klebsiella pneumoniae* (cKP), these novel variants demonstrate heightened virulence characteristics, characterized by increased mucoviscosity and hypervirulence. Consequently, they are capable of inducing severe community-acquired infections and metastatic dissemination in immunocompetent individuals [3].

The epidemiology of HvKp infection is still not well comprehended in terms of its source and transmission route. However, it is believed that intestinal colonization plays a crucial role in the development of infection. Susceptible factors for HvKp infection include diabetes mellitus, male gender, and Asian ethnicity [5]. Despite the absence of prior immunosuppressive therapy, known malignancies, or risk factors for immunodeficiency, the patient in question had poorly managed diabetes mellitus for over two decades. This individual exhibited all three risk factors commonly found in East Asian diabetic men.

HvKP infections exhibit a higher prevalence in the Asian Pacific Rim, although they are also being observed globally. Furthermore, HvKp demonstrates the capability of metastatic dissemination and induces infections in various anatomical locations. HvKP is capable of instigating *Klebsiella pneumoniae* invasive syndrome (KPIS) through hematogenous dissemination, leading to the development of brain abscess, suppurative meningitis, endophthalmitis, and necrotizing fasciitis [6]. The patient presented with HvKP septicemia accompanied by invasive pulmonary and severe intracranial infection, satisfying the diagnostic criteria for KPIS. Given the highly invasive and aggressive clinical features of HvKP, the patient rapidly manifested symptoms such as high fever (39.1 °C), sepsis, respiratory failure, and ultimately fell into a comatose state.

The urgent requirement for a prompt and precise diagnostic approach arises from the remarkably virulent nature of HvKP, which would greatly assist in guiding and facilitating the management and therapy of HvKP-infected patients. Presently, the absence of efficient techniques to distinguish between classical cKP and HvKP strains frequently leads to delays in diagnosing and treating HvKP infections. Clinical laboratories currently lack the ability to distinguish between cKp and HvKp. However, recent advancements have demonstrated that certain biomarkers and quantitative siderophore production can be utilized to predict HvKp strains. These biomarkers include capsules, siderophores, lipopolysaccharides, fimbriae, outer membrane proteins, and type 6 secretion system. In the case at hand, the analysis of cerebrospinal fluid using metagenomic next-generation sequencing (mNGS) revealed the presence of several virulence factors in HvKP, namely capsule (rmpA), siderophores (*iutA, iucA, iucB, iucC, iucD, iroB, iroC, iroD*), and fimbriae (*fimH*). Therefore, it is recommended to employ mNGS or virulence-associated genomics testing when appropriate conditions permit.

The etiology of intracranial infection is typically bacterial, with staphylococci and streptococci being the most prevalent pathogens acquired within the community. *Klebsiella pneumoniae*, an opportunistic pathogen, is particularly significant in causing both community and hospital-acquired infections, accounting for 10 % of intracranial infections in Taiwan [7]. The administration of appropriate initial antibiotics is a crucial prognostic factor in adult bacterial meningitis [8]. The majority of HvKp isolates exhibit resistance solely to ampicillin, while remaining susceptible to aminoglycosides and cephalosporins [9]. In recent times, there has been a growing prevalence of carbapenem-resistant HvKp strains that exhibit heightened resistance to antimicrobial agents due to the acquisition, accumulation, and dissemination of resistant genes [10]. The limited efficacy of antimicrobial therapy against carbapenem-resistant HvKp poses significant challenges to both global public health and clinical interventions. However, it is fortunately that the HvKp strains under consideration in this instance retain susceptibility to beta-lactam antibiotics, encompassing those with beta-lactamase inhibitors and carbapenems. Sensitivity antibiotics were administered to eradicate HvKp, resulting in the clearance of the cerebrospinal fluid (CSF) and the absence of microorganisms on the Gram-stained smear or in the CSF culture. The treatment duration for intracranial infections, such as meropenem and amikacin, often exceeds the conventional timeframe of 14–21 days. The evaluation of anti-infection strategies heavily relies on the absence of abnormalities in cerebrospinal fluid analysis. In recent times, there has been a growing utilization of adjunctive intrathecal or intraventricular aminoglycoside therapy, particularly when cultures fail to clear by the fourth or fifth day. However, it is imperative to acknowledge that the unique attributes of each patient exert a substantial influence on determining the precise duration of treatment, thereby necessitating an individualized approach. The establishment of recommended treatment duration may entail the systematic analysis of extensive sample sizes.

This case report highlights a diabetic patient who experienced a severe intracranial infection caused by community-acquired HvKp. The patient exhibited signs of HvKP septicemia, accompanied by invasive pulmonary and severe intracranial infection, consistent with KPIS. Successful treatment was achieved through the administration of appropriate sensitivity antibiotics, leading to the patient's eventual recovery. HvKp demonstrates heightened virulence characteristics, capable of inducing severe and potentially lethal infections in immunocompetent hosts. This instance serves as a prompt for medical practitioners to consider the potential occurrence of central nervous system or systemic infections caused by HvKp under appropriate circumstances.

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CRediT authorship contribution statement

Gongjie Ye contributes to the manuscript writing; Lei Yang participates in data analysis and interpretation; Zhouzhou Dong contributes to the critical review of the intellectual content of the article.

Competing interests

The authors declare that they have no competing interests.

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Declarations

None.

Ethics approval and consent to participate

The study is supported by the patient's wife and she has signed informed consent.

Consent for publication

Not applicable.

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