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Rare Case of *Klebsiella Pneumoniae* Liver Abscess Complicated with Infective Endocarditis and Aortic Root Abscess in a Patient Without Diabetes

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Abstract

Liver abscesses are common in Taiwan. Although Gram-negative *Klebsiella* species are the most common pathogens associated with liver abscesses, cases of liver abscess with infective endocarditis (IE) are rare. Herein, we report the case of a liver abscess caused by *Klebsiella pneumoniae* in a patient who presented with consciousness disturbance after 7 weeks of antibiotic treatment. In conjunction with the brain magnetic resonance imaging findings, cerebrospinal fluid analysis revealed septic emboli. Large aortic valve vegetation, which was not initially evident, was identified during follow-up transthoracic echocardiography and later progressed into aortic root abscess formation. Therefore, the patient received porcine aortic valve replacement, from which he recovered well. We highlight the importance of prompt detection of concomitant IE, particularly in patients with degenerative aortic valves. (J Intern Med Taiwan 2023; 34: 50-56)

Key Words: Aortic root abscess, Infective endocarditis, *Klebsiella pneumoniae*, Liver abscess, Transthoracic echocardiography

Introduction

Klebsiella species are environmental Gram-negative bacteria (GNB) that colonize the human gastrointestinal tract and often cause common ailments, such as urinary tract infections, pneumonia, intra-abdominal infections, and liver abscesses, which may further progress to severe bacteremia. Among other less common infections associated with *Klebsiella* are osteomyelitis; necrotizing fasciitis; endophthalmitis; meningitis; and spleen, kidney, psoas muscle, spine, and prostate abscesses[1]. Since the 1980s, *Klebsiella pneumoniae* has become the leading cause of liver abscesses in Taiwan, thereby

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surpassing *Escherichia coli* and contributing to the spread of extrahepatic infections[1,2].

In contrast to infections caused by gram-positive microorganisms, of which *Streptococcus* and *Staphylococcus* are the most commonly identified genera[3], GNB-induced infective endocarditis (IE) is less prevalent, with a reported incidence of 1%–10%[4]. Generally, GNB-induced IE is classified into two categories: HACEK (indicating *Haemophilus spp.*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, or *Kingella spp.*) and non-HACEK. Within the non-HACEK category, the most common causative pathogens are *E. coli* and *Pseudomonas aeruginosa*[5,6]. *Klebsiella*-induced IE is uncommon, accounting for less than 1% of general IE cases, and is associated with a high in-hospital mortality rate[7]. A recent review highlighted that the aortic valve is the most commonly involved region, especially among immunocompromised individuals, such as those with diabetes, end-stage renal disease, alcoholism, malignancy, or a history of intravenous drug abuse[8]. Particularly in Taiwan, diabetes mellitus has been identified as the most prevalent underlying cause of *K. pneumoniae* liver abscesses[9]. Even patients without diabetes may be susceptible to concomitant IE as a result of incomplete liver abscess treatment, which should raise clinicians' concerns in daily practice.

Case presentation

A 74-year-old male patient without diabetes and with a medical history of gastric ulcer and benign prostatic hyperplasia presented with complaints of general weakness, poor appetite, and fever persisting for several days. The patient was admitted to the gastrointestinal ward of our hospital under the impression of *K. pneumoniae* bacteremia with a liver dome abscess, which was confirmed through computed tomography (Figure. 1) and abdominal echo.

Upon admission, laboratory data revealed bandemia (white blood cell count = 9.4 × 10^3/μL, segmental neutrophils = 76.0%, and band = 8.0%), anemia (hemoglobin = 10.8 g/dL), thrombocytopenia (platelets = 60 × 10^3/μL), and an elevated C-reactive protein (CRP) level (23.40 mg/dL). His coagulation function was, however, within the normal range (prothrombin time = 12.5 s, activated partial thromboplastin time = 32.7 s), and his hemoglobin A1C level was also normal (4.6%).

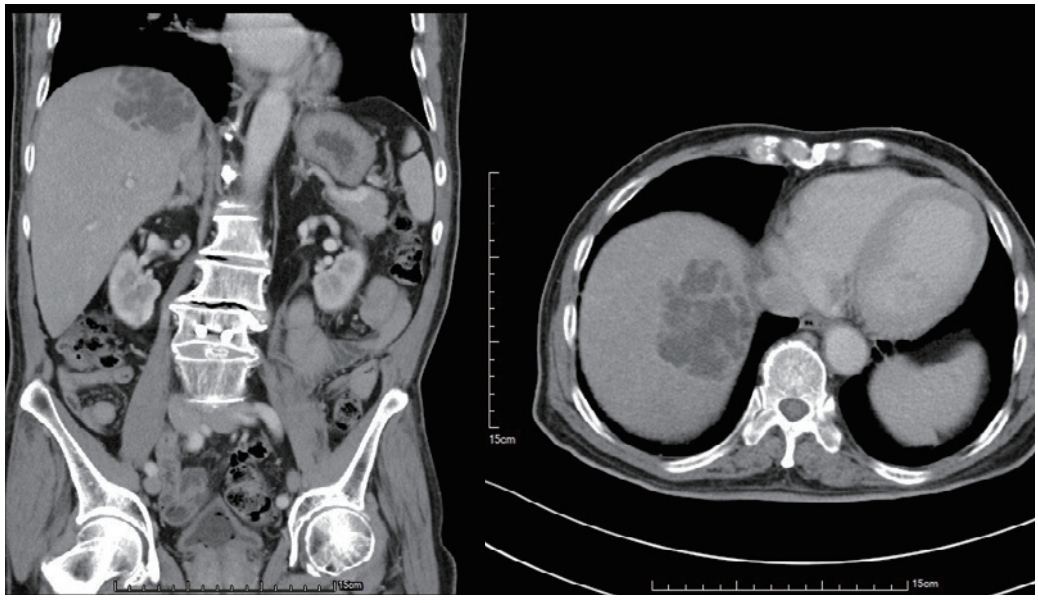

Figure 1. Liver abscess, right superior segment.

The patient's venous blood gas values revealed respiratory alkalosis resulting from hyperventilation and decreased CO2 levels (pH = 7.555, PCO2 = 29.9 mmHg, PO2 = 77.4 mmHg, HCO3− = 26.7 mmol/L, and BE-b = 5.2 mmol/L). In addition, biochemistry revealed impaired hepatic function with elevated bilirubin (aspartate aminotransferase = 134 U/L, total bilirubin = 7.65 mg/dL) and mild acute kidney injury (creatinine = 1.15 mg/dL, estimated glomerular filtration rate = 62.16 ml/min/1.73m^2). The patient's electrolyte levels revealed mild normonatremia and hypokalemia (Na = 138 mmol/L, K = 3.2 mmol/L).

Blood culture revealed *K. pneumoniae*. Therefore, ultrasound-guided aspiration was performed, and 30 mL of yellow pus was obtained, whose culture revealed the presence of *K. pneumoniae.* According to the susceptibility test, antibiotic treatment was initiated with intravenous cefoperazone/sulbactam and then switched to ceftriaxone on day 10 of hospitalization as per the recommendation of an infection specialist. Subsequently, the patient was discharged from the hospital with a prescription for the oral antibiotic cefixime (100 mg/capsule, twice daily) after 14 days of intravenous antibiotic treatment. During a follow-up appointment in the outpatient clinic, ultrasound was used to confirm a regressive change of the patient's pyogenic liver abscess from 4.2 to 2.0 cm, along with an improved CRP level of 5.04 mg/dL.

However, the patient was admitted to the emergency department again 1 month after the previous discharge with complaints of intermittent fever (37°C to 39°C) and weakness. Physical examination revealed a painful expression during epigastric palpation, audible systolic murmur at the upper-right sternal border, and consciousness disturbance, with a Glasgow coma scale score of E3V2-3M5.

Computed tomography was performed to confirm the regressive change of the previous liver abscess. Brain magnetic resonance imaging was performed on the suspicion of septic emboli. The results, however, revealed presumed embolic infarcts at the left occipital region, right corona radiata, and bilateral centra semiovale. Initial transthoracic echocardiography (TTE) revealed a calcified aortic valve without visible valvular vegetation (Figure. 2A), along with mild to moderate aortic regurgitation and mild aortic stenosis (peak pressure gradient = 29 mmHg). However, subsequent transesophageal echocardiography (TEE) failed because of the patient's agitation and poor cooperation. Cerebrospinal fluid (CSF) was analyzed on suspicion of central nervous system infection. The

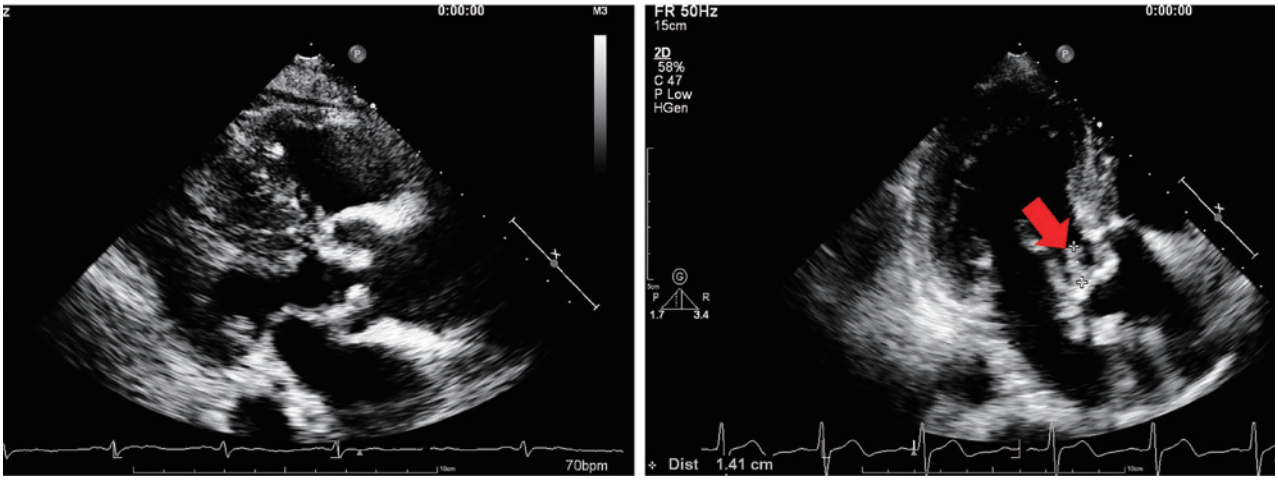

Figure 2. (A) Calcified aortic valve without visible valvular vegetation. (B) Large vegetation (1.41 cm in length, red arrow) over the calcified aortic valve.

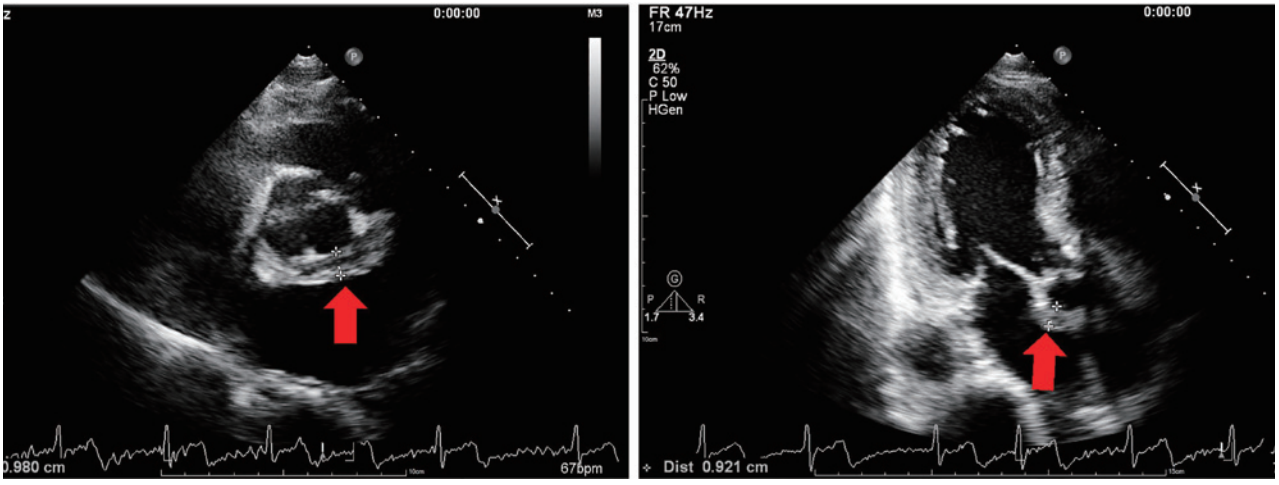

Figure 3. Suspicious aortic root abscess formation between the left coronary cusp and left atrium (red arrow).

results revealed a normal CSF/serum glucose ratio of 0.53 (CSF glucose = 54 mg/dL, serum glucose = 102 mg/dL), an elevated white blood cell count (49 × 10/9 cells/μL, with lymphocyte predominance, 67%), and a total protein level of 87.3 mg/dL, indicating septic emboli in conjunction with the brain MRI findings, but neither bacteria nor fungi were cultured.

Blood culture again revealed *K. pneumoniae* infection, with identical results to those of previous aspirated abscess and blood sample cultures, indicating the same strain. Therefore, as determined by the susceptibility test, intravenous ceftriaxone was administered to treat the infection. Because of the brain embolic infarcts, a specialist in echocardiography was consulted based on the strong suspicion of IE, who also suggested additional TEE testing under anesthesia. Because of the patient's consciousness disturbance and unstable respiration pattern, TTE was arranged after consultation with the attending gastroenterologist and the patient's family. During the TTE, a large vegetation measuring 1.41 cm was observed over the calcified aortic valve (Figure. 2B). The aortic stenosis had also progressed moderately (peak pressure gradient = 58 mmHg). Subsequently, 5 days later, TTE revealed an echolucent area and an increase in wall thickness between the left coronary

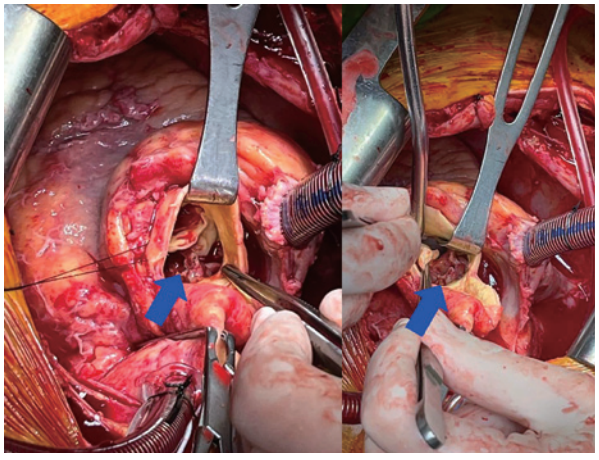

Figure 4. Annular abscess cavity (blue arrow), measuring approximately 2 × 3 cm, between the noncoronary and left coronary sinus.

cusp and the left atrium, suggesting an aortic root abscess (Figure. 3), which was confirmed during surgery (Figure. 4). A large annular abscess cavity, measuring approximately 2 × 3 cm, was observed at the aortic annulus between the noncoronary and left coronary sinus. However, as recommended by an experienced cardiovascular surgeon, no root surgery was performed. Instead, after the annular abscess cavity was repaired with a Dacron graft patch, a 27-mm porcine valve was implanted with interrupted Teflon Pledge 2-0 TiCron. After completing a 6-week meropenem regimen, the patient

gradually recovered and was discharged with a CRP level of 0.8 mg/dL. Although no microorganism was cultured from the surgical samples of aortic valve tissue at follow-up, the fact that the same *K. pneumoniae* was cultured from aspirated abscess and blood samples in two hospital courses suggested that it was the causative pathogen.

Discussion

To our knowledge, this is the first report of an aortic root abscess caused by *K. pneumoniae* in Taiwan. However, our patient did not have diabetes and was not immunocompromised. Such a unique course, along with the increasing trend of *K. pneumoniae* infection, emphasizes the importance of timely detection of concomitant IE, especially for patients with degenerative aortic valves.

GNB-induced IE, including both the HACEK and non-HACEK categories, accounts for approximately 4%–5% of all endocarditis cases[5,10], and non-HACEK cases have a high mortality rate of 20%–30%[4]. Although *E. coli* and *P. aeruginosa* continue to be the most prevalent pathogens causing non-HACEK cases[6,11], the incidence of liver abscesses induced by *K. pneumoniae* is rising in East Asia, especially in Taiwan and Korea[2].

Although the aortic valve remains the most commonly involved region, cases of liver abscess complicated by mitral valve and tricuspid valve IE have been reported[10,12]. For example, Liu et al. highlighted an unusual case of *K. pneumoniae* endocarditis developing with a stalk of left ventricular vegetation attached to the interventricular septum[13]. Srinivas et al. presented a case of *K. pneumoniae* endocarditis with simultaneous destruction of both the mitral and aortic valves[14]. Another study reported that the incidence of perivalvular abscesses secondary to IE is approximately 7.5% and 14% in patients with native and prosthetic aortic valves, respectively[15]. In a comprehensive systematic review of studies in Greece, Ioannou et al. highlighted that the rate of perivalvular abscesses with *K. pneumoniae* endocarditis is 27.9%, higher than the rates for endocarditis caused by other *Klebsiella* species[8].

Infections by *Klebsiella* species are common in Asia. However, some cases have been reported in North America[16], and two cases of liver abscess and concomitant IE were reported in non-Asian patients living in Switzerland with no history of travel to Asia[17]. These findings should remind clinicians of the trend of spreading infection. Along with liver abscesses, the increasing trend of *K. pneumoniae* infections with secondary IE, such as community-acquired pneumonia, cystitis, and splenic abscesses[18-20], albeit uncommon, has raised some concerns.

Although hypervirulent strains of *K. pneumonia* are the main causative pathogens of infection, Wu et al. highlighted that classic strains of *K. pneumonia* also similarly contribute to bacteremia and infections of other body sites[21]. In addition to IE, invasive or hypervirulent strains of *K. pneumonia* are responsible for other extrahepatic complications, such as bacteremia and eye, central nervous system, bone, and soft tissue infections[22,23].

IE involving a calcified aortic valve caused by *K. pneumoniae* has rarely been reported as a complication of incomplete liver abscess treatment. Although TTE initially failed to prove it, this scenario was confirmed through echocardiography during follow-up. Cardiac MRI is another useful tool for the early diagnosis of IE. However, we did not use this modality in our study because of our limited experience. In addition, because of the inadequate laboratory facilities and capabilities of our hospital, we could not perform further pathogenic strain analyses, including hyperviscosity, capsular type, and virulent plasmid gene analyses, which are recommended in future cases involving a similar medical scenario.

Conclusion

Although GNB rarely induce IE, in diabetic and nondiabetic patients with *K. pneumoniae*–caused liver abscesses and bacteremia, concomitant extrahepatic IE infection should raise concerns in daily practice. In this study, we emphasized the ready availability and noninvasive nature of TTE. If a patient's condition prohibits a TEE assessment, then TTE can serve not only as an alternative modality for the diagnosis of IE but also as a crucial tool for following up disease changes, as in our case. However, one-time TTE to rule out IE may be insufficient. Without close TTE follow-up, the progression of aortic root abscesses may remain undetected.

Data Availability Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation, to any qualified researcher.

Ethics Statement

The study was approved by the ethics committee of Shin Kong Wu Ho-Su Memorial Hospital, and the patient's family gave written consent to participate in the study.

Author Contributions

All authors contributed in this patient care, diagnosis and treatment, and in writing this article.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Acknowledgments

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非糖尿病患罹患肺炎克雷伯氏菌肝膿瘍併發感染性心內膜炎及主動脈根膿瘍

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摘 要

格蘭氏陰性菌種肺炎克雷伯氏菌是台灣地區引發肝膿瘍最常見的病原體，然而鮮少有案例導致感染性心內膜炎。我們於此提出一罕見病例，肇因於肺炎克雷伯氏菌肝膿瘍之非糖尿病患，雖經過7個星期的抗生素藥物治療，卻在後續病情追蹤時發生意識改變。腦部核磁共振影像與腦脊髓液穿刺檢驗顯示感染敗血性血栓。並經由連續追蹤胸前心臟超音波掃描，確認併發感染性心內膜炎及主動脈根膿瘍，病患於後續接受主動脈根膿瘍清創手術。因此，對於具有退化性心臟瓣膜的病患，格蘭氏陰性菌種導致的肝膿瘍敗血症仍不可輕忽其惡化擴展為感染性心內膜炎的機率。