Endogenous endophthalmitis and liver abscess syndrome secondary to *Klebsiella pneumoniae*: report of three cases from Qatar

Ahmed AR Mohamad Al Ani¹, Abdel-Naser Elzouki¹, Ali Rahil¹, Fouad Al-Ani²

¹Departments of Medicine, Hamad General Hospital, Hamad Medical corporation, Weil Cornell Medical College, Doha, Qatar
²Accident and Emergency, Hamad General Hospital, Hamad Medical corporation, Weil Cornell Medical College, Doha, Qatar

**1. Introduction**

*Klebsiella pneumoniae* (*K. pneumoniae*) is an important cause of community and nosocomial–acquired infection worldwide[1]. It is most frequently causes infection in hospitalized patients and occurs primarily in those who have impaired host defenses, including patients with diabetes mellitus, alcoholism, malignancy, immunosuppressive therapy[2]. It is, however, an uncommon cause for community–acquired infections in individuals without any underlying predisposing medical conditions[3].

Endophthalmitis is a severe inflammation of the internal coats of the eye. It can be caused by exogenously introduction of contaminating microorganisms via penetrating trauma or postoperative, or endogenously via hematogenous spread from infected distant sites. Patients with impaired host defense mechanisms, including those with diabetes mellitus, are more prone to this complication[4]. Different etiologic microorganisms have been found to cause endophthalmitis that include bacteria and fungi. In patients with diabetes mellitus, *K. pneumoniae* is the most prevalent microorganism[5]. Endogenous endophthalmitis is a rare but devastating disease that may frequently results in visual loss despite appropriate and early antibiotic treatment. Recent reports have suggested an increased incidence of endogenous endophthalmitis in East Asia, particularly in Taiwan, where the major source of infection has been liver abscess secondary to *Klebsiella pneumoniae*. Here we report three cases who presented in Qatar with severe endogenous endophthalmitis associated with *Klebsiella pneumoniae* septicemia secondary to pyogenic liver abscess in a diabetes mellitus setting.

**ABSTRACT**

Endogenous endophthalmitis is a rare but devastating disease that may frequently results in visual loss despite appropriate and early antibiotic treatment. Recent reports have suggested an increased incidence of endogenous endophthalmitis in East Asia, particularly in Taiwan, where the major source of infection has been liver abscess secondary to *Klebsiella pneumoniae*. Here we report three cases who presented in Qatar with severe endogenous endophthalmitis associated with *Klebsiella pneumoniae* septicemia secondary to pyogenic liver abscess in a diabetes mellitus setting.
2. Case reports

2.1. Case 1

A 47-year old Filipino male who was previously healthy until one month prior to his presentation, when he started to have productive cough with yellowish and occasionally blood stained sputum associated with fever, headache, left sided pleuritic chest pain, and right eye pain and redness with decrease vision over the last two weeks. He also admitted to have lower abdominal pain with dysuria, nausea and vomiting. No history of recent travel abroad. There was no relevant family or occupational history. On examination, the patient’s temperature was 39.3 °C, blood pressure was 107/65 mmHg, and pulse was in sinus rhythm with a rate of 110 beats per minute. His oxygen saturation was 95% on room air. General examination was unremarkable except for the right eye which was congested with pus in the anterior chamber and loss of vision, findings were consistent with endophthalmitis. The right pupil was normal in size and reactive to light. The left eye was normal. Chest examination was remarkable for left basal coarse crackles. Abdominal examination revealed tenderness in the right hypochondrium with tender palpable liver 16 cm below costal margin. Examination of other systems was unremarkable.

Laboratory investigations revealed white cell count 22.3×10^3 cells/mm^3 (4–10×10^3 cells/mm^3), hemoglobin 14.3 g/dL (13–17 g/dL), platelets 79×10^3 per cubic millimeter (150–400×10^3 per cubic millimeter), erythrocyte sedimentation rate 90 mm/h, random blood glucose concentration 23.4 mmol/L (3.3–5.5 mmol/L), glycosylated hemoglobin (HbA1c) 11.5%, negative ketone bodies in the blood, serum sodium (Na) 125 mmol/L (135–145 mmol/L), serum chloride (Cl) 94 mmol/L (96–110 mmol/L), serum potassium (K) 3.9 mmol/L (3.6–5.1 mmol/L), corrected serum calcium (Ca) 3.06 mmol/L (2.1–2.6 mmol/L), blood urea 8.7 mmol/L (1.7–8.3 mmol/L), creatinine 87 µmol/L (62–124 µmol/L), total serum protein 55 g/L, albumin 29 g/L (35–50 g/L), total bilirubin 51 µmol/L (3.5–24 µmol/L), alkaline phosphatase (ALP) 226 IU/L (40–129 IU/L), alanine aminotransferase (ALT) 34 IU/L (<40 IU/L), aspartate transaminase (AST) 18 IU/L (<40 IU/L), C-reactive protein 328 mg/L (<5 mg/L), parathyroid hormone 89 pg/mL (15–65 pg/mL), and normal serum cortisol level (614 nmol/L) as well as lipid and coagulation profiles. Blood film revealed marked neutrophilic leukocytosis with toxic neutrophils and few reactive lymphocytes. Chest X-ray showed multiple bilateral cavitary lesions in the right upper and middle lung zones and left middle and lower lung zones (Figure 1). Blood cultures, from both aerobic and anaerobic bottles, showed Gram-negative bacilli (K. pneumoniae). Three samples for sputum examination for acid-fast bacillus were negative. Urine microscopy remarkable only for white blood count 370 leukocytes/µL and the urine culture reported on growth in 48 h. Serology for HIV and viral hepatitis B and C were negative.

Abdominal ultrasound showed an ill-defined echogenic mass sized 5 cm×4.6 cm in the right liver lobe and another one of 2.7 cm×2.5 cm caudal to the first lesion. CT scan chest and abdomen show bilateral pleural effusion with multiple opacities in lungs fields and enlarged mediastinal lymph node as well as findings consistent with liver abscess and small prostate abscess (Figure 2).

CT Chest-Abd-Pelvis

The patient was stabilized with intravenous fluids and despite control of diabetes with insulin and antibiotic treatment with intravenous ertapenem for 16 d, the right eye vision was lost. Hypercalcemia resolved and serum calcium returned back to normal. Nuclear scan of the neck revealed small ectopic area of abnormal uptake in the right upper mediastinum, and the patient was reluctant to accept surgical
2.2. Case 2

A 48-year old Philipino old male, known case of diabetes mellitus since 1996 on metformin presented to the emergency department with left eye pain and progressive loss of vision. The pain was localized and there was no discharge. This was preceded by a one week history of nausea, vomiting and high grade fever, which comes on and off and associated with night chills. Patient then noticed that his urine became dark in color associated with bilateral painful leg swelling. Vital signs examination revealed temperature 39.4 °C, blood pressure 140/60 mmHg, pulse was in sinus rhythm with a rate of 120 beats per minute and oxygen saturation 100% on room air. Eyes examination showed normal right eye but congested left eye with tender sclera, surrounded by erythema and associated with marked reduction of the vision. Apart from bilateral tender leg swelling and bilateral decrease air entry in both lungs by auscultation, the rest of general and systemic examinations were unremarkable. The patient was referred urgently to the ophthalmologist.

B–scan ocular ultrasound of the left eye showed superior choroidal swelling, hyperechoic responses in the vitreous humour, and a flat retina, the right eye was grossly normal with moderate non–proliferative diabetic retinopathy on fundal examination and he was diagnosed as left eye endophthalmitis. Initial blood tests showed a white blood count 17.2×10³ cells/mm³ (4–10×10³ cells/mm³), hemoglobin 14.63 g/dL (13–17 g/dL), platelets 42.5×10³ per cubic millimeter (150–400×10³ per cubic millimeter), D–Dimer 424 mg/L (normal up to 0.55 mg/L), a random blood glucose concentration of 17.2 mmol/L (3.3–5.5 mmol/L), positive serum ketone bodies 2+, serum Na 128 mmol/L (135–145 mmol/L), serum Cl 87 mmol/L (96–110 mmol/L), serum K 4.3 mmol/L (3.6–5.1 mmol/L), serum bicarbonate 18 mmol/L (21–28 mmol/L), creatinine 87 µmol/L (62–124 µmol/L), total serum protein 48 g/L, albumin 21 g/L (35–50 g/L), total bilirubin 101 µmol/L (3.5–24 µmol/L), serum ALP 176 IU/L (40–129 IU/L), serum ALT 121 IU/L (0–40 IU/L), serum AST 50 IU/L (0–40 IU/L), HbA1c 10.7%, serum amylase 105 IU/L (13–53 IU/L). Blood cultures, from both aerobic and anaerobic bottles, showed Gram–negative bacilli (K. pneumoniae). Liver aspirate culture was also positive for K. pneumoniae. Serology for HIV and viral hepatitis B and C were negative.

Chest CT revealed bilateral prominent interstitial markings with small patchy opacity of left zone (Figure 3).

Abdominal ultrasound examination showed a well defined loculated right lobe liver abscess of the size of 4.3 cm×3.5 cm, in which a drain was inserted and 15 mL of very thick (tooth paste like) dark pus was drained. Echo–cardiography and ultrasound Doppler of both lower limbs were normal.

CT scan abdomen showed liver abscess (Figure 4). MRI examination of both legs showed diffuse cellulitis of the left leg with collection (oedema) (Figure 5). Bone scan didn’t show osteomyelitis.

Figure 3. CT scan chest small patchy opacity of left zone.

Figure 4. CT scan abdomen shows liver abscess with drainage tube inside the abscess.

Figure 5. MRI examination of both legs shows diffuse cellulitis of the left leg with inflammatory changes, no intramuscular abscess or collection.

The patient was stabilized with intravenous fluid and was empirically given intravenous tazocin and ciprofloxacin.
then stopped and started on ceftriaxon 2 g intravenous injection (IV) once a day. The ophthalmologist was started him on atropine eye drops, injection of vancomycin 1000 mg and ceftazidine 500 mg in left eye and continued on vancomycin and ceftazidine eye drops. The patient was scheduled for vitrectomy but he refused. The treatment was continued for two weeks, and the liver abscess was drained, repeated blood cultures were negative and patient became a febrile and he was discharged.

Figure 6. MRI paraspinal and intraspinal shows epidural abscess causing cord compression.

2.3. Case 3

A 51-year old Philippine male patient with no significant past medical history presented to the emergency department with high grade fever and yellow discoloration of the sclera of two weeks duration, this was proceeded by dry cough. The patient is ex-smoker, not alcohol consumer. On examination, temperature was 38.6 °C, blood pressure was 130/78 mmHg, and pulse was in sinus rhythm with a rate of 110 beats per minute. His oxygen saturation was 98% on room air, he had yellow sclera, chest auscultation revealed bilateral left lower zone crepitation’s and abdominal examination revealed hepatomegaly (liver span 15 cm). The other systemic examinations were unremarkable.

Initial blood tests showed a white cell count 17.3×10^3 cells/mm³ (4–10×10^3 cells/mm³), hemoglobin 11.1 g/dL (13–17 g/dL), platelets 150×10^4 per cubic millimeter (150–400×10^4 per cubic millimeter), normal blood urea and serum creatinine, and a random glucose concentration of 14 mmol/L (3.3–5.5 mmol/L) with positive serum ketone bodies 2+. The serum Na 129 mmol/L (135–145), serum Cl 90 mmol/L (96–110 mmol/L), serum K 3.7 mmol/L (3.6–5.1 mmol/L), bicarbonate 25 mmol/L, total serum protein 68 g/L, albumin 21 g/L (35–50 g/L), total bilirubin 122 µmol/L (3.5–24 µmol/L), ALP 204 IU/L (40–129 IU/L), ALT 81 IU/L (0–40 IU/L), AST 50 IU/L (0–40 IU/L), HbA1c 9.8%, serum amylase 16 IU/L (13–53 IU/L). Serology for HIV and viral hepatitis B and C markers as well as anti-amoeba antibody were negative. Blood cultures, from both aerobic and anaerobic bottles, showed Gram-negative bacilli (K. pneumoniae).

Ultrasound examination showed multiple well-defined heterogeneous predominantly hypo echoic lesions at the right lobe of the liver representing multiple abscesses, the largest measure 8.5 cm×6.7 cm with surrounding edema, and ultrasound guided drain was inserted. Liver aspirate culture was positive for K. pneumoniae. Chest X-ray showed perihilar and paramediastinal patchy shadowing, an opacity in the left apical, right paracardiac region and left supradiaphragmatic region, impression multiple areas of inflammatory process. Echo cardiography was normal.

The patient was empirically given ceftriaxon 2 g IV once a day and IV metronidazole three times a day (was discontinued after blood culture results) for two weeks.

Two days after admission, patient complained of decreased vision in the right eye, and was started by the ophthalmologist on cyclopentolate eye drops and intravitreal antibiotic. Patient improved, became afebrile, his vision back to normal and blood sugar was controlled with insulin. He was discharged on oral cefuroxime to complete 6 weeks antibiotics, oral antidiabetic therapy and prednisolone eye drops. Blood culture before discharge was negative.

In the first follow up, visit two weeks after discharge, CT scan abdomen was repeated and showed complete resolution of the liver abscess.

Six weeks after discharge, the patient presented with severe low back pain for one week followed by lower abdominal pain and urinary retention one day prior to his presentation. His back pain was not radiating to the lower limbs and not associated with numbness, but aggravated by any movement and relieved by lying down. Patient had 20 kg weight loss in the last three months. On examination, the temperature was 36.9 °C, blood pressure was 139/84 mmHg, and pulse was in sinus rhythm with a rate of 72 beats per minute. His oxygen saturation was 99% on room air. There was paraspinal tenderness in the mid thoracic region. Examination of the lower limbs, showed increase tone and decrease power (Grade 3/5) with brisk reflexes and non sustained clonus. Other systemic examinations were unremarkable.

Blood tests were remarkable for a white cell count 11.5×10^3
cells/mm³ (4–10 cells/mm³), erythrocyte sedimentation rate 74 mm/h, a random blood glucose concentration of 23.4 mmol/L (3.3–5.5 mmol/L), HbA₁c 9.8%, total serum protein 55 gm/L, albumin 29 gm/L (35–50), serum Na 125 mmol/L (135–145 mmol/L), serum Cl 94 mmol/L (96–110 mmol/L), serum K 3.9 mmol/L (3.6–5.1 mmol/L), total bilirubin 51.4 µmol/L (3.5–24 µmol/L), with normal serum transaminase and international normalized ratio.

Urine culture revealed no growth and sputum for acid–fast bacillus (three samples) were negative. Tuberculin test was positive (18 mm). Chest X-ray showed scoliotic deformity at the dorsal spine without obvious lung parenchymal lesions. There was also a paraspinal shadow at the level of D8–D10 but vertebrae looked normal. Abdominal ultrasound showed focal hypoechoic lesion sequelae of inflammatory changes. CT scan chest revealed multiple cavities and nodular opacities with fibrotic band in the lungs, and an osteolytic lesion at D9 and D10 vertebral bodies with anterior longitudinal ligament calcification. MRI showed spines paraspinal and intraspinal epidural abscess (T9–T10) that cause cord compression (Figure 6).

Fine needle aspiration from the paraspinal abscess revealed acute inflammatory process with granulation tissue. Culture was negative for bacterial growth and acid fast bacilli. Polymerase chain reaction of aspirate was also negative for Mycobacterium tuberculosis.

Patient was assessed by neurosurgeon and underwent laminectomy. Post laminectomy (D9 and D10) histopathology revealed fragment of soft tissue, bony fragment and fibro–cartilaginous tissue showing mild acute and chronic inflammation with no granuloma or malignant cells. Patient received IV antibiotics (ceftriaxone 2 g once a day with metronidazole 500 mg three times a day for 3 weeks).

Patient was discharged with gradual improvement in the lower limbs weakness (on Foley catheter) and transferred for rehabilitation unit for physiotherapy. Patient advised to continue IV ceftriaxone for another 3 weeks as an outpatient, in addition to metformin (1 g twice daily), deep vein thrombosis prophylaxis (dalteparin 2500 units subcutaneous) and to follow with the infectious disease team for positive tuberculin test.

3. Discussion

Although nosocomial K. pneumoniae infections occur worldwide, some types of community–acquired infections have been described in only few geographic areas. It includes K. pneumoniae, urinary tract infection and, primarily in East Asia, particularly in Taiwan, a pyogenic liver abscess syndrome that typically associated with endogenous endophthalmitis[3,5–7]. Most cases of endogenous endophthalmitis are due to fungal infection and gram positive bacteria in immune compromised patients. Endogenous endophthalmitis secondary to K. pneumoniae, a gram negative bacterium, is a rare but often devastating septic metastatic infection. It accounts for 2%–8% of all endophthalmitis cases[3]. Diabetes mellitus has been identified as the major risk factor for the development of endogenous endophthalmitis secondary to K. pneumoniae in patients with liver abscesses and this was present in up to 40% of the cases[5,12–13]. One of our three patients (case 2) was a known case of diabetes mellitus for 15 years and the other two patients were diagnosed as having diabetes mellitus for the first time during the workup of their presentations. It was reported that in type 2 diabetes mellitus with poor glycemic control there is impaired phagocytosis of capsular serotype K1 or K2 K. pneumoniae and there is high prevalence of phagocytic–resistant capsular serotype in liver abscesses[3,13,14].

Blood cultures in the three cases were positive for K. pneumoniae and sensitive to all antibiotics except ampicillin and this phenomenon was similar to the previously reported cases from USA[15].

Five major virulence factors of K. pneumoniae are known to contribute to the pathogenesis of infection. These are the capsular serotype, hypermucoviscousity phenotype, lipopolysaccharide, siderophores, and pili[3,16]. Among all, the capsular serotype (in particular the strain K1) was found significantly associated with pyogenic liver abscess and endogenous endophthalmitis[3,17]. Typically, this strain is capable of producing a mucoviscous exopolysaccharide web when a loop is passed through a colony[17,18]. Hence the gene, encode a 43 kD outer membrane protein, was named mucoviscosity–associated gene (MagA) and was located within an operon that is specific to the serotype K1 capsular polysaccharide gene clustered[19]. The K. pneumoniae strain which carries this gene is more resistant to human complement–mediated serum and phagocytosis killing suggesting an enhanced virulence and pathogenicity[20]. The serotype of the isolated K. pneumoniae in our patients was not performed but the virulent and devastating clinical course of the disease in the three cases may suggest the presence positivity of K1 strain and MagA gene. Rapid detection of this hypervirulent strain that causes this syndrome allows earlier diagnosis and treatment.

Occasionally, the ocular infection is the presenting manifestation of sepsis in patients with disseminated K. pneumoniae infection[12]. And it was the presenting manifestation in the first and second case. The visual outcome in these two patients was poor in spite of intensive therapy by the ophthalmologist and this is similar to other case reports[20–21]. The outcome of vision in the third case was complete recovery of the affected eye and this is
probably because of aggressive and immediate intervention by the ophthalmologist because there was no delay as the patient developed the eye symptoms while in the hospital.

In conclusion, we report three cases who presented in Qatar with severe endogenous endophthalmitis associated with K. pneumoniae secondary to pyogenic liver abscess in a diabetes mellitus setting. A high clinical suspicion allows immediate diagnosis and treatment. Early antibiotic therapy remains the cornerstone of treatment. It suggests that this syndrome is becoming a global health problem and is not confined in East Asia. This devastating disease should be suspected in diabetic patients presented with Klebsiella liver abscess and vigorous search for intraocular infection, as early and appropriate antibiotic treatment could save the visual loss of such patients.

Conflict of interest statement

We declare that we have no conflict of interest.

References