

# Invasive *Klebsiella* Syndrome with Liver Abscess and Endogenous Endophthalmitis

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**Background:** Invasive *Klebsiella* syndrome is an emerging infectious condition that frequently involves pyogenic liver abscess (PLA) and metastatic complications such as endogenous endophthalmitis (EE). This condition is often associated with diabetes mellitus and can result in poor visual prognosis despite treatment.

**Case Description:** We present the case of a 53-year-old diabetic female who developed EE secondary to a *Klebsiella pneumoniae* liver abscess. The patient initially presented with fever, fatigue, and abdominal pain, later developing ocular redness and reduced visual acuity. Abdominal ultrasound and computed tomography (CT) confirmed the presence of a multilocular liver abscess. Blood cultures were negative likely due to prior antibiotic use before admission, but *Klebsiella pneumoniae* was isolated from both the liver abscess and intraocular fluid. She was treated with intravenous (IV) meropenem and metronidazole, along with intravitreal vancomycin and ceftazidime. Despite early percutaneous drainage and antibiotic therapy, the patient's vision did not improve, ultimately requiring evisceration.

**Conclusion:** This case highlights the importance of early recognition of invasive *Klebsiella pneumoniae* infections and their metastatic potential. Physicians should consider liver abscess as a possible source of infection in patients presenting with EE. Despite aggressive treatment, the prognosis remains poor, particularly in diabetic patients.

**Keywords:** liver abscess, *Klebsiella pneumoniae*, endogenous endophthalmitis

## Introduction

*Klebsiella pneumoniae* (*K. pneumoniae*), a Gram-negative bacterium, is associated with a wide range of infections, including pulmonary and urinary tract infections, as well as more severe conditions such as liver abscesses, endogenous endophthalmitis, and meningitis.<sup>1</sup> The incidence of *K. pneumoniae*-induced pyogenic liver abscess (PLA) varies geographically, with a significantly higher prevalence in East and Southeast Asia compared to Western countries.<sup>1-3</sup> This syndrome disproportionately affects individuals with diabetes mellitus, which is a major predisposing factor due to impaired immune responses.<sup>4</sup> Compared to classic *K. pneumoniae* infections, which are often nosocomial and linked to multi-drug resistance, hypervirulent strains (hvKP) have enhanced invasiveness even in immunocompetent individuals. These strains are frequently associated with the K1 and K2 serotypes and exhibit a hypermucoviscous phenotype, which can be identified by the positive string test.<sup>5,6</sup> Endogenous endophthalmitis (EE) is an intraocular infection characterized by the involvement of the vitreous, the aqueous humor, or both. EE carries a particularly poor prognosis for visual acuity when it occurs in conjunction with KLA.<sup>7,8</sup> According to a report by Jackson et al, among the entire patient population suffering from EE, 44% retained only light perception (LP) in terms of visual acuity, and a quarter of the patients necessitated an evisceration.<sup>9</sup> On the other hand, Yang reported that in the subset of patients whose EE was secondary to PLA triggered by *K. pneumoniae*, 48% were left with visual acuity at or below the LP level, and 41% required an evisceration.<sup>8</sup> In this report, we present the case of a diabetic female with *K. pneumoniae*-induced liver abscess and EE.

This case underscores the aggressive nature of hypervirulent *K. pneumoniae* and highlights the importance of early recognition and a multidisciplinary treatment approach to prevent devastating complications.

## Case Report

A 53-year-old female patient with pre-existing type 2 diabetes mellitus (HbA1c: 8.52%) presented to the emergency department after two weeks of experiencing fatigue, malaise, pharyngitis, and intermittent fever. On the seventh day after symptom onset, she sought medical care at a local hospital, where she was initially diagnosed with acute pharyngitis. Despite completing a one-week course of amoxicillin/clavulanate, her symptoms showed no improvement. Additionally, three days before her emergency department visit, she developed symptoms including epigastric abdominal pain, ocular redness, and reduced visual acuity in her right eye, all of which contributed to her decision to visit to the emergency department.

Upon her arrival, the patient was febrile with a temperature of 38.5°C. Her heart rate was 110 beats per minute, and her blood pressure was 150/90 mmHg. Respiratory examination revealed normal lung sounds with no evidence of pneumonia. Neurological examination showed no signs of meningitis, such as neck stiffness or altered mental status. However, later imaging revealed multiple brain abscesses, suggesting metastatic septic emboli. The ocular examination revealed a loss of visual acuity in her right eye, measured at hand motion (Figure 1). A relative afferent pupillary defect (RAPD) was observed. Slit lamp examination revealed severe anterior chamber inflammation, corneal edema, hypopyon, and lens opacity. Clinical signs of orbital cellulitis were evident, including proptosis, limitation in eye movements, and periorbital redness and swelling. The patient's condition progressed from endophthalmitis to panophthalmitis, indicated by worsening pain, increased swelling, and changes in the appearance of the eye, such as increased purulent discharge and scleral thinning. Initial laboratory tests are summarized in Table 1. Given that the patient had no history of eye trauma or previous eye surgeries, a presumptive diagnosis of EE in her right eye was made. After obtaining aqueous and vitreous samples, intravitreal injections of vancomycin (1.0 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL) were administered. The patient presented with EE accompanied by abdominal pain, suggesting a possible abdominal source of infection. Therefore, additional abdominal imaging tests were performed. Abdominal ultrasound and computed tomography (CT) scan showed an ill-defined, multilocular low density lesion in segment 3 of her liver, what was confirmed for an abscess (Figure 2). Vitreous cultures came back positive for *K. pneumoniae*. Ultrasound-guided percutaneous drainage of the mass was performed, and the culture of the fluid collected from the liver abscess was also positive for *K. pneumoniae*, confirming the diagnosis of EE secondary to KLA. The antibiotic sensitivities of the cultured *Klebsiella pneumoniae* showed susceptibility to meropenem, ceftriaxone, ciprofloxacin, and gentamicin. The organism was resistant to ampicillin. Given these sensitivities, the patient was treated with intravenous meropenem and metronidazole. The rationale behind the use of intravenous metronidazole was to cover potential anaerobic bacteria that could coexist with *Klebsiella pneumoniae* in polymicrobial infections, particularly given the patient's complex presentation with multiple sites of infection. Further systemic evaluation was performed. Magnetic resonance imaging (MRI) of the brain revealed proptosis, vitritis, orbital cellulitis in the right eye, and multiple brain nodules, suggesting the presence of brain abscesses (Figure 3). A lumbar puncture was also performed. Her cerebrospinal fluid (CSF) appeared clear and colorless, and laboratory test results are summarized in Table 1. No organisms were observed on Gram stain.



**Figure 1** The right eye is significantly erythematous with substantial eyelid swelling (yellow arrow).

**Table 1** Laboratory Characteristics of Patient

| Laboratory Test                    | Result       | Reference Range |
|------------------------------------|--------------|-----------------|
| Hemoglobin (g/L)                   | 131          | 120–170         |
| Hematocrit (%)                     | 41.6         | 34–50           |
| White blood cell (G/L)             | <b>21.26</b> | 4–11            |
| %Neutrophils (%)                   | 74.1         | 45–75           |
| Platelets (G/L)                    | <b>171</b>   | 200–400         |
| Procalcitonin (ng/mL)              | <b>0.9</b>   | <0.5            |
| Blood urea nitrogen (mg/dL)        | 10           | 7–20            |
| Creatinine (mg/dL)                 | 0.76         | 0.7–1.5         |
| HbA1C (%)                          | 8.52         | 4–7             |
| Glucose (mg/dL)                    | 140          | 70–110          |
| Aspartate aminotransferase (U/L)   | <b>52</b>    | 9–48            |
| Alanine aminotransferase (U/L)     | 14           | 5–49            |
| Total bilirubin (mg/dL)            | 0.96         | 0.2–1           |
| Direct bilirubin (mg/dL)           | 0.24         | 0–0.2           |
| Lactate dehydrogenase (U/L)        | 155          | 140–280         |
| Protein (mg/dL)                    | 65           | 50–80           |
| <b>Cerebrospinal fluid</b>         |              |                 |
| Cell count (cells)/mm <sup>3</sup> | 35           |                 |
| Lymphocyte (%)                     | 90%          |                 |
| Other cells (%)                    | 10%          |                 |
| CSF Glucose (mg/dL)                | 65           | 45–80           |
| CSF Protein (mg/dL)                | <b>34.46</b> | 15–45           |

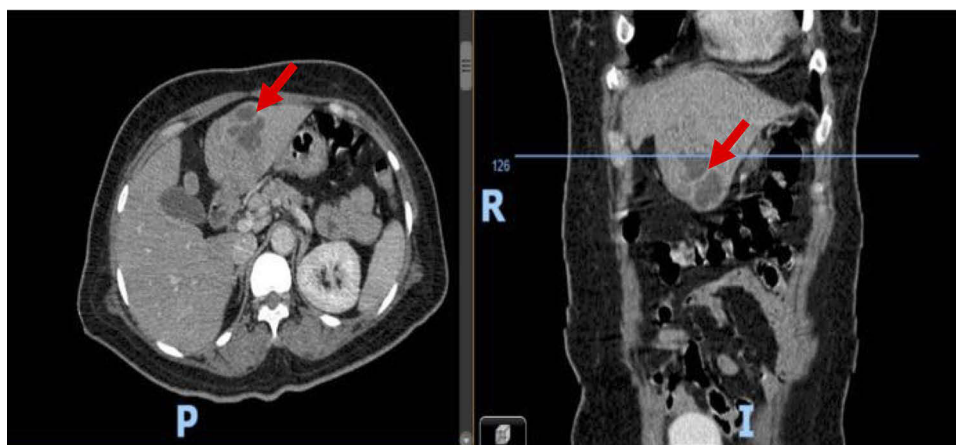
**Abbreviations:** HbA1c, glycated hemoglobin; CSF, cerebrospinal fluid.

Echocardiogram and CT scans of the chest were unremarkable. Despite these interventions, the patient continued to experience escalating eye pain, eyelid swelling, and elevated intraocular pressure. After consultation with the ophthalmology department, the patient underwent evisceration. After the surgery, the eye pain and swelling resolved.

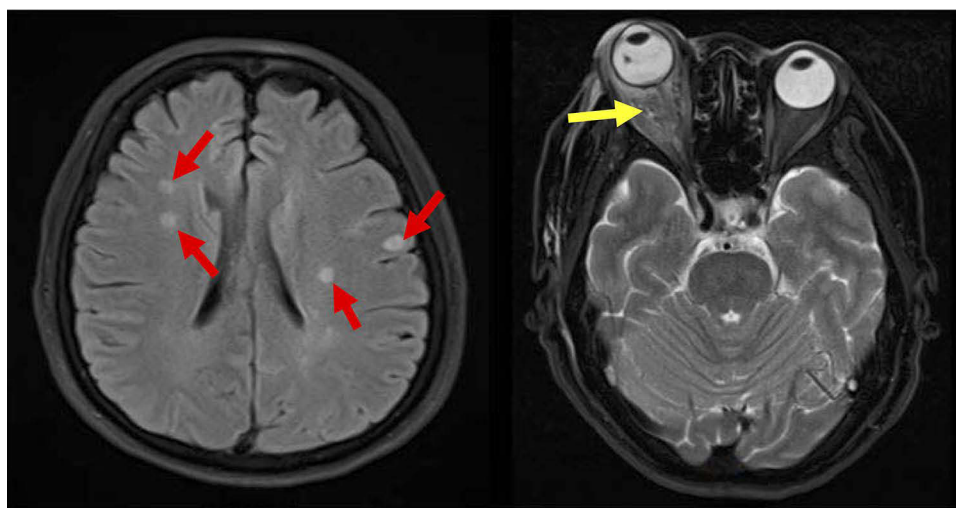
After completing two weeks of IV antibiotic therapy, our patient was discharged in a stable condition and prescribed oral antibiotics, specifically amoxicillin/clavulanate 878/125 mg twice daily for an additional four weeks. By this time, blood cultures returned negative results, and imaging showed a reduction in the size of the liver abscess and the brain lesions. In subsequent follow-up examinations, the patient's other eye remained calm and comfortable, no further complications were reported.

## Discussion

Liver abscesses can be classified into pyogenic, amebic, and fungal abscesses, each requiring different management strategies. Amebic liver abscesses, due to *Entamoeba histolytica*, are more frequent in endemic areas and are treated primarily with metronidazole, with drainage reserved for large or complicated cases.<sup>10</sup> Fungal liver abscesses, often



**Figure 2** Abdominal computed tomography reveals a 30-mm multilocular mass in segment 3 of the liver (red arrow).



**Figure 3** Brain magnetic resonance imaging reveals proptosis, vitritis, and orbital cellulitis in the right eye (yellow arrow), as well as multiple brain nodules (red arrow), suggesting the presence of brain abscesses.

caused by *Candida* species, are typically seen in immunosuppressed patients and require antifungal therapy, with drainage indicated in refractory cases.<sup>10</sup> PLA has a severe prognosis, particularly when caused by *K. pneumoniae*.<sup>10</sup> *K. pneumoniae* is often a constituent of the normal intestinal microbiota in healthy individuals. It has the capability to translocate to the liver via the portal venous system or by breaching the intestinal epithelial barrier.<sup>11</sup> *K. pneumoniae* is the predominant bacterial strain responsible for the development of secondary infections.<sup>8</sup> Patients affected by KLA typically exhibit symptoms such as fever, tenderness in the right upper quadrant of the abdomen, nausea, vomiting, diarrhea, increased white blood cell count, as well as elevated levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and bilirubin. Invasive *Klebsiella pneumoniae* syndrome is characterized by the combination of a PLA with extrahepatic complications. Common metastatic sites include the central nervous system (CNS) (eg, meningitis, brain abscesses), the eyes (endogenous endophthalmitis), and soft tissues (necrotizing fasciitis). This syndrome has been increasingly reported in East and Southeast Asia, with the highest prevalence in Taiwan, South Korea, Singapore, Hong Kong, and Vietnam.<sup>7</sup> The onset of endogenous ocular infection often leads to a rapid worsening in clinical condition. Symptoms of ocular inflammation typically emerge within 2–10 days following the onset of systemic illness, although there can be a delayed onset of several weeks. In certain cases, the

ocular infection may serve as the initial manifestation of sepsis.<sup>12</sup> The entry site of *Klebsiella pneumoniae* is often through the gastrointestinal tract, where it is part of the normal intestinal microbiota. It can translocate to the liver via the portal venous system or by breaching the intestinal epithelial barrier, leading to liver abscess formation. In our case, the patient had been experiencing fever, malaise, and nausea for a duration of two weeks. However, it was the ocular symptoms that prompted the patient to visit the emergency room. The patient sought medical attention only after experiencing visual failure. For patients having sepsis symptoms without a clear infection source, a prompt abdominal ultrasound examination is recommended. Nevertheless, abdominal CT imaging demonstrates higher sensitivity in detecting abscesses compared to ultrasound. Liver abscesses typically present as thick enhancing wall and centrally hypoattenuating lesions. In some instances, they may contain gas, which varied from multiple bubbles to a large gas collection with an associated fluid level. Additionally, a single nonloculated low-density area within the liver may be observed.<sup>13</sup> CT imaging of this patients reveals a multilocular mass with characteristics like abscess on segment 3 of the liver. In terms of microbiological definition, the invasive properties of *K. pneumoniae* are characterized by a hypermucoviscous phenotype, particularly those belonging to capsular serotypes K1 and K2, are known for their ability to evade neutrophil-mediated killing, allowing for hematogenous dissemination.<sup>6</sup> These strains can be identified using the string test, in which bacterial colonies produce a viscous string >5 mm when stretched with an inoculation loop.<sup>6</sup> While the string test is a simple method to screen for hypervirulent *K. pneumoniae*, PCR-based testing for virulence-associated genes such as *rmpA* (regulator of mucoid phenotype A) and *magA* (mucoviscosity-associated gene A) provides a more definitive diagnosis.<sup>6</sup> *K. pneumoniae* EE is confirmed by positive swab culture from the affected eyes or blood cultures.<sup>8</sup> The visual prognosis is generally unfavorable when sight is limited to the extent of perceiving hand motions. On the other hands, individuals who have good vision at the time of diagnosis are more likely to have better visual outcomes.<sup>8</sup> In a study by Yang et al, it was found that a delay of more than two days in initiating treatment for EE led to severe visual outcomes.<sup>8</sup> Similarly, Chen et al reported that several factors were associated with poor visual outcomes, including poor initial visual acuity (OR, 4.6; 95% CI, 1.6–13.4;  $p = 0.004$ ), positive *K. pneumoniae* culture in the aqueous or vitreous humor (OR = 4.9, 95% CI 0.9–26.4,  $p = 0.059$ ), and the detection of EE before liver abscess (OR = 5.1, 95% CI 1.6–26.6,  $p = 0.007$ ). These factors were identified as significant risk factors for unfavorable visual outcomes in patients with EE.<sup>14</sup> Our patient exhibited indicators of an unfavorable prognosis. Specifically, ocular symptoms had persisted for 3 days before the diagnosis of endogenous endophthalmitis was made, and visual acuity was already significantly impaired upon admission. Furthermore, culture analysis of the aqueous humor confirmed the presence of *K. pneumoniae*. Notably, the patient was immediately administered intravenous and intravitreal antibiotics before the accurate diagnosis of EE was established. Despite these interventions, the patient continued to experience escalating eye pain, swelling of the eyelids, and elevated intraocular pressure, ultimately necessitating evisceration.

Our case adds to the existing body of knowledge by highlighting the importance of early recognition and multidisciplinary management in patients presenting with concurrent liver abscess and endogenous endophthalmitis, particularly in diabetic patients. This case underscores the need for vigilance in patients presenting with both abdominal and ocular symptoms, contributing to improved diagnostic and therapeutic strategies.

The organs most commonly affected by *K. pneumoniae* in cases of extrahepatic syndrome, in decreasing order of occurrence, are the lungs, ocular system, central nervous system and rare presentations, including prostatic abscesses and endocarditis.<sup>6</sup> In our case, CT scans of the chest were unremarkable, but MRI of the brain showed multiple brain nodules which suggested brain abscess. However, our patient demonstrated a normal cell count, glucose level and protein level in the CSF, and no organisms were detected upon Gram stain examination. This observation is understandable considering that the patient had already initiated antibiotic treatment at the time of specimen collection.

Diabetes is a major risk factor for developing *K. pneumoniae* EE in patients with a liver abscess.<sup>15</sup> According to Lin et al, individuals with poorly controlled type 2 diabetes have difficulty in eliminating *K. pneumoniae* serotypes K1 or K2.<sup>16</sup> Lin et al also found a high occurrence of *K. pneumoniae* serotypes in liver abscesses that are resistant to phagocytosis. This resistance contributes to their prevalence in liver abscess cases and specifically in endophthalmitis.<sup>17,18</sup> Our patient had poor glycemic control with her hemoglobin A1C measurement of 8.52%, indicating ineffective management of blood glucose levels over the past three months.



The decision to perform drainage for a liver abscess depends on several factors, including abscess size, location, and the patient's clinical condition. Percutaneous drainage is generally recommended for abscesses measuring  $\geq 5$  cm, as these larger abscesses are less likely to resolve with antibiotics alone.<sup>19</sup> For patients with severe sepsis or an APACHE II score of  $\geq 15$ , early percutaneous drainage is strongly advised to control the infection source and reduce the risk of systemic complications.<sup>19</sup> In this case, ultrasound-guided percutaneous drainage was performed based on established clinical criteria. The patient had a 30-mm multilocular liver abscess, which, despite being at the threshold for drainage, posed a high risk of poor antibiotic penetration and persistent infection. Additionally, the presence of severe sepsis, endogenous endophthalmitis, and brain abscesses indicated hematogenous dissemination, necessitating rapid source control. Given that empirical antibiotics had failed and blood cultures were negative, aspiration provided microbiological confirmation of *Klebsiella pneumoniae*, allowing targeted therapy. In addition to early percutaneous drainage of the liver abscess, the empirical choice of antibiotics in our case and the duration of treatment align with existing literature.<sup>18</sup> We administered meropenem to the patient for several reasons. Firstly, the patient was in a critical condition with sepsis and bacteraemia. Meropenem is effective against a broad range of bacteria, making it suitable for treating severe infections. Secondly, the patient had multiple infection sites, involving the liver, right eye, and brain. Meropenem is known for its ability to penetrate various tissues, including the central nervous system, making it an appropriate choice for treating infections in these locations. The duration of treatment is generally guided by the resolution of fever, the size of liver abscess and the number of neutrophils. In the provided case, a complete two-week course of antibiotic therapy, which incorporate meropenem and metronidazole, was administered. The failure of amoxicillin/clavulanate in this case was likely due to  $\beta$ -lactamase production by *K. pneumoniae*, rendering it resistant to this antibiotic.<sup>1</sup> Additionally,  $\beta$ -lactam antibiotics have poor penetration into multiloculated liver abscesses, necessitating both higher antibiotic concentrations and drainage.<sup>1,10,11</sup> The initial use of amoxicillin/clavulanate delayed appropriate therapy, highlighting the importance of early microbiological diagnosis and targeted antimicrobial treatment. For EE, intravitreal antibiotics are mandatory to achieve therapeutic intraocular concentrations. The standard regimen for bacterial endophthalmitis includes intravitreal vancomycin (1 mg/0.1 mL) and ceftazidime (2.25 mg/0.1 mL).<sup>20</sup>

## Conclusion

In conclusion, this case report serves as a reminder that when encountering patients with endogenous endophthalmitis, physicians should consider the possibility of a liver abscess. Physicians should be aware of not only the capacity for extrahepatic septic metastases but also their associated complications. Immediate administration of a comprehensive multidisciplinary therapy is crucial in order to prevent complications of liver abscess, including endogenous endophthalmitis.

## Ethical Approval and Consent for Publication

Written informed consent has been provided by the patients to have the case details and any accompanying images published. Ethical approval is not required for this study according to the guidelines, and institutional approval was not required to publish the case details.

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## Disclosure

The authors declare they have no competing interest for this study.

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