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A UNIQUE CASE OF HYPERVIRULENT *KLEBSIELLA PNEUMONIAE* INVASIVE SYNDROME WITH ENDOGENOUS ENDOPHTHALMITIS AND LEFT RENAL VEIN THROMBOSIS WITHOUT LIVER ABSCESS

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ABSTRACT

Introduction: This case report presents a rare instance of hypervirulent *Klebsiella pneumoniae* invasive syndrome (KPIS) without hepatic involvement. It highlights an atypical presentation as this syndrome is characterized by liver abscesses.

Case Presentation: A 54-year-old female of South Asian descent presented to the emergency department with abdominal pain, fever, chills, nausea, and vomiting. Lab investigations showed hyperglycaemia, leukocytosis, and elevated procalcitonin. Imaging revealed bilateral acute pyelonephritis with early abscess formation in the left kidney, bilateral pleural effusions, diffuse multi-lobar consolidations, minimal ascites, and left renal vein thrombosis. The patient was treated as a case of septic shock secondary to hypervirulent *K. pneumoniae* with complications evolving into acute pyelonephritis and endogenous endophthalmitis. *K. pneumoniae*, known for its polysaccharide capsule, can lead to severe complications in immunocompromised patients, such as endogenous endophthalmitis, liver abscess, and pyelonephritis. Endophthalmitis, a critical ocular emergency, can result in permanent vision loss. The patient's ocular outcomes remain uncertain due to a lack of follow-up, but prompt interdisciplinary intervention led to the resolution of other comorbidities.

Conclusion: This case highlights the importance of considering hypervirulent *K. pneumoniae* as a cause of severe infection without liver abscess. It also underscores the importance of immediate multidisciplinary management to address the systemic complications associated with this infection and the importance of connecting different symptoms to one aetiology.

KEYWORDS

Hypervirulent, *Klebsiella pneumoniae*, *Klebsiella pneumoniae* invasive syndrome, endogenous endophthalmitis

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LEARNING POINTS

- *Klebsiella pneumoniae* invasive syndrome (KPIS) should be considered in patients with positive *Klebsiella pneumoniae* infection affecting more than one organ system.
- KPIS may present atypically, such as in the absence of liver abscesses and with the presence of thrombosis.
- Hypervirulent and hypermucoviscous strains of *Klebsiella pneumoniae* should be considered in cases of KPIS.

INTRODUCTION

Klebsiella pneumoniae, a Gram-negative bacillus, is commonly associated with respiratory and urinary tract infections[1]. Diminished immune responses, especially in patients with diabetes mellitus, are identified as a predisposing factor. Hypervirulent *K. pneumoniae*, initially found in the Asia-Pacific region, is now recognized globally and typically affects patients of Asian descent[2]. This strain is associated with a rare clinical condition known as *Klebsiella pneumoniae* invasive syndrome (KPIS), characterized by a primary liver abscess with metastatic infection[1]. This is the first case report of a patient with hypervirulent *K. pneumoniae* without liver abscess in the Middle East.

CASE DESCRIPTION

A 54-year-old South Asian female presented to our emergency department with a 4-day history of epigastric pain, nausea, vomiting, and fever. On arrival, vitals showed a high-grade fever of 39.5 °C, heart rate of 134 bpm, respiratory rate of 20 bpm, and borderline blood pressure of 98/62 mmHg. Despite appearing ill and diaphoretic, she was alert and oriented, with no findings on examination to localize the potential source of infection. She was admitted to the High Dependency Unit (HDU) as a case of impending septic shock; initially resuscitated with crystalloid fluids and started on broad-spectrum antibiotics. Initial blood investigations were remarkable for high septic markers *(Table 1)*, and pan cultures were sent. A contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis was done to rule out an intra-abdominal source and revealed bilateral acute pyelonephritis with early abscess formation in the left kidney, along with left renal vein thrombosis and bilateral pleural effusion *(Fig. 1)*. Initial transthoracic echocardiogram showed no endocardial vegetations. Following initial resuscitation, the patient developed pulmonary oedema despite receiving only 30 ml/kg intravenous (IV) fluids. Chest X-ray showed diffuse lung consolidations with bilateral pleural effusions. IV fluids were judiciously reduced, and her respiratory distress improved with IV diuretics. A repeat echocardiogram showed normal cardiac function and valve morphology.

Empirical antibiotics were escalated to IV carbapenems as septic markers were persistently elevated, then adjusted per antibiogram, with the following course: meropenem and doxycycline for 5 days, then ertapenem for 3 days, and finally ceftriaxone. Anticoagulation for provoked left renal vein thrombosis was initially withheld due to thrombocytopenia. CT chest with contrast showed septic pulmonary emboli *(Fig. 2)*, and repeat platelet count improved, after which low molecular weight heparin was started. The newly diagnosed diabetes mellitus required insulin therapy. Subsequently, the patient developed acute left eye pain with decreased visual acuity, peri-orbital pain, conjunctival injection, and a hypopyon. The ophthalmology team diagnosed her with left eye endogenous endophthalmitis (EE); she was treated with moxifloxacin, tobramycin and cyclopentolate eye drops. A B-scan revealed subretinal collections suggestive of retinochoroidal abscess, prompting the administration of intravitreal antibiotics - vancomycin and ceftazidime. Despite initial improvement, her vision worsened, leading to a left eye vitrectomy.

Despite adequate antibiotics, clinical deterioration prompted a chest X-ray revealing pleural effusions. A pleural

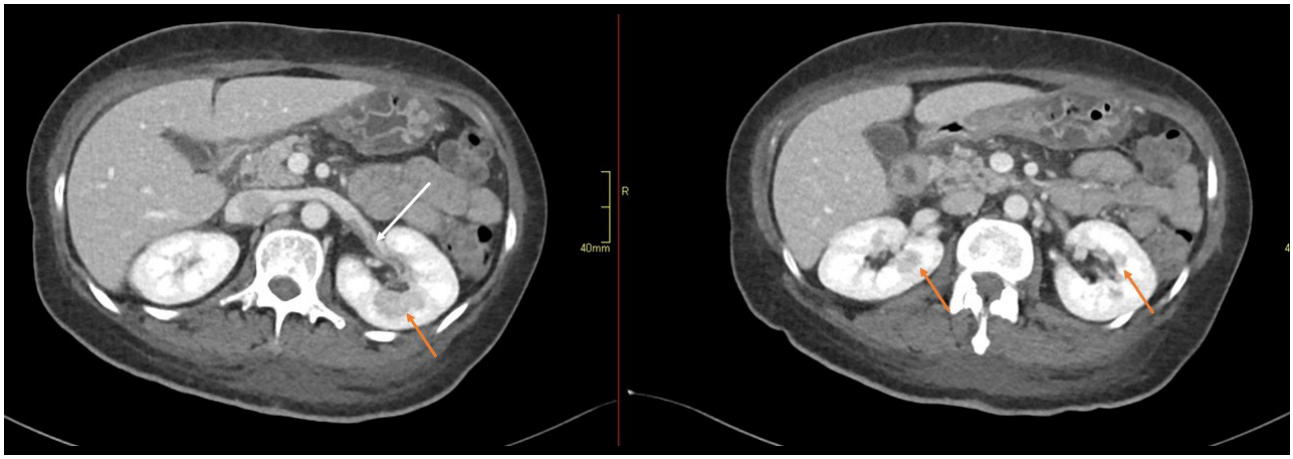

Figure 1. Contrast-enhanced computed tomography scan showing bilateral patchy renal parenchymal hypodensities suggestive of pyelonephritis (orange arrows) and left renal vein thrombosis (white arrow).

Test	On admission	After 2 weeks	After 4 weeks	Normal values
POCT glucose (mg/dl)	252	231	174	65-140
HbA1c (%)	14	-	-	< 5.7
White blood cell count (x10^3/µl)	20.5	9	7.6	3.6-11
Haemoglobin (g/dl)	13.2	11.1	10	12-15
Platelets (x10^3/µl)	101	550	436	150-410
Procalcitonin (ng/ml)	30.83	0.14	0.07	< 0.1
C-Reactive protein (mg/l)	299.9	144.4	45	< 5
Serum ketones (mmol/l)	3.5	-	-	0.1-0.6
Creatinine (mg/dl)	0.65	0.38	0.37	0.5-0.9
eGFR (ml/min/1.73 m^2)	104.6	119	119.8	> 60
Lactate dehydrogenase (U/l)	296	201	211	105-222
Troponin T (ng/l)	9	N/A	N/A	< 14
NT-proBNP (pg/ml)	2,426	92.16	N/A	< 125
Prothrombin time (s)	14.8	N/A	N/A	11-14
Amylase (U/l)	24	N/A	N/A	28-100
Total bilirubin (mg/dl)	0.96	0.22	N/A	0-1
Alkaline phosphatase (U/l)	142	95	N/A	35-104
Alanine transaminase (U/l)	18	7	N/A	0-31
Total protein (g/dl)	6	8	N/A	6.6-8.7
Albumin (g/dl)	2.8	2.6	2.6	3.4-4.8
Globulin (g/dl)	3.2	5.4	N/A	2.8-3.4
Sodium (mmol/l)	133	136	139	136-145
Potassium (mmol/l)	3.4	3.5	3.7	3.3-4.8
Chloride (mmol/l)	103	98	101	98-108
Bicarbonate (mmol/l)	18.3	27.3	27.7	20-28
Urea (mmol/l)	35	9	13	12-40
Anion gap (mmol/l)	11	10	11	6-14
Urine protein	1+	N/A	N/A	Negative
Urine glucose	4+	4+	N/A	Negative
Urine bilirubin	-	-	N/A	Negative
Ketone (urine routine)	3+	N/A	N/A	Negative
Budding yeast	N/A	N/A	3+	Negative
Blood culture	-	N/A	N/A	Negative
Urine culture	*Klebsiella pneumoniae*	*Candida krusei*	*Enterococcus faecium*, *Candida krusei*, *Candida dubliniensis*	Negative
Respiratory culture	N/A	*Candida albicans*	*Candida albicans*	Negative

Abbreviations: HbA1c, hemoglobin A1C; POCT, point-of-care testing; eGFR, estimated glomerular filtration rate; NT-proBNP, N-terminal pro b-type natriuretic peptide; N/A, not available as it was not performed.

Table 1. Lab investigations with results at 3 different timeframes: on admission, after 2 weeks, and after 4 weeks.

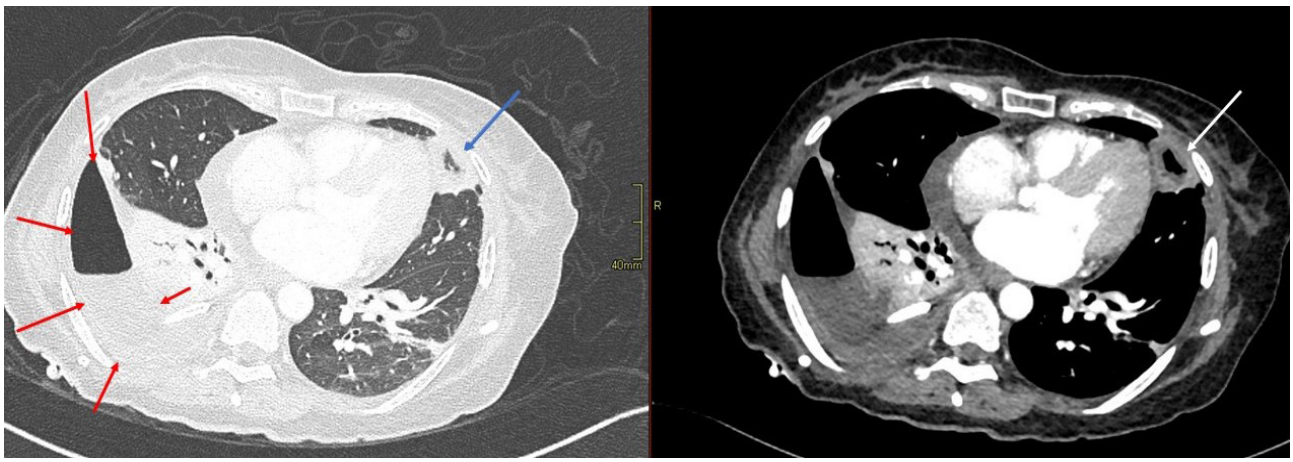

Figure 2. Multiple variable-sized peripheral nodular densities showing hypodense centre indicative of possible early necrotic changes. In particular, empyema (red arrows), lung window (blue arrow) and venous phase (white arrow) demonstrate septic emboli.

tap was performed to rule out pleural tuberculosis, and an empirical anti-tuberculosis treatment (ATT) was started with levofloxacin. The pleural fluid was reported as negative for acid fast bacilli. The patient spiked fever again, pan-cultures were repeated, and antibiotics were escalated to piperacillin-tazobactam. Urine and respiratory culture grew *Candida krusei* and *Candida albicans* respectively, thus fluconazole was added. A respiratory swab was collected which tested positive for human metapneumovirus. Following this, the patient developed a right pyopneumothorax, requiring an intercostal drain insertion.

With regard to the clinical outcomes following treatment with antibiotics and vitrectomy, the hypopyon resolved but she was advised to continue with prednisolone, brimonidine and moxifloxacin eye drops and follow-up in the out-patient clinic. The pyelonephritis resolved, but there was some pleural effusion noted on the last chest X-ray, and as per recommendations of pulmonology team she would require chest physiotherapy and follow-up in the clinic. She was advised to continue on the ceftriaxone course for a total of 6 weeks from date of hospitalization.

DISCUSSION

K. pneumoniae is a Gram-negative organism, consisting of a polysaccharide capsule with specific stereotypes (K1 and K2) causing increased susceptibility to metastatic complications in diabetic patients. The organism disseminates haematogenously where the polysaccharide capsule can offer protection against phagocytosis and thereby cause complications like EE, pyelonephritis, as well as liver abscesses[3,4]. These multi-systemic adverse effects are typically caused by hypervirulent *K. pneumoniae* strains resulting in KPIS[1]. As per a study in Korea which investigated the outcomes of EE due to Klebsiella, six risk factors were identified which included diabetes mellitus[5], as in the presented case. Liver abscesses are known to be one of the most common complications in KPIS, however this patient presented with renal and ocular infections. A similar case in a 39-year-old Malaysian female has been reported with similar eye findings[6]. However, the presentation of EE in association with pyelonephritis is a rare finding. The complication of renal vein thrombosis specifically in this condition has not been described extensively. Lurz et al reported a case of renal vein thrombosis in the presence of *K. pneumoniae* pyelonephritis in the USA[7]. However, coagulopathies are well-known to be associated with Gram-negative bacterial infection, especially when leaning towards sepsis and disseminated intravascular coagulation[8,9].

In terms of the ocular involvement, our patient was lost to follow-up hence late complications could not be properly assessed. Previous cases show a range of outcomes from blindness in 35.9% of the patients in the Korean study[5] and rupture of the globe needing evisceration in a case in Canada[4] to complete resolution in the case from Malaysia[6]. Our case is the first recorded case of *K. pneumoniae*-induced endogenous endophthalmitis associated with pyelonephritis and renal vein thrombosis without liver abscess in the Middle East.

CONCLUSION

It is imperative to consider hypervirulent and hypermucoviscous strains of *K. pneumoniae* in patients with disseminated infection and multi-system involvement. KPIS can be suspected in patients without liver abscess. Early diagnosis, multidisciplinary intervention, and timely management are crucial in preventing severe outcomes such as permanent vision loss or sepsis leading to mortality.

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