Fatal Community-Acquired Bloodstream Infection Caused By Klebsiella Varicola: A Case Report

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Short Report

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Abstract

Background Klebsiella pneumoniae infection leads to significant concerns because of its varied manifestation and resultant mortality. While recent genetic structure analysis reveals that the higher virulence and mortality could be from its subspecies rather than Klebsiella pneumoniae. However, which is often misdiagnosed and underestimated in clinic because it's difficult to distinguish Klebsiella pneumoniae from its subspecies using classic clinical examinations. This case study is the first in clinic to report the fast and fatal effect of Klebsiella subspecies, and serve as reference for doctors diagnosing similar diseases.

Case presentation A 52-years male patient was admitted to hospital due to unknown high fever. All examinations excluded the viruses, fungi, mycoplasma/chlamydia and parasitic infection. Classic bacterial culture revealed the klebsiella pneumonia, however sensitive antibacterial adheres to drug susceptibility results failed to improve patient's symptoms. His condition worsened and rapidly entered sepsis and subsequent sepsis shock, died within 72 hours of symptom onset. The PMseq-DNA Pro High throughput gene detection was acquired on second day after death revealing the mixed infection of klebsiella variicola and klebsiella pneumoniae. Clinic evidences suggested that Klebsiella variicola rather than klebsiella pneumoniae contributed to patient's poor prognosis.

Conclusions: This is the first case reported that patient died from klebsiella subspecies infection within short period of time. Which suggests that we should be alert to the clinical hazards and fatal effect of klebsiella subspecies. Classic method is limited in guiding the anti-infection therapy for complex cases, early genetic detection should be recommended in the diagnosis and management of complex infection.

Introduction

The klebsiella causing infection is a well-known type of infection with its high incidence and mortality. It causes outbreaks of nosocomial infections and even drug resistance, and can lead to infection in the community among health-care patients or people with underlying immunodeficiency [1]. Based on genetic analysis, the klebsiella pneumoniae (K. pneumoniae) contains three polygroups: klebsiella pneumoniae (KpI), K.quasipneumoniae (KpII) and K.variicola(KpIII) [2]. KpI is the most frequent group, followed by KpIII and KpII [1, 3]. Klebsiella is usually defined as classic klebsiella (Ck) and hypervirulent klebsiella (Hvkp) according to its invasiveness or virulence, while subspecies of Klebsiella (KpII and KpIII) present the higher virulence [3]. Currently, approximately 20% of human isolates assumed to be K. pneumoniae are in fact K. variicola/ or K. quasipneumoniae [1]. It's difficult to distinguish KpI from KpII and KpIII using classic clinical laboratory examinations [4]. Therefore, clinical hazards and importance of KpII and KpIII is often overlooked.

Case Presentation
A 52-year old male presented with unexplained high fever, bellyache and headache for one day, and subsequently was admitted to Intensive Care Unit with diarrhea, and confusion. He had no medical history other than 5 years of history of type 2 diabetes and 7 years of history of Gout. On admission. Physical examinations revealed the temperature of 40°C and without obvious abnormal signs.
Laboratory examinations revealed the slightly deteriorated hepatorenal function, clotting function and increased inflammatory parameters (Table 1–3). Chest radiograph showed the manifestations of inflammatory response, while other imaging results showed no obvious abnormalities (Fig. 1–3). Doctors excluded the diagnosis of infection of virus, nmycobacteria, mycoplasma/chlamydia and autoimmune diseases by laboratory (Table 4). Traditional bacteria culture of blood sample showed the bacterial of klebsiella pneumonia that are sensitive to almost all antibiotics (Table 5). Treatments included anti-inflammation (intravenous Meropenem 1gram per 6hours + intravenous caspofungin 70 milligrams/initial dose). However, patient's condition rapidly deteriorated within hours of admission with decreased blood pressure and reduced oxygen saturation. Life support therapies including mechanical ventilation and vasoactive drugs could not improve patient’s condition. He suffered cardiac arrest on second day of admission, and was declared clinically death after several rescue efforts. The PMseq-DNA Pro High throughput gene detection was conducted on secondary day, and result was acquired on fourth day revealing the infection of klebsiella pneumoniae and klebsiella variicola (Fig. 4). The bone marrow biopsy supported the severe bacterial infection (Fig. 5).

| Items      | Results(1st) | Reference range |
|------------|--------------|-----------------|
| TBIL(µmol/L) | 19.4         | 3.6–20.5        |
| TP(µmol/L)  | 49.8         | 65–85           |
| ALB(g/L)    | 31.4         | 40–55           |
| ALT(U/L)    | 156          | 9–50            |
| AST(U/L)    | 182          | 15–40           |
| SCREA(µmol/L) | 160         | 57–97           |
| UREA(µmol/L)| 12.40        | 3.1–8           |
| GLU(mmol/L) | 13.89        | 3.9–6.1         |
| K+(mmol/L)  | 3.22         | 3.5–5.5         |
| UA(µmol/L)  | 591          | 210–420         |

On admission, the blood sample was collected, Liver and renal function was examined. Results were acquired about 2 hours after sample collection.
### Table 2
The clotting function parameters tested after transferring

| Items       | Results | Reference range |
|-------------|---------|-----------------|
| 3P          | Negative| Negative        |
| D-D (µ g/ml)| 60.75↑  | 0 ~ 1           |
| FDP (µ g/ml)| 128.5↑  | 0 ~ 5           |
| PT (sec)    | 18.3↑   | 9.2 ~ 12.2      |
| INR         | 1.59↑   | 0.8 ~ 1.2       |
| APTT (sec)  | 67.6↑   | 21.1 ~ 36.5     |
| TT (sec)    | 23.4↑   | 14 ~ 21         |
| Fbg (g/l)   | 22.58   | 1.8 ~ 3.5       |

On admission, the blood sample was collected, Clotting was examined. Results were acquired about 1 hours after sample collection.

### Table 3: The inflammatory parameters results on admission

| Items       | Results | Reference range |
|-------------|---------|-----------------|
| WBC (x10⁹) | 1.20    | 3.5-10          |
| #NEUT (x10⁹)| 0.63   | 1.8-6.3         |
| %NEUT      | 52.5    | 40-75           |
| MONO (x10⁹) | 0.05  | 0.1-0.6         |
| %MONO      | 4.2     | 3-10            |
| #LYMBP (x10⁹) | 0.39 | 1.1-3.2         |
| %LYMBP    | 32.5    | 20-50           |
| RBC (x1012)| 1.83   | 3.5-5.5         |
| HGB (g/L)  | 52.0    | 114-163         |
| %HCT      | 15.60   | 35-50           |
| PLT (x10⁹) | 10.0   | 125-350         |
| CRP mg/L   | 230.33  | 0-5             |
| PCT        | >100    | 0-0.046         |

On admission, the blood sample was collected, Blood routine including CRP, PCT was examined. Results were acquired about 1 hours after sample collection.
Table 4
Results related to Virus, mycobacteria, mycoplasma/ chlamydia and autoimmune disease.

| Items          | Results | Reference |
|---------------|---------|-----------|
| RSV-IGM       | Negative| Negative  |
| ADV-IGM       | Negative| Negative  |
| IFZA-IGM      | Negative| Negative  |
| IFZB-IGM      | Negative| Negative  |
| HPIVs-IGM     | Negative| Negative  |
| MP-IGM        | Negative| Negative  |
| CP-IGM        | Negative| Negative  |
| CBV-IGM       | Negative| Negative  |
| CAV-IGM       | Negative| Negative  |
| ECHO-IGM      | Negative| Negative  |
| LP-IGM        | Negative| Negative  |
| 2019-nCoV     | Negative| Negative  |
| EB-DNA (copies/ml) | < 5E + 2 | < 5E + 2 |
| EB-DNA        | Negative| Negative  |
| CMVDNA DL(copies/ml) | < 5E + 2 | < 5E + 2 |
| CMV DNA DX    | Negative| Negative  |

**t1**  
Test method: Blotting

|        | Results | Reference |
|--------|---------|-----------|
| A-PR3  | Negative| Negative  |
| A-MP0  | Negative| Negative  |
| A-GBM  | Negative| Negative  |

**t2**  
Test method: Fluorescence

|        | Results | Reference |
|--------|---------|-----------|
| cANCA  | Negative| Negative  |
| pANCA  | Negative| Negative  |

After patient admission, the blood sample was collected, parameters related to Virus, mycobacteria, mycoplasma/chlamydia and autoimmune disease were examined.
Table 5
Results of bacterial culture and drug sensitivity

| Specimen          | Blood                              |
|-------------------|------------------------------------|
| Equipment         | Phoenix100                         |
| Items             | Bacterial culture + Antimicrobial Susceptibility |
| Results           | Klebsiella Pneumoniae              |

| Antibiotics          | MIC | Results Interpretation | Breakpoints |
|----------------------|-----|------------------------|-------------|
| Cefotaxime           | ≤ 1 | S                      | S ≤ 1; R ≥ 4 |
| Cotrimoxazole        | ≤ 20| S                      | S ≤ 2/38; R ≥ 4/76 |
| Tigecycline          | ≤ 0.5| S                      |             |
| Levofoxacin          | ≤ 0.12| S                     | S ≤ 0.5; R ≥ 2 |
| amikacin             | ≤ 2 | S                      | S ≤ 16; R ≥ 64 |
| Imipenem             | ≤ 0.25| S                      | S ≤ 1; R ≥ 4 |
| Er Ertapenem         | ≤ 0.12| S                      | S ≤ 0.5; R ≥ 2 |
| Cefepime             | ≤ 0.12| S                      | S ≤ 2; R ≥ 16 |
| Ce Foperazone/sulbactam | ≤ 8 | S                      | S ≤ 16; R ≥ 64 |
| Ceftriazone          | ≤ 0.25| S                      | S ≤ 1; R ≥ 4 |
| Ceftazidime          | ≤ 0.12| S                      | S ≤ 4; R ≥ 16 |
| Cefoxitin            | ≤ 4 | S                      | S ≤ 8; R ≥ 32 |
| Cefuroxime axetil    | 4 | S                      |             |
| Cefuroxime           | 4 | S                      | S ≤ 4; R ≥ 32 |
| Piperacillin/Tatabatam | ≤ 4| S                      | S ≤ 16/4; R ≥ 128/4 |
| Amoxicillin/clavulanate | ≤ 2| S                      | S ≤ 8/4; R ≥ 32/16 |
| ESBL                 | Neg | -                      |

Blood sample was properly collected and examined following the standards of bacterial culture. Results of bacterial and antimicrobial susceptibility were acquired after 24 hours later.

Discussion And Conclusions
Klebsiella is a Gram-negative bacterium within the enterobacteriaceae family. It usually causes the opportunistic nosocomial infection or community-required infection among hospitalized patients or community people. Klebsiella mainly colonized in human gut but also has been isolated from other body surfaces such as hand, face, and skin, even from other sources including water, plants and soil [1, 5]. It contains several subspecies manifesting with varied clinical performance. Klebsiella pneumoniae subspecies infection has led to significant concerns because of its varied manifestation and resultant mortality [6].

Recent research revealed the diabetes is a significant risk factor for hypervirulent Klebsiella pneumoniae infection and for causing serious complications [7-9]. This patient’s medical history could contribute to his underlying immunodeficiency and was possibly responsible for fatal bloodstream infection. Although both klebsiella pneumoniae and klebsiella variicola were found from the blood sample, the klebsiella variicola could play the more viral role to patient’s prognosis, because all treatments targeting to klebsiella pneumoniae failed to improve patient’s condition. Moreover, klebsiella variicola associated with the more frequent cause of bloodstream infection and higher mortality [3, 4].

It is difficult to distinguish Klebsiella pneumoniae and its subspecies by classic method of bacterial culture, which may lead to misdiagnosis or delay diagnosis and treatment [4]. As shown in this case, Klebsiella pneumoniae was found in blood culture and was sensitive to antibiotics used in this case, but treatments did not respond well. Recent clinical observations showed tigecycline and polymyxin display higher rates of treatment success in hypervirulent klebsiella infection than other antibacterial drugs such as carbapenem [10], combination of treatments is preferred to monotherapy in cases of severe infections [11, 12]. Unfortunately, no treatments targeting klebsiella variicola infection were conducted because of the delayed result and the rapid progression of illness.

Klebsiella pneumoniae subspecies can bring the fatal influence to health-care patients. Currently, the clinical importance of Klebsiella subspecies is overlooked, whilst clinical lethal sepsis cases identified as Klebsiella pneumoniae infection should actually be its subspecies due to the limitation of clinical examination. This case alerts clinicians to raise awareness of Klebsiella subspecies infection, especially unexplained fever or other features among health-care people. Meanwhile, This case highlights the need to introduce genetic techniques into current clinical practices, especially in the early diagnosis of severe infections.

**Declarations**

**Ethics approval and consent to participate**

This report was conducted according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Guizhou Provincial People's Hospital.

**Consent for publication**
Written informed consent was obtained from the patient’s daughter for publication of this case report and any accompanying images.

**Availability of data and material**

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

We confirm that the manuscript has been approved by all authors listed in the manuscript. All authors declare that they have no competing interests.

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**Authors’ contributions**

Dali Long and Yuhui Wang completed the collection of clinical data. Jinlong Wang, Sijie Mu, Li Chen and Xianqing Shi contributed to the compilation of data and production of charts. Jianquan Li analyzed all data and wrote the manuscript.

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**Abbreviations**

Not applicable

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**Figures**
Figure 1

The Chest radiograph on admission After admission, chest radiograph was performed, results showed that the manifestations of bilateral lung inflammation: The fuzzy bilateral lung markings, multiple patchy and patchy hyperdense shadows.

Figure 2
The electrocardiogram on November 8, 2020 The electrocardiogram was performed after admission, results showed that Sinus tachycardia 140/min and mild change of T wave.

![Figure 3](image)

**Figure 3**

The result of Abdominal ultrasonography on admission The abdominal ultrasonography was conducted on admission. results showed that Gallbladder wall thickening, left renal cyst the sonograms of liver, pancreas, spleen and right kidney were normal

| Type | Genera          | Numbers of sequences | Species                  | Numbers of sequences |
|------|-----------------|----------------------|--------------------------|----------------------|
| G-   | Klebsiella      | 68405                | klebsiella pneumoniae    | 243747               |
|      |                 |                      | klebsiella variicola     | 543                  |

**Figure 4**

The PMseq-DNA Pro high throughput gene detection from blood sample To identify the pathogenic bacteria for bloodstream, the blood sample was collected on second day after admission. And the gene detection of blood sample was performed. Results showed that the bacterial type is the G-, bacterial genera is Klebsiella, and there are 68405 of sequences number. Also, results revealed that there are two species of klebsiella: klebsiella pneumoniae and klebsiella variicola, their sequence number are 243747 and 543 respectively.
Figure 5

The bone marrow biopsy result. The bone marrow biopsy was conducted on the secondary day after admission. Results were acquired after 48 hours after examination and showed there are a few scattered and unidentified cells and macrophages phagocytizing blood cells.