Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
50(1) 1–9

DOI: 10.1177/03000605211069284
journals.sagepub.com/home/imr
SAGE

Left eye enucleation caused by multi-systemic *Klebsiella pneumoniae* invasive syndrome

Yanquan Liu[1], Hongquan Zhu[1], Yue Yin[2] and Zhimin Yan[1]

Abstract

Klebsiella pneumoniae is generally considered the most common pathogenic bacterium causing community-acquired pneumonia. In recent years, cases of liver abscess caused by the bacterium and its spread have been reported in Asia and other parts of the world. This clinical symptom of liver abscess caused by hypervirulent *K. pneumoniae* and its migrating infection is also called invasive *K. pneumoniae* liver abscess syndrome (IKPLAS). This study explored the clinical characteristics, diagnosis, and treatment of an elderly patient with IKPLAS who experienced multi-organ failure caused by the infection. The treatment of the patient was difficult, and despite our efforts, the invasive infection led to eye enucleation. This paper is expected to improve our understanding and awareness of this disease in the clinic.

Keywords

Klebsiella pneumonia, invasive Klebsiella pneumoniae liver abscess syndrome, invasive syndrome, enucleation, liver abscess, multi-organ infection, hypervirulence

Date received: 10 July 2021; accepted: 1 December 2021

Introduction

Most cases of invasive syndrome associated with *Klebsiella pneumoniae* are caused by its highly virulent variant (HvKP). HvKP has high invasiveness and virulence, and patients infected with HvKP are more likely to develop infection in multiple organ systems. The distant transfer and spread of HvKP are mainly related to its

[1]Clinical Medicine Research Center, Department of Intensive Medicine, The First Affiliated Hospital of Gannan Medical University, Ganzhou, Jiangxi, China
[2]Fujian Medical University Union Hospital, Fuzhou, Fujian, China

Corresponding author:
Zhimin Yan, Deputy Chief Physician, Clinical Medicine Research Center, The First Affiliated Hospital of Gannan Medical University, No. 128, Jinling West Road, Zhanggong District, Ganzhou, Jiangxi Province 341000, China.
Email: yanzhimin81@tmu.edu.cn

capsular polysaccharide, iron uptake protein, and important virulence genes, and the pathogen endangers human life and health globally. This paper summarizes the clinical data of a patient with invasive syndrome caused by *K. pneumoniae* who was recently admitted to the First Affiliated Hospital of Gannan Medical University, and the clinical characteristics and treatment of this case were analyzed in combination with a literature review to improve our understanding of invasive syndrome caused by *K. pneumonia*. These findings should help ensure the early and timely treatment of patients with invasive syndrome, minimize the incidence of sequelae, and provide a reference for clinical diagnosis and treatment.

Case presentation

A woman in her late 60s complained of "recurrent fever for 5 days and blindness in her left eye for 3 days". This patient developed fever without an obvious cause on April 26, 2021 (peak temperature, 38.6°C) with chills, but there was no cough, sputum, nausea, vomiting, diarrhea, or other discomfort. On April 29, 2021, she developed sudden blindness in her left eye, lacrimation, and photophobia. She was treated at a local municipal hospital. Testing for COVID-19 was first completed by nucleic acid detection. The possibility of new coronary pneumonia was dismissed. The patient was treated with levofloxacin eye drops, prednisolone acetate ophthalmic suspension, and other medicines. On May 1, 2021, she developed fever again (maximum body temperature, 39.8°C). The patient's left eye was red, swollen, and painful, and the clinical symptoms were more obvious. Other symptoms included an obvious runny nose, dizziness, chills, and body aches, but the patient had no sore throat, cough, sputum, chest tightness, shortness of breath, or other symptoms. Consequently, she was referred to the outpatient clinic of our hospital.

The outpatient examination revealed the following findings in routine blood analysis: white blood cell count (WBC), 7.4×10^9/L, hemoglobin, 122 g/L; platelet count (PLT), 26×10^9/L; C-reactive protein (CRP), 303.47 mg/L; and procalcitonin (PCT), 38 ng/mL. In addition, negativity for respiratory pathogens was confirmed, and head and lung computed tomography (Figure 1) revealed that the density of the upper lobe of the right lung was increased, with cavities and fluid visible in the upper lobe, indicating abscess. Meanwhile, the assessment of the liver revealed multiple low-density shadows in the left liver, which may have been indicative of liver abscess. The patient was diagnosed with pulmonary infection and admitted to the Emergency Department of our hospital on May 2, 2020. The Emergency Department performed cardiac ultrasound, hepatobiliary and pancreatic color Doppler ultrasound, and other examinations in consideration of diagnoses of pulmonary infection, liver abscess, and left orbital cellulitis. The patient was provided treatments such as imipenem/cilastatin sodium and moxifloxacin to treat the infection, as well as fluid replacement and treatments to protect liver function, and the patient's body temperature normalized. To provide further diagnosis and treatment, the patient was transferred to the Department of Infectious Diseases in our hospital with diagnoses of septicemia, lung infection, liver abscess, and cellulitis of the left eye. Since the onset of the patient's symptoms, her mental health, sleep habits, and diet had been poor, although her urine remained normal and her weight did not change significantly. The patient denied any history of heart disease, diabetes, hepatitis, tuberculosis, typhoid fever, and bacillary dysentery. She also had no history of smoking, drinking, drug, or food allergies. Her family's economic conditions and

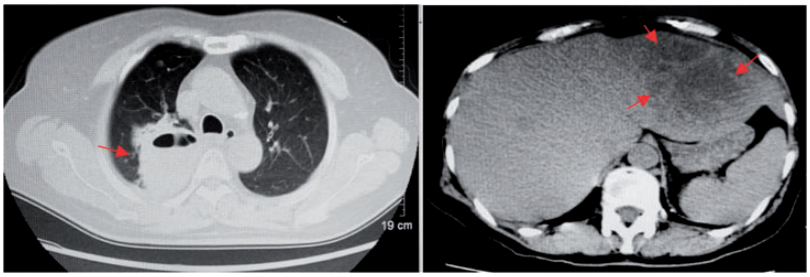

Figure 1. Head and lung computed tomography revealed that the density of the upper lobe of the right lung was increased, with cavities and fluid visible in the upper lobe, indicating potential abscess, and assessment of the left liver lobe revealed multiple low-density shadows, suggesting liver abscess.

living environment were acceptable. Her remaining history, personal history and family history, were unremarkable.

The patient's physical examination after admission revealed the following findings: temperature, 36.5°C; pulse, 85 beats/minute; respiratory rate, 20 breaths/minute; and blood pressure, 120/75 mmHg. The patient was conscious with lacrimation and swelling of the left eye, accompanied by yellow purulent discharge, difficulty opening the eye, and no movement of the eye in any direction. Meanwhile, there were no abnormalities of the right eye and eyelid (Figure 2). Her breath sounds were rough, and no dry and wet rales were heard in her lungs. Her heartbeat was regular with no cardiac murmurs.

The patient's abdomen was flat, soft, and symmetrical, and abdominal wall varicosity, creeping waves, and other abnormalities were not detected. There was no edema in either lower extremity, and pathological signs were not identified.

After admission, we recorded the following data for the patient: WBC, 23.4×10^9/L; hemoglobin, 95 g/L; PLT, 36×10^9/L; CRP, 309.88 mg/L; and PCT, >100 ng/mL. The results of blood biochemical analysis were as follows: blood glucose, 7.32 mmol/L; alanine aminotransferase, 96 IU/L, aspartate aminotransferase, 103 IU/L; alkaline phosphatase, 228 IU/L; gamma-glutamyl transferase, 275 IU/L; potassium, 3.17 mmol/L; calcium, 1.88 mmol/L; total protein, 47.1 g/L; and albumin, 23.4 g/L. Hemoculture and drug susceptibility testing indicated the presence of *K. pneumoniae*. Magnetic resonance imaging of the head (Figure 3) revealed multiple small round signals on both frontal/parietal lobes, indicative of brain abscesses. Examination of the urinary system and color Doppler ultrasound revealed multiple cysts in the liver, chronic cholecystitis, and bilateral abdominal cavities and pleural effusion. Examinations of serial indices of female-specific tumors; pathogenic antibodies against infecting respiratory tract microbes; routine screening for toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus; antineutrophil cytoplasmic antibodies; and galactomannan revealed no abnormalities.

Regarding the treatment plan, the patient underwent close monitoring of blood glucose, and based on the results of blood etiology tests, the patient was treated with a series of antibiotics as follows: imipenem and cilastatin sodium (1.0 g, q8h, ivgtt) + moxifloxacin (0.4 g, qd, ivgtt) from May 2, 2020 to May 7, 2020; ceftriaxone (2.0 g, qd, ivgtt) from May 7, 2020 to May 14, 2020; azithromycin (0.5 g, qd, ivgtt) from May 7, 2020 to May 21, 2020; meropenem (0.5 g, q8h, ivgtt) from May 14, 2020

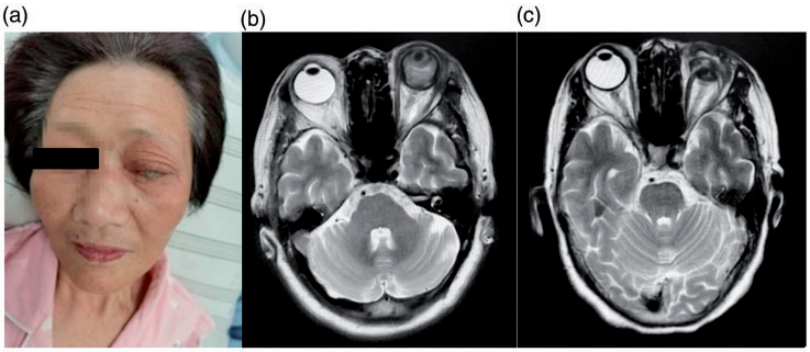

Figure 2. The patient's left eye symptoms (a) and imaging data (b) and her postoperative imaging data (c).

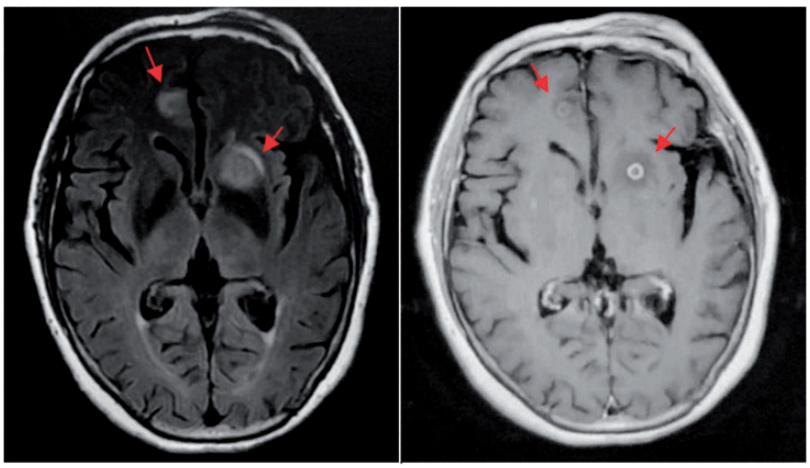

Figure 3. Head magnetic resonance imaging revealed multiple small round signals in both frontal/parietal lobes, indicative of brain abscess.

to May 16, 2020; and amikacin (0.6 g, qd, ivgtt) and cefoperazone sodium/sulbactam sodium (3.0 g, q8h, ivgtt) from May 16, 2020 to May 21, 2020.

In addition, an ophthalmologist in our hospital was contacted for consultation, and the patient received treatment to lower her intraocular pressure as well as intraocular ceftazidime. Our hospital endocrinologists guided hypoglycemic treatment. At the same time, we performed lumbar puncture and conducted routine cerebrospinal fluid and biochemical and culture examinations. In addition, the patient was administered human albumin to correct hypoproteinemia, reduced glutathione to protect the liver, mannitol to reduce intracranial pressure, and other supportive treatments to reduce intraocular pressure, replace lost fluids, and correct electrolyte disturbances. After the aforementioned diagnostic and treatment modalities, the patient's inflammation indices decreased, and no bacteria were detected on multiple blood cultures. Repeated imaging revealed that the liver abscess was reduced, and the patient was discharged.

The patient was immediately referred to the Department of Ophthalmology in our hospital to continue treatment after being discharged from our department. The Department of Ophthalmology admitted the patient with a diagnosis of infective endophthalmitis of the left eye. After admission, physical examination revealed that the patient had difficulty opening her eyes, her eyes could not move autonomously in different directions, and she had no light perception or visual function. An ophthalmologist in our hospital indicated that the patient's eyes were necrotic, and they lacked physiological function. On June 8, 2020, the patient's left eye was surgically removed under local anesthesia. The surgery was smooth, and cefoperazone sodium/sulbactam sodium was given postoperatively. For deep anti-infective treatment, the patient was administered levofloxacin eye drops and prednisolone acetate ophthalmic suspension; however, her left eyelid remained slightly swollen, the conjunctiva was slightly inflamed, but there was no leakage or purulent discharge at the surgical suture. The patient was discharged from the Department of Ophthalmology on June 13, 2020, and she has undergone continued follow-up to date. The patient has undergone tests and other laboratory tests twice, and no metastatic or recurrent infections have been detected. In addition, the psychiatric and mental health assessment by the Department of Psychology and the physical fitness assessment by the Department of Rehabilitation were also performed. The patient's general condition, quality of life, and ability to care for herself were acceptable.

Discussion

K. pneumoniae, which is classified in Enterobacteriaceae, is a gram-negative, facultative anaerobic bacillus with abundant capsules, and it often colonizes the skin, nasopharynx, and intestines in humans.[1] *K. pneumoniae* is a common cause of community-acquired infections and nosocomial infections. Based on the presence of capsular polysaccharides, *K. pneumoniae* can be divided into 78 serotypes. K1 and K2 are the most common serotypes, and they display strong virulence and pathogenicity.[2] *K. pneumoniae* often causes lung, abdominal, and urinary tract infections. It is the leading cause of bacterial liver abscesses in Chinese people.[3] In the clinical diagnosis of *K. pneumoniae* liver abscess, in addition to liver abscess lesions, some patients may also have acute infections such as lung infection, central nervous system infection, intraocular infection, and necrotizing fasciitis.[1] This syndrome with multi-site involvement is currently called IKPLAS or invasive syndrome.

The past and personal history of the patient in this case was not remarkable. She arrived at the hospital with symptoms of repeated fever and sudden blindness in her left eye. Excluding non-specific fever and blindness with eye swelling and purulent discharge, there were no other symptoms of discomfort. The patient first visited a local municipal hospital, and the hospital immediately eliminated COVID-19 as a cause through nucleic acid testing. The patient was treated with levofloxacin eye drops, prednisolone acetate ophthalmic suspension, and other medicines. However, the patient's symptoms were not improved, and her left eye was red, swollen, and painful with purulent discharge. There were obvious symptoms such as a runny nose, dizziness, chills, and body aches, revealing a trend of rapid deterioration.

Later, this patient was referred to the outpatient clinic of our hospital. Emergency blood testing dismissed the possibility of hematological disease, but her CRP and PCT levels were elevated, indicating inflammation. Imaging uncovered inflammatory lesions in the lungs and

abscesses in the liver, suggesting inflammation and infection. The Emergency Department of our hospital provided the patient with imipenem, cilastatin sodium, and moxifloxacin as anti-infective therapies, as well as fluid replacement and other treatments. After the patient's body temperature returned to normal, she was referred to our department. After laboratory and imaging examinations, she was clearly diagnosed with IKPLAS, brain abscess, liver abscess, liver cyst, lung infection, and infective endophthalmitis of the left eye. After confirming the diagnosis, the woman was treated with standardized antibiotics as soon as possible. The control effect of the infection was good, but her ocular symptoms worsened.

Although imaging of this elderly patient revealed the presence of abscesses in the brain and liver, the patient refused abscess drainage, which is the primary and standard abscess treatment, during hospitalization because of the potential traumatic risk of puncture drainage. She was only willing to accept drug-based conservative treatment, and she provided written notification of her refusal to undergo drainage. After a series of anti-infective treatments, imaging revealed that the abscess had shrunk, and her inflammatory indices were significantly lower, indicating that the treatment was effective. During follow-up, we recommended that the patient be transferred to the Department of Ophthalmology of our hospital for further specialized treatment. The physical examination at the initial admission revealed that the patient's left eye was inflamed and swollen accompanied by yellow purulent discharge. In addition, the patient struggled to open her left eye, which could not move spontaneously in all directions, and the eye lacked light perception and visual function. An ophthalmologist in our hospital concluded that the left eye was necrotic without physiological function, and the patient was treated for left eye enucleation under local anesthesia.

In the 1980s, Taiwanese scholars were the first to report a case of liver abscess caused by *K. pneumoniae*.[4] Although such cases are rare, nearly 70% of liver abscesses in mainland China are caused by this bacterium.[3] In addition to causing liver abscesses, *K. pneumoniae* causes metastatic infections in other parts of the body because of its further spread along the bloodstream, potentially causing irreparable body damage. Previous studies from various countries illustrated that *K. pneumoniae* strains isolated from patients with IKPLAS in Asia and strains isolated from patients in other regions are significantly different in terms of genetics and phenotypes, and serotypes K1 or K2 are the dominant forms.[5] Thus, *K. pneumoniae* is more virulent and aggressive in Asia, and Asian populations are more likely to develop IKPLAS. Chiu *et al.*[6] reported a clinical case of *K. pneumoniae* invasive syndrome caused by a non-healing wound after foot trauma. The middle-aged male patient was treated with antibiotics (piperacillin/tazobactam 4.5 g q8h, vancomycin 1 g q12h) and emergency double-calf amputation to control the infectious foci of necrotizing fasciitis after admission. Unfortunately, the patient developed endophthalmitis on the third day after amputation. Chiu and colleagues performed left eye vitrectomy and provided intravitreal antibiotics during the operation (ceftazidime 2 g), followed by a 10-day course of intravenous ceftazidime. The patient's condition gradually improved, but only light perception was restored in the left eye, with vision being nearly completely lost.

The pathogenesis of IKPLAS is currently unclear. The most important factor is diabetes or impaired glucose tolerance.[7] During hospitalization, our patient had high fasting blood glucose levels, indicating possible diabetes. Diabetes or impaired

glucose tolerance has been identified as an independent risk factor for *K. pneumoniae* liver abscess. Patients with diabetes are 3.6- to 11-fold more likely to develop liver abscess associated with endophthalmitis than people without diabetes, and the former patients are extremely prone to irreversible vision loss.[8] In addition, impaired glucose regulation can lead to decreased phagocytosis of neutrophils and difficulty in control inflammation. Patients presenting with IKPLAS with coincident meningitis and endophthalmitis have the highest disability and mortality rates.[9] During our patient's hospitalization, we formed an intra-hospital multi-disciplinary team to manage her treatment. Experts in our hospital discussed that the possible pathogenic mechanism of IKPLAS involves the destruction of the host's gastrointestinal mucosal protective barrier, the spread of normal colonizing bacteria throughout the body, biliary dissemination, and bloodstream transmission. However, in the infected host (i.e., a patient with IKPLAS), the risk factors include diabetes, alcoholism, malignant tumors, chronic obstructive pulmonary disorder, glucocorticoid therapy, and immunosuppression. In addition, past histories of liver abscess, liver cirrhosis, and urinary tract stones may be potential risk factors for IKPLAS.

At the same time, some scholars identified six independent risk factors that can predict severe complications of *K. pneumoniae* liver abscess: $PLT < 150 \times 10^9/L$, alkaline phosphatase $>300\,U/L$, air cavity formation in the abscess, Acute Physiology, Age and Chronic Health Evaluation II (APACHE II) score >40, absence of broad-spectrum cephalosporins in the initial treatment, and absence of timely drainage.[10] Of course, some studies have found that APACHE II scores ≥ 20, acute respiratory failure, and shock are the biggest positive predictors of metastatic infection at any site. When the APACHE II score exceeds 16, metastatic infection, septic shock, acute respiratory failure requiring mechanical ventilation, and the formation of air cavities on imaging are significant predictors of death, and drainage of the abscess cavity is a protective against death in patients with IKPLAS.[11]

Although *K. pneumoniae* is prone to drug resistance and the prevalence of extended spectrum beta-lactamase (ESBL)-producing strains is increasing annually, ESBL-positive *K. pneumoniae* is relatively rare in patients with IKPLAS, and it is relatively sensitive to antibacterial drugs.[12] Because patients with IKPLAS have multi-organ infections in addition to liver abscesses, the condition is dangerous, and its progression is rapid. Concerning the choice of antibiotics for treating IKPLAS, we recommend a course of antibiotics with efficacy against ESBL-positive bacteria for 4 to 6 weeks, and the treatment regimen should not be altered prior to drug sensitivity testing. Concerning treatment during hospitalization, timely abscess puncture and drainage will help relieve the condition and facilitate patient recovery.[13]

In general, our patient did not pay attention to the first signs of her disease. When the condition had progressed to the point of irreversibility, she visited a hospital, but she was treated with conventional treatments that did not correct IKPLAS. The entire treatment process of female patients is tortuous, and efforts should be made to prevent eye enucleation caused by invasive infection. For this reason, when some patients present with unexplained fever and a series of unrelated symptoms, hemoculture and imaging should be performed as soon as possible to confirm the diagnosis, and IKPLAS should be excluded quickly. When the diagnosis is confirmed, anti-infective treatment should be selected according to the results of drug sensitivity testing, and abscess drainage should be performed in a timely and effective manner to

optimize the outcome of the prognosis of the patient.

Conclusion

We have reported a rare case invasive syndrome caused by *K. pneumoniae* in an elderly woman. This aggressive infectious disease caused the patient to lose one eye and severely impaired her quality of life and social interactions. These findings highlight the need for clinicians to be aware of IKPLAS in daily clinical practice. It may be essential for us to deepen the understanding of IKPLAS and provide effective anti-infective treatment or perform standard surgery or drainage as soon as possible. In addition, we should pay more attention to the patient's own quality of life and provide appropriate care to ensure the improvement of the patient's prognosis.

Availability of data and material

All data generated in this study are included in the uploaded manuscript.

Ethics statement

The reporting of this study conforms to the CARE guidelines.[14] Detailed patient information has been de-identified. The study protocol was approved by the ethics review committee of the First Affiliated Hospital of Gannan Medical University. The patient provided consent for the treatment. Written informed consent was obtained from the patient for the publication of this case report and the accompanying images.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and publication of this article: The study was funded by the National Natural Science Foundation of China (81300428) and sponsored by the Science and Technology Fund Project of Jiangxi Provincial Health Commission (SKJP520201086-202130697).

ORCID iD

Yanquan Liu https://orcid.org/0000-0001-6826-0456

References

1. Sink JR, Pasculle WA, Shah NB, et al. Disparate Domains: Cryptogenic Invasive Klebsiella pneumoniae Liver Abscess Syndrome. *Am J Med* 2017; 130: 673–677.
2. Coutinho RL, Visconde MF, Descio FJ, et al. Community-acquired invasive liver abscess syndrome caused by a K1 serotype Klebsiella pneumoniae isolate in Brazil: a case report of hypervirulent ST23. *Mem Inst Oswaldo Cruz* 2014; 109: 970–971. DOI: 10.1590/0074-0276140196.
3. Tian LT, Yao K, Zhang XY, et al. Liver abscesses in adult patients with and without diabetes mellitus: an analysis of the clinical characteristics, features of the causative pathogens, outcomes and predictors of fatality: a report based on a large population, retrospective study in China. *Clin Microbiol Infect* 2012; 18: E314–E330. DOI: 10.1111/j.1469-0691.2012.03912.x.
4. Liu YC, Cheng DL and Lin CL. Klebsiella pneumoniae liver abscess associated with septic endophthalmitis. *Arch Intern Med* 1986; 146: 1913–1916.
5. Fung CP, Hu BS, Chang FY, et al. A 5-year study of the seroepidemiology of Klebsiella pneumoniae: high prevalence of capsular serotype K1 in Taiwan and implication for vaccine efficacy. *J Infect Dis* 2000; 181: 2075–2079.
6. Chiu HHC, Francisco CN, Bruno R, et al. Hypermucoviscous capsular 1 (K1) serotype Klebsiella pneumoniae necrotising fasciitis and metastatic endophthalmitis. *BMJ Case Rep* 2018; 11: e226096. doi: 10.1136/bcr-2018-226096
7. Wang HH, Tsai SH, Yu CY, et al. The association of haemoglobin A1C levels with the clinical and CT characteristics of Klebsiella pneumoniae liver abscesses in patients with

diabetes mellitus. *Eur Radiol* 2014; 24: 980–989.
8. Sheu SJ, Kung YH, Wu TT, et al. Risk factors for endogenous endophthalmitis secondary to klebsiella pneumoniae liver abscess: 20-year experience in Southern Taiwan. *Retina* 2011; 31: 2026–2031.
9. Yang PW, Lin HD and Wang LM. Pyogenic liver abscess associated with septic pulmonary embolism. *J Chin Med Assoc* 2008; 71: 442–447.
10. Korsten P, Vasko R, Gross O, et al. Endophthalmitis, liver abscess, and cerebral and pulmonary emboli in a 48-year-old Vietnamese man. *Internist (Berl)* 2014; 55: 722–725. DOI: 10.1007/s00108-014-3484-z.
11. Liao CY, Yang YS, Yeh YC, et al. Invasive liver abscess syndrome predisposed by Klebsiella pneumoniae related prostate abscess in a nondiabetic patient: a case report. *BMC Res Notes* 2016; 9: 395. DOI: 10.1186/s13104-016-2188-y.
12. Chan DSG, Archuleta S, Llorin RM, et al. Standardized outpatient management of Klebsiella pneumoniae liver abscesses. *Int J Infect Dis* 2013; 17: e185–e188.
13. Yang KC, Shrestha T, Kolakshyapati M, et al. Occult community acquired Klebsiella pneumoniae purulent meningitis in an adult. *Medicine (Baltimore)* 2018; 97: e11017. DOI: 10.1097/MD.0000000000011017.
14. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.