

The Clinical Characteristics, Imaging Findings, and Treatments for the Severe Infection of Klebsiella Pneumonia in ICU: A Case Series Report

Yuxi Wang, Yu Wang, Jiaying Wang, Cheng Xu, Jinggang Yu, Lili Zhou, Xiaoni Kang, Hepeng Fu and Yuxiang Zhang*

Department of Intensive Care Unit, 309th hospital of Chinese People of Liberation of Army, Beijing, China

***Corresponding author:** Yuxiang Zhang, Department of Intensive Care Unit, 309th hospital of Chinese People of Liberation of Army (PLA), No. 17 Heishanhu Road, Haidian District, Beijing 100091, China; Email: 15810550308@163.com

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ABSTRACT

Background: Klebsiella pneumoniae is an important pathogen that can cause community- and hospital-acquired infection in association with the characteristics of high mortality, hyper virulent and highly transmissible. The aim of the study was to elucidate the clinical characteristics, imaging features and treatments for the severe infections of Klebsiella pneumoniae.

Method: We reported a series of 4 classical cases, including 3 male patients and 1 female patient with the average 62.75 years old, to demonstrate the clinical characteristics, imaging findings and treatment for the lethal pathogen. Each case has its unique features, focusing on different aspects.

Case presentation: Case 1 briefly introduces the classical carbapenem sensitive Klebsiella pneumoniae (CSKP) induced severe pneumoniae. Case 2 presents a general picture of CSKP induced pyogenic liver abscess (CSKP-PLA). Case 3 is focused on the CRKP induced cholecystitis and the infection of biliary system. Uniquely, Case 4 describes a story of CRKP bloodstream infection (CRKP-BSI) after kidney transplantation (KTx).

Conclusions: *Klebsiella pneumoniae* can cause severe infection manifested in various clinical characteristics, including severe pneumoniae abscess, pyogenic liver abscess, cholecystitis, sepsis after renal transplantation and so on. Imaging features of the infection are diversified, playing a role in guiding physicians to detect the signs of the pathogen in the early stage of infection. Effective therapeutic approaches are mainly focused on the combined regimen associated with the surgical mini-invasive approaches in necessary. Strictly implementation of infection prevention and control policy (**IPC**) is the key to prevent the further spreading of the pathogen in the hospital settings and communities in the whole world.

Keywords: *Klebsiella pneumoniae*; Clinical characteristics; Imaging findings; Treatments

Abbreviations: **ALB:** Albumin; **ALT:** Alanine Aminotransferase; **AST:** Aspartate Aminotransferase; **BNP:** Brain Natriuretic Peptide; **BNP:** Brain Natriuretic Peptide; **BUN:** Blood Urea Nitrogen; **CPR:** Cardio-Pulmonary Resuscitation; **CRE:** Creatine; **CRKP:** Carbapenem Resistant *Klebsiella pneumoniae*; **CRKP-BSI:** Carbapenem Resistant *Klebsiella pneumoniae* Bloodstream Infection; **CRRT:** Continuous Renal Replacement Therapy; **CSKP:** Carbapenem Sensitive *Klebsiella pneumoniae*; **CSKP-PLA:** Carbapenem Sensitive *Klebsiella pneumoniae* Induced Pyrogenic Liver Abscess; **CT:** Computed Tomography; **DCD:** Donation after Cardiac Death; **Hb:** Hemoglobin; **ICU:** Intensive-Care-Unit; **IPC:** Infection Prevention and Control Policy; **KP:** *Klebsiella pneumoniae*; **KPC:** *Klebsiella pneumoniae* Carbapenemase; **KP-C:** *Klebsiella pneumoniae* induced Cholecystitis; **KTx:** Kidney Transplantation; **LVA:** Last Vacuum Aspiration; **MODS:** Multiorgan Dysfunction Syndrome; **N%:** Neutrophil; **PCT:** Procalcitonin; **PLA:** People of Liberation Army, Pyrogenic Liver Abscess; **PLT:** Platelet; **PTCD:** Percutaneous Transhepatic Cholangial Drainage; **PTD:** Percutaneous Transhepatic Drainage; **PTGBD:** Percutaneous Transhepatic Gallbladder Drainage; **SICU:** Surgical Intensive-Care-Unit; **SOT:** Solid Organ Transplant; **SPE-KPLA:** Septic Pulmonary Embolism caused by a *Klebsiella pneumoniae* Liver Abscess; **TBIL:** Total Bilirubin; **TNI:** Troponin I; **TP:** Total Protein; **VSD:** Vacuum Sealing Drainage; **WBC:** White Blood Cell

BACKGROUND

Klebsiella pneumoniae (**KP**) is an important gram-negative pathogen with capsule to resistant to environmental attacks, responsible for severe diseases such as septicemia, pneumonia, urinary tract infections, biliary systems infections, and soft tissue infections, associated with community- and hospital-acquired infections [1]. Based on the phenotypic characteristic, *Klebsiella pneumoniae* strains can be divided into two classes: the classical *Klebsiella pneumoniae* strains and the hypervirulent *Klebsiella pneumoniae* strains. Hypervirulent *Klebsiella pneumoniae* strains are usually sensitive to antibiotics, but can cause life-threatening community-acquired infections in young and healthy host, such as liver abscesses, pneumoniae, meningitis, and endophthalmitis, and therefore associated with high morbidity and mortality, with the ability to metastatically spread, an unusual feature for enteric Gram-negative bacilli in the non-immunocompromised hosts [2]. To date, the majority of the hypervirulent *Klebsiella pneumoniae* has been reported in Asian, raising the controversy of genetic predisposition vs. the geospecific strain acquisition [2].

Noticeably, among various infections caused by *Klebsiella pneumoniae*, *Klebsiella pneumoniae* induced pyogenic liver abscess (**KP-PLA**) has more been regarded as an emerging public health problem worldwide and is frequently diagnosed in patients with metabolic diseases and has a higher risk for septic metastatic infection, leading to sepsis even multiorgan dysfunction syndrome (**MODS**), with the in-hospital mortality 20% in KP-PLA and 21.4% in primary KP-PLA with metastatic infection, respectively [3]. In addition to the surgical approaches, antibiotic therapy and continuous renal replacement therapy (**CRRT**) are effective treatment for KP-PLA. Besides, *Klebsiella pneumoniae* induced cholecystitis (**KP-C**) is also a rare type of infection of the pathogen, few articles have reported. The surgical drainage from gallbladder to alleviate the severity in combination with the effective combinational antibiotic treatment is usually the effective therapeutic approach.

In recent years, many cases of the carbapenem resistant *Klebsiella pneumoniae* bloodstream infections (**CRKP-BSI**) after renal transplantation from donation after cardiac death (**DCD**) have been reported. Undoubtedly, kidney transplantation is considered the definitive treatment for end-stage kidney diseases with manifested survival benefits over dialysis [4]. With a limited donor pool and an expanding transplant waiting list, it's necessary to take advantage of the organ from infected donated after donor cardiac death (**DCD**) [5]. However, significant incidence of infectious complication (approximately 80%) has been observed in the kidney transplant recipients, especially in the first year following renal transplantation [6]. It has been reported that mortality associated with the infections caused by *Klebsiella pneumoniae* carbapenemase (**KPC**)-producing Enterobacteriaceae is 28-68% [7-12] and in solid organ transplant (**SOT**) recipients, the mortality can be as high as 71% [12-17].

Known risk factors for the acquisition of infections with *K. pneumoniae* include old age, malnutrition, chronic alcohol toxification, diabetes, chronic respiratory tract disease, and multiorgan dysfunction syndrome [18-22].

Compared with the risk factors of acquisition of infection with *Klebsiella pneumoniae*, the risk factors of acquisition of Carbapenem resistant *Klebsiella pneumoniae* include old age, hematological malignancies, cancer, solid organ or stem cell transplantation, immunosuppressant therapy, surgery, mechanical ventilation, prolonged use of invasive devices (ex. Indwelling tubes or drainage tubes), use of antimicrobial agents, and a high Acute Physiology and Chronic Health Evaluation score [7-9, 23,24].

Given the high mortality and various clinical features of the lethal pathogen, there is a need for study to distinctively present cases and describe the severe infections of *Klebsiella pneumoniae*. In the present study, we have presented a series of cases in an attempt to elucidate the clinical characteristics, imaging features and treatments for the severe infections of *Klebsiella pneumoniae*.

METHOD

This is a retrospective study. Four patients were chosen from the medical records from January 2015 to January 2017 who are typical representatives of the different types of infection of *Klebsiella pneumoniae* and once treated in Intensive-care-unit (ICU) department of the 309th hospital of PLA. The 309th hospital of People Liberation of Army is a 1430-bed tertiary care teaching hospital with a 20-bed comprehensive Intensive-care-unit (ICU) and a 10-bed surgical Intensive-care-unit (SICU) and approximately 40,000 hospital admissions per year in Beijing, China.

The research project has been approved by the Ethics Committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

CASE PRESENTATION

Case 1

A 60-year-old female patient complained of intermittent wheezes for one month, fever and cough with brick-red sputum for half one month that exacerbated for one week. The past medical history included hypertension, hyperlipidemia, diabetes and postoperative excision of the tuberculosis of the right lymphoid nodes. Laboratory test showed that white blood cell (WBC) $19.40 \times 10^9/L$, Neutrophil 91.5%, procalcitonin (PCT) 74.860ng/ml, Brain Natriuretic Peptide (BNP) 12820pg/ml. Based on her laboratory results, she received Meropenem for the antibiotic treatment initially. However, she presented with loss of consciousness and cyanosis after the treatment. Physical examination showed obvious wheezy phlegm sound in the bilateral lungs. Tracheal intubation and mechanical ventilator were, therefore, applied. Multiple sputum and urine cultures yielded the carbapenem sensitive *Klebsiella pneumoniae* strains. Meropenem (2g, q8h) was continually applied for the antibiotic treatment. Afterwards, the patient's condition was waving, lingering and difficult to cure.

On the 15th days after admission, she presented with intermittent fever. Twice sputum cultures grew the *Stenotrophomonas maltophilia* strain and the auscultation of lungs showed the augmented wheezy phlegm sound. Meropenem (2g, q8h) and levofloxacin (0.5g, qd) were, therefore, adjusted for the regimen of antibiogram. However, she continually developed fever, with the highest degree 39°C. Vancomycin (0.5g, qd) was, therefore, added to the antibiogram to target the coccus strains with adjuvant therapy. Tracheotomy was performed and the sputum cultures yielded multi-drug resistant *Acinetobacter baumannii* strains. Therefore, Tigecycline (50 mg q12h after a 100mg loading dose) was added to the antibiogram.

Upon completion of the above antibiogram, she still developed intermittent fever, complained of wheezes and cough with phlegm. The computed tomography of lung showed the signs of lung infection and the formation of cavitation (Figure 1). To seek for the further treatment, she

was transferred to ICU department of our hospital. A combinational treatment, consisting of Meropenem (1g, q8h), Minocycline (100mg, q12h) and Voriconazole (200mg, q12h), was applied for the antibiotic treatment. After a serial treatment, she successfully received the ventilator weaning and was switched to the low flow oxygen inhalation treatment, without any signs of wheezes and dyspnea.

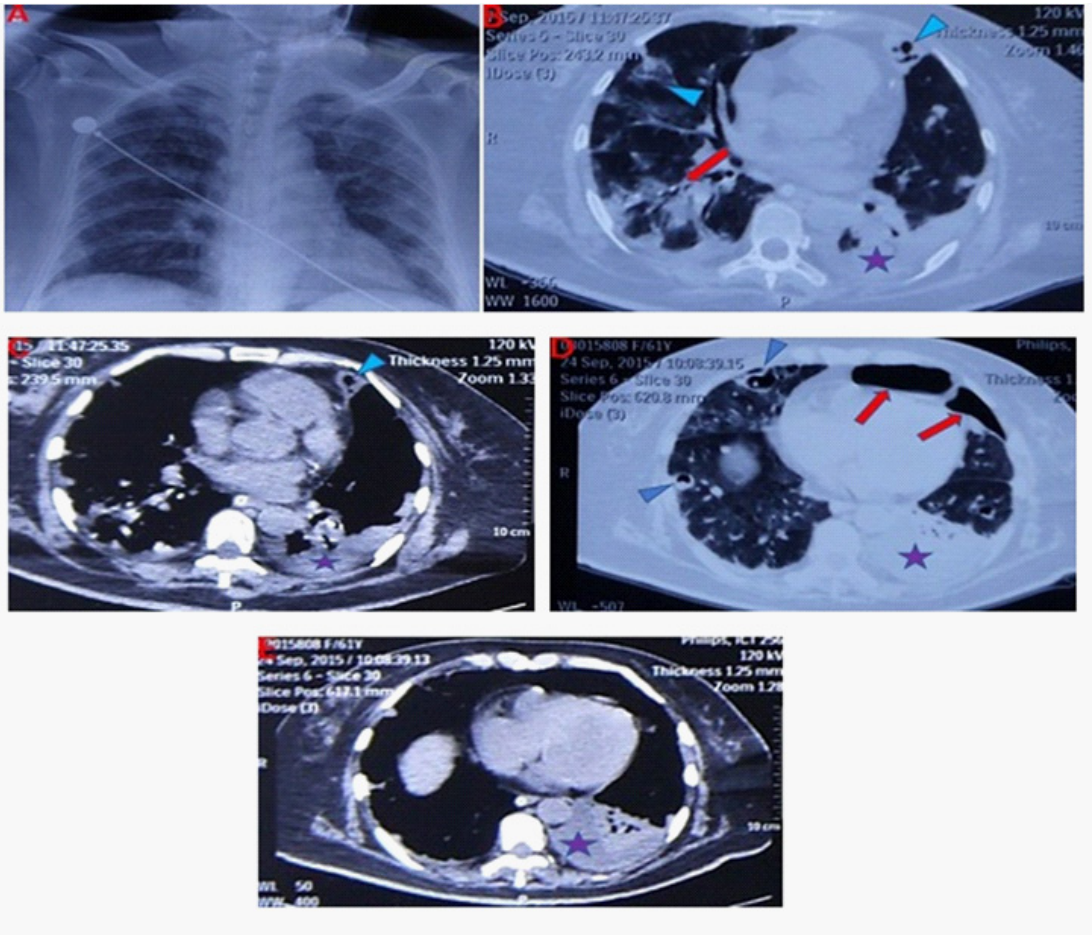


Figure 1: The imaging findings of lung abscess with Septic Shock.

- A. Chest radiograph revealed multiple alveolar consolidation in the bilateral lungs.
- B. The lung window of cross-section view of computed tomography scan showed multiple consolidation with “the air bronchograms sign”(arrows), multiple peripheral wedge-shaped shadows in the right lung (arrowheads) and nodular opacities in the left lung. The left lung abscess and the formation of loculated pleural effusion (asterisk) were observed.
- C. The mediastinum window of cross-section view of computed tomography scan showed cavitory nodule (arrowhead), loculated pleural effusion (asterisk) in the left lung.

- D. Seventeen days later, a repeated computed tomography in the same image plane showed newly formation of bilateral lung abscess (arrowheads), pleural effusion (asterisk) and pneumothorax (arrow).
- E. A repeated mediastinum window of cross-section view of computed tomography scan showed lung alveolar consolidation and pleural effusion (asterisk).

In view of the improved condition, she was transferred to pneumology department. New combinational treatment, including Teicoplanin, Piperacillin, and Tazobactam, was made up for the antibiotic treatment. However, the sputum culture yielded multidrug resistant *Klebsiella pneumoniae*. Therefore, Minocycline was added to the antibiogram. Afterwards, the antibiogram was adjusted to Moxifloxacin, combined with Minocycline, Cefoperazona /Sulbactam. Later, it was changed to Levofloxacin, Minocycline, Cefoperazona/Sulbactam. During the treatments, she had swollen lower limb that had been detected no thrombus in the vessels by the vascular ultrasound. Combined with other adjunctive therapies, she had a good recovery. Two months after the admission, thoracic CT scan showed the good recovery of the lung. She was then transferred to her regional hospital for the continuation of therapy.

Case 2

A 53 years old male patient complained of fever with nausea and vomiting for 5 days that exacerbated with abdominal pain for 1 day. The highest degree of temperature came to 38.9°C. Laboratory results showed that alanine aminotransferase (**ALT**) 98.0U/L, aspartate aminotransferase (**AST**) 204U/L, total bilirubin (**TBIL**) 27.0umol/L, total protein (**TP**) 60.0g/L, albumin (**ALB**) 30.0g/L, platelet (**PLT**) $25 \times 10^9/L$. Physical examination showed the percussion pain in the hepatic region. Previous medical history included diabetes for more than 10 years and orally intaking Acarbose for controlling of blood glucose with unsatisfactory outcome, long-term alcohol drinking and suffered from hepatitis B for 5 years. The computed tomography of abdomen in the regional hospital showed the space-occupying lesions in the liver that indicated pyogenic liver abscess (**PLA**) and the free air under the phlegm and around the liver (Figure 2). He was then diagnosed as space-occupying lesions in the liver that suspected to be pyogenic liver abscess. To seek for further examination and treatment, he was transferred to hepatological surgery department of our hospital. He presented with intermittent fever, with the temperature about 39°C. Afterwards, he received the percutaneous transhepatic drainage (**PTD**) for the invasive surgical treatment. However, he did not have good recovery and developed intermittent fever with condition waving, lingering and difficult to cure, and temperature ranging from 38°C to 39°C. A combinational therapy, consisting of Cefotaxime/Sulbactam (3g, q8h) and Etimicin Sulfate (100ml, qd) was applied for the antibiotic therapy, combined with other anti-febrile, rehydration and nutritional support therapy. Later, the antibiogram was switched to Meropenem (1g, q8h). Unfortunately, he presented with agitation with loss of consciousness. The blood gas analysis indicated type I respiratory failure.

In view of the uncontrolled sepsis despite maximal treatment, he was transferred to ICU department for infection management. Urgently, the patient was put on tracheal intubation and mechanical ventilator. Meanwhile, Meropenem (1g, q8h, pumping for 3 hours), Tigecycline (50mg, q12h after a 100mg loading dose) and Ornidazole (0.5g, bid) were commenced for antibiotic therapy. A series of therapies were performed for him, such as the inhibition of inflammatory reaction by Ulinastatin, the phlegm-resolving, the acid-inhibition, the inhibition of digestive enzymes by somatostatin, fasting, clysis and laxation, and nutritional support therapy. Besides, the immunoglobulin was intravenously injected to neutralize the inflammatory mediators and strengthen body resistance. Ultrasonic examination of abdomen indicated the increased volume of abdominal fluid. Therefore, abdominal puncture and drainage was performed, with intermittently complementing the human serum albumin. Meanwhile, platelets, red blood cells, plasma and colloid were infused to maintain the nutrition and fluid balance status. Most important of all, continuous renal replacement therapy (**CRRT**) was performed to maintain the acid-base and inner environment balance. The culture of drainage of liver yielded carbapenem sensitive *Klebsiella pneumoniae* and the culture of drainage of abdominal cavity grew *Enterococcus faecium*. Additionally, the culture of sputum yielded multi-drug resistant *Acinetobacter baumannii*. The antibiogram was switched to the combination of Piperacillin/ tazobactam, Tigecycline and Caspofungin. However, he didn't have good recovery, with severe sepsis. On the 7th day after admission, emergent exploratory laparotomy under general anesthesia was performed, combined with abdominal necrosectomy, ultrasonic-guided incision of the liver abscess with drainage and the percutaneous transhepatic cholangial drainage (**PTCD**). After the surgery, the above combinational therapy was continued in combination with other adjunctive therapy. Satisfactorily, he had a good recovery and successfully went through the ventilator-weaning procedure and was independence of CRRT. On the 18th days after admission, he was then transferred back to hepatological surgery department for continuation of infection management and other treatments, and discharged with good recovery half a month later.

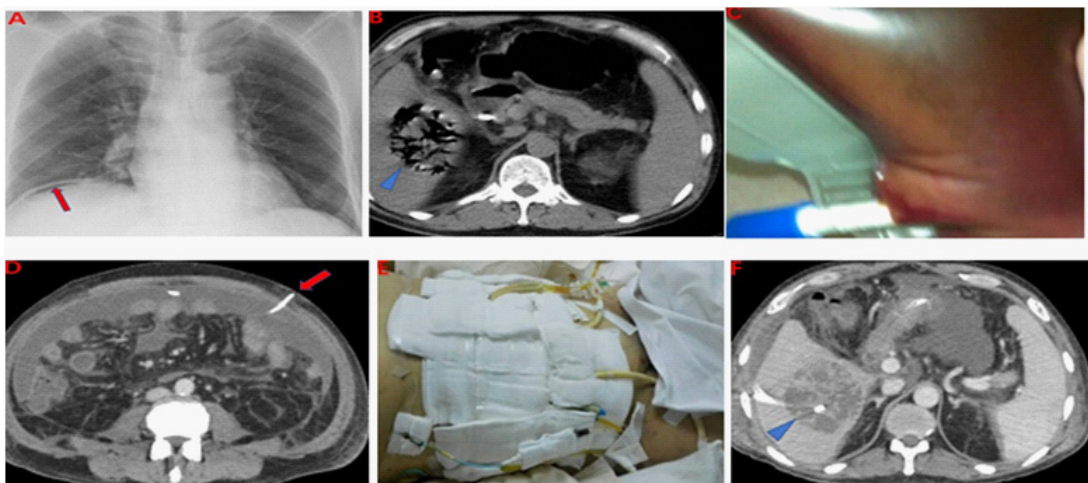


Figure 2: The imaging findings in the treatment of pyogenic liver abscess (PLA).

- A. The abdominal X-ray scan showed that there was free air under the diaphragm (arrow).
- B. The computed tomography (CT) of abdomen showed an abscess (arrowhead) within the right lobe of the liver.
- C. The aspiration drainage was performed using Pigtail drainage device. The *Klebsiella pneumoniae* strains were identified by the purulent fluid culture.
- D. Seven days later, the aspiration drainage (arrowhead) had been performed using Pigtail drainage placed in abdomen.
- E. The exploratory laparotomy had been performed. About 1500ml purulent fluid had been aspirated, meanwhile 5 catheters placed during the surgery.
- F. Seventeen days later, a repeated computed tomography of abdomen showed the abscess (arrowhead) in the right lobule of liver and the absorption of abdominal fluids.

Case 3

An 85 years old male patient complained of low degree fever with nausea and vomiting for one day, admitted to Cadre ward of our hospital. Previous medical history included hypertension and sequelae of cerebral infarction. Computed tomography of chest and abdomen showed the signs of infection of bilateral lungs with more obvious for right lung, the distension of gastric cavity and the accumulated air and liquid in the cavity of intestine (Figure 3). Physical examination at admission showed the basic vital signs included heart rate 115/min, breath rate 35/min, blood pressure 105/60mmHg, and oxygen saturation 65%. Besides, he was in a dementia state and auscultation of lungs showed coarse breathing sound in the bilateral lung with the low volume of the breathing sound in the right lung. The phlegm-wheezing sound was heard. He was, therefore, transferred to ICU department for further treatment. Laboratory results showed White Blood

Cells (**WBC**) $5.10 \times 10^9/L$, Neutrophil (**N%**) 87.6%, Hemoglobin (**Hb**) 68g/L, Creatine (**CRE**) $158.2 \mu\text{mol}/L$, Blood Urea Nitrogen (**BUN**) $10.1 \text{mmol}/L$, Brain Natriuretic Peptide (**BNP**) $374 \text{ng}/\text{ml}$, Troponin I (**TNI**) $0.04 \text{ng}/\text{ml}$. Based on the laboratory results and the symptoms, he was put on tracheal intubation and mechanical ventilator. Meropenem (1g, q8h) and Teicoplanin (0.4g, qd) were commenced, combined with complementation with red blood cells, plasma and rehydration. Meanwhile, other treatments was made up for him, such as the inhibition of hemorrhage by omeprazole, somatostatin and octreotide. Upon finishing the above treatment, he had a good recovery of pneumoniae and received tracheotomy on the 9th days of admission. However, his fever developed and the temperature was constantly above 38°C during the 11th to 14th day after admission. Laboratory result showed the obvious uplifting of the level of transaminase and bilirubin. Physical examination indicated the percussion pain in the gallbladder region. Computed tomography of abdomen showed the signs of abdominal fluid and swollen gallbladder with the characteristic traits of “double-layer sign”, indicating the signs of cholecystitis. Therefore, on the 15th day after admission, the percutaneous transhepatic cholangial drainage (**PTCD**) was performed. The bile juice smear reported the infection of gram negative bacteria four hours later. Four days later, the culture of drainage of bile juice yielded carbapenem resistant *Klebsiella pneumoniae*. Tigecycline and Ornidazole were, therefore, added to the antibiogram. One month after the admission, thorough the above antibiotic treatment, he had a good recovery and successfully went through the ventilator-weaning procedure and switched to low fluid oxygen inhalation ($3L/\text{min}$), with alleviation of lung infection and cholecystitis and improvement of other laboratory indexes. Besides, the mental state of the patient was improved and the recovery of the gastrointestinal function and the immunological status was satisfied.

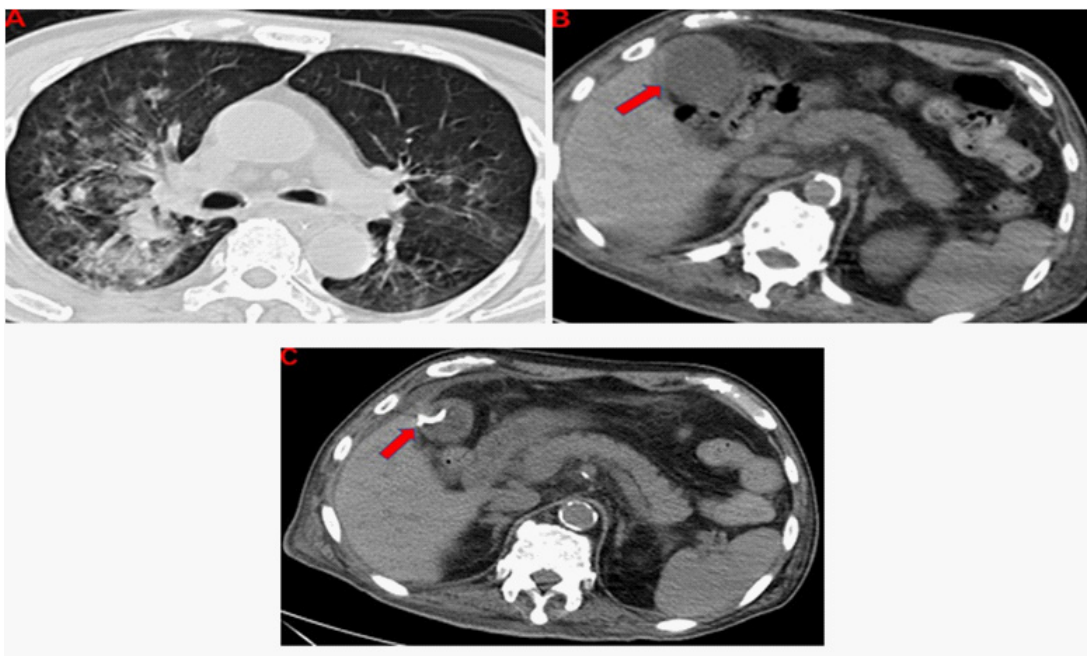


Figure 3: The computed tomography (CT) of chest and abdomen during the treatment for cholecystitis caused by *K. pneumoniae*.

- A. The lung window of the cross-section view of computed tomography scan showed patchy ground-glass opacities in the right lower lobule of the lung.
- B. 7 days later, the patient was febrile again. The computed tomography showed the sign of acute acalculous cholecystitis that was manifested by enlarged gallbladder and the thickened wall of gallbladder (arrow).
- C. The ultrasound guided percutaneous transhepatic gallbladder drainage (arrow) was performed on the elderly with acute acalculous cholecystitis for the treatment.

Case 4

A 53-year-old male patient with hypertension and end stage renal failure due to diabetic nephropathy on dialysis received a cadaveric renal transplant in other medical center with unknown donor and matching information. The allograft vessels were anastomosed to the external iliac artery and vein respectively. He was put on tacrolimus 4mg twice daily, mycophenolate mofetil 360mg twice daily and methylprednisolone 500mg once daily after transplant for immune suppression. Postoperatively, he had a slow recovery with normal temperature initially. Serum creatinine level was 573.3 μ mol/L. A few days later, he had intermittent fever and persistent malaise, complained of right lower quadrant pain. On the 15th days after renal transplantation, there was pleural of effusions and purulent fluids from the incision in the transplant kidney

region. Multiple cultures of blood, sputum and purulent fluid from the incision grew carbapenem resistant *Klebsiella pneumoniae* strains (**CRKP**). Tigecycline (50mg, q12h after a 100mg loading dose) and Meropenem (1g, q8h) were, therefore, commenced and Tacrolimus and Mycophenolate Mofetil were discontinued, except for the methylprednisolone and prednisolone. A computed tomography (CT) scan of the chest showed there were patchy shadows in the right lower lobe of the lung; Multiple nodular shadows in the bilateral lung; Increased volume of pleural effusion than before; Newly formed pneumothorax; Newly formed consolidation in the right lower lobe of the lung (Figure 4). Considering the possibility of infection of *Klebsiella pneumoniae* overlapping with fungus, a combinational therapy, consisting of Tigecycline, Meropenem and Minocycline, were further enhanced to strengthen the anti-infective therapy after discussion with the respiratory physician, meanwhile, Immunoglobulin was injected to maintain the immunological function.

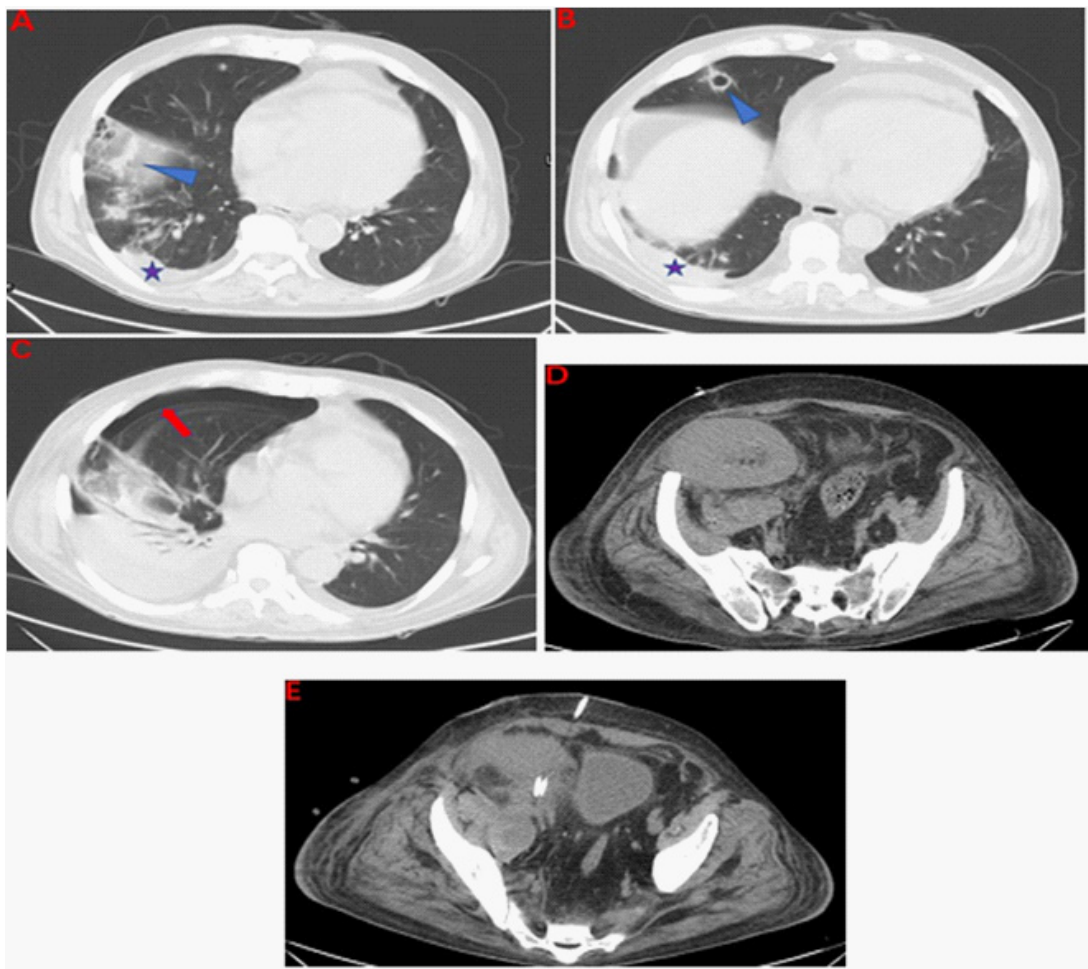


Figure 4: The characteristic imaging findings of thoracic cavity and pelvic cavity during the treatment of infection of *K. pneumoniae* after the renal transplantation.

- A. The computed tomography of the chest showed peripheral wedge-shaped shadows (arrowhead) and pleural effusion (asterisk) on the 27th days after admission.
- B. The chest CT showed lung abscess and pleural effusion on the same day.
- C. Ten days later, chest CT showed a wide range of consolidation within the right lower lobe of the lung and the pneumothorax in the right lung (arrow).
- D. The CT scan of the abdomen and pelvis showed peripheral collection of the purulent fluid, with the size about 3.8×3.5cm under the lower tip of the grafted kidney.
- E. Emergent ultrasonic-guided percutaneous drainage for peripheral collection of purulent fluid was performed 71 days after renal transplantation.

Upon completion of the course of the above antibiotics, the temperature of the patient returned to the normal range. However, he still complained of shortness of breath, tightness of the chest and aggravated fatigue. Therefore, on the 35th day after the renal transplantation, he was transferred from transplant surgery unit to our intensive care unit (**ICU**) department. Owing to the acute onset of pneumothorax, urgently, the right thoracic closed drainage surgery was performed, meanwhile orthopedic surgeon was invited to perform continually vacuum sealing drainage (**VSD**) in the surgical area through last vacuum aspiration (**LVA**). The antibiogram was adjusted to Meropenem (2g, q8h), Tigecycline (100mg, q12h). However, he still developed chills and fevers, with the highest temperature 40.2°C. Multiple ultrasound and CT examinations showed there was pleural of perinephric effusion around the transplanted kidney. Fluid aspiration of the perinephric collection was performed, with the culture yielding the same multidrug resistant *Klebsiella Pneumoniae* as the urine culture, therefore adjusting the dose of antibiotics (Meropenem 2g, q8h) and prolonging the pumping time (3 hours and 30 minutes). However, he still developed intermittent fever. Ultrasound examination showed increased volume of perinephric fluid around the transplanted kidney and massive fluids enclosed the blood vessels, while there were no indication of local puncture and drainage. After communication with the patient's family and the urinary surgeon, he received the exploratory surgery for the transplanted kidney in the surgery room. During the procedure of the surgery, there was no findings of hematoma and abscess. However, the level of hemoglobin and platelets were continually dropped, therefore, blood transfusions with various blood products, such as platelets, fibrinogen, prothrombin and recombinant human coagulation factor VII α , were performed, especially after the finding of the massive bloody drainage fluids in the retroperitoneal drainage tube.

During the night of the 75th day after renal transplantation, the patient's blood pressure suddenly dropped to 50/30 mmHg, accompanied with the loss of consciousness, immediately performing the bedside tracheal intubation and assisted mechanical ventilator, meanwhile providing plenty of fluid for the expansion of volume of systemic circulation and rehydration. The rescue was continued to the next day, however, the patient's blood pressure still could not

be maintained. Cardio-pulmonary resuscitation (**CPR**) was immediately performed, with various first-aid medicine infused. After informing his family members of the disease, the family refused to continue the treatment. With the allowance of the chief physician, the patient was automatically discharged.

DISCUSSION

As the most lethal pathogen, no matter in the hospital and community, *Klebsiella pneumoniae* has attracted the attention of many medical experts to devote their life to fight with it with various “weapons” in the whole world. However, the outcome is not optimistic as expected. The rate of worldwide spreading of *Klebsiella pneumoniae* has become faster than imagination and the severity of the complication that it causes is astonishing and usually is extremely hard to handle. In many ICU departments of hospital worldwide, the mortality of the infection of *K pneumoniae* is more than 67.6%, pulling the alarm of the severity of the lethal infection [25].

From the cases that we have presented, we can acknowledge that the clinical characteristics caused by the pathogen are protean, ranging from the simple pneumoniae with hard-to-handle fever, the pyrogenic liver abscess that can be detected by the imaging apparatus, the cholecystitis that can be neglected by the inexperienced physician to the deadly complication after renal transplantation. All of the cases lead to septic shock and multiorgan dysfunction syndrome (**MODS**), with the use of mechanical ventilator. Among the cases, 2 cases were treated with the continual renal replacement therapy (**CRRT**). The effective therapeutic approaches of the above cases was focused on the combinational therapy, consisting of Meropenem and Tigecycline, and various appropriate surgical treatment, such as exploratory laparotomy for pyogenic liver abscess, ultrasonic-guided incision of the liver abscess with drainage, percutaneous transhepatic gallbladder drainage (**PTGBD**), the drainage for the perinephric effusion, the drainage for abdominal cavity, and so on. Besides, the outcome of treatment was differential, including survival for 3 cases, and death for 1 case. In the analysis of drug resistant profile of the pathogens, the results are also diversified, including 2 cases for carbapenem resistant *Klebsiella pneumoniae* and 2 cases for carbapenem sensitive *Klebsiella pneumoniae*.

The imaging features that the cases have shown are various with distinct characteristics. From the imaging findings of simple pneumoniae that caused by *K. pneumoniae*, we can come to the featured observation that there are multiple alveolar consolidation distributed in the bilateral lungs, with the characteristic trait of “air bronchogram sign”. Multiple peripheral wedge-shaped shadows and nodular opacities can be seen in the bilateral field of lung. The cavitary nodules and loculated pleural effusion can be observed. Occasionally, under the severe circumstances, pneumothorax can be caused by the pathogen which can be shown on the chest X-ray. As for the pyrogenic liver abscess (**PLA**) that caused by *K. pneumoniae*, the sign of “free air under the diaphragm” can be detected by abdominal X-ray, but can also be misleading for physicians. The computed tomography of abdomen is necessary to further clarify the the focus of infection.

Peripheral nodules with or without cavities, a feeding vessels sign, and peripheral wedge-shaped opacities have been previously reported as the typical chest CT findings indicative of septic pulmonary embolism caused by a *Klebsiella pneumoniae* liver abscess (**SPE-KPLA**) [26-29]. Apart from the same imaging features of PLA, the cholecystitis caused by *K. pneumoniae* can be shown on the computed tomography of abdomen, with the trait of “enlarged gallbladder and the thickened wall of gallbladder”, as known of the “double-layer sign”. With regard to the characteristic imaging features of the infection of *K. pneumoniae* after renal transplantation, a wide range of imaging findings on the CT can be seen, including the accumulated fluid zone around kidney, the metastatic lung abscess and pleural effusion, and the diffused lesions in the soft tissue. Most important of all, the growth of *K. pneumoniae* on the culture can be definitive and the imaging features only play an adjunctive role to guide the physicians.

Therefore, as the guardians of health, we must ask the question that “what’s the effective therapeutic approach to treat it?” Unfortunately, there is no absolute effective therapy for the pathogen, however, there are some therapeutic consensuses have been come to. With regards to the Carbapenem sensitive *klebsiella pneumoniae*, the chosen of the antibiotics can mainly focused on the result of antibiotic susceptibility testing. Appropriate and prolong combined treatment (Tigecycline + Carbapenem, Tigecycline + Fosfomycin, Fosfomycin + Aminoglycoside, Third generation cephalosporin + β - lactamases inhibitor etc.) can be successful in the treatment of cases caused by carbapenem resistant *Klebsiella pneumoniae* (**CRKP**). Among the cases, there was only 1 case (case 3) utilizing high dose Tigecycline (100 mg, q12h after a 200mg loading dose) in the treatment. De Pascale et al. have conducted the research to come to the conclusion that Tigecycline that utilized at dose higher than standard treatment can be utilize to treat severe infections with satisfactory outcome [30]. In the early stage of the infection, utilization of appropriate combined treatment strategy, full dose and full course, can bring a relatively ideal outcome for the patient. Imaging techniques are helpful for the diagnosis of the infection owing to the imaging characteristic. It is critical to retrieve the reliable positive culture during the early stage of treatment, guiding the application of the antibiotics. Besides, utilization of properly mini-invasive approaches, such as drainage, can alleviate the severity of the symptom to a large extent. Strain genotyping should be performed to optimize further treatment protocols in such cases.

Noticeably, in 2017, there was a fatal outbreak of the ventilator associated pneumoniae caused by a new emerging hypervirulent *Klebsiella pneumoniae* strain in Zhejiang, China [31]. Hypervirulent *K pneumoniae* has the ability to cause life-threatening, community-acquired infections such as liver abscesses, pneumonia, meningitis, and endophthalmitis in young and healthy individuals and is therefore associated with high morbidity and mortality, with the characteristics of hypervirulent, multidrug resistant, and highly transmissible, gaining the virulence by the acquisition of a roughly 170 kbp virulence plasmid [2].

Since the above characteristics, an improved infection prevention and control policy (**IPC**) and some advanced preventative measurements are urgently to be carried out to keep the

carbapenem resistant *Klebsiella pneumoniae* from spreading further. Importantly, worldwide surveillance of these carbapenem resistant *K pneumoniae*, implementation of stricter control measures and invention of new preventive apparatus are needed to prevent these emerging multi-resistant, hypervirulent, highly transmissible super-bacteria from further disseminating in hospital settings and the community in the whole world.

CONCLUSION

Klebsiella pneumoniae can cause severe infection manifested in various clinical characteristics, including severe pneumoniae abscess, pyogenic liver abscess, cholecystitis, sepsis after renal transplantation and so on. Imaging features of the infection are diversified, including the peripheral nodules with or without cavities, a feeding vessels sign, and peripheral wedge-shaped opacities on the chest scan or the diffused lesions in the soft tissue around the infected organs on the computed tomography and so on. Although the effective therapeutic options are limited, current beneficial therapeutic approaches are mainly focused on the combined regimen, associated with the necessary surgical mini-invasive approaches. During the early stage of treatment, It is critical to retrieve the reliable positive culture to guide the application of the antibiotics. Most importantly, strictly implementation of infection prevention and control policy (IPC) is the key to prevent the further spreading of the pathogen in the hospital settings and communities in the whole world.

AUTHORS' CONTRIBUTIONS

YZ designed and supervised the study. YW collected and analyzed the medical records, and wrote the manuscript, while YZ monitored the study. HF provided the collection of the valuable articles with the assistance of the searching on the PubMed. All of the authors read and approved the final manuscript.

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