Am J Clin Exp Urol 2024;12(4):194-199
www.ajceu.us /ISSN:2330-1910/AJCEU0157135

Case Report

A case series of emphysematous pyelonephritis in COVID-positive patients

Sajal Gupta[1], Abheesh Varma Hegde[1], Naresh Kumar Kaul[2], Sandesh Parab[3], Tarunkumar Prakash Jain[3], Mukund Andankar[3], Hemant Ranganath Pathak[3]

[1]Department of Urology and Renal Transplantation, Father Muller Medical College, Mangalore, Karnataka-575002, India; [2]Max Speciality Hospital, Vaishali Nagar, Delhi, India; [3]Department of Urology and Renal Transplantation, B.Y.L. Nair Ch. Hospital and Topiwala National Medical College, Dr. A Nair Road, Mumbai-400008, India

Received April 10, 2024; Accepted July 16, 2024; Epub August 25, 2024; Published August 30, 2024

Abstract: Emphysematous pyelonephritis (EPN) is a rare infectious disease affecting the renal and perirenal tissues, wherein gas formation occurs in the renal parenchyma, perinephric tissues, or collecting systems. It can be life threatening with mortality rates upto 60%. Here, we report a case series of EPN during the COVID pandemic with COVID test-positive patients who were diagnosed based on clinical signs, symptoms, and CT scans. One patient was conservatively managed, one underwent nephrectomy, and the others were treated with percutaneous drainage and pigtailing. Despite being critically ill, all the patients recovered uneventfully. Owning to the rarity of the lesion and variations in the clinical spectrum, the diagnosis of EPN is challenging. EPN requires early diagnosis and prompt management. The interventional technique depends on the clinical status of the patient and the severity of the lesion. Although the threshold of intervention is low in normal clinical practice, in covid patients, we tried to manage patients conservatively and intervened only when unavoidable.

Keywords: Emphysematous pyelonephritis (EPN), diabetes mellitus (DM), ER (emergency room), hydroureteronephrosis (HUN), total leucocyte count (TLC), haemoglobin (Hb), random blood sugar (RBS), intensive care unit (ICU), percutaneous drainage (PCD), hypertension (HTN)

Introduction

Emphysematous pyelonephritis (EPN) is a rare life-threatening acute necrotizing infection affecting the renal parenchyma and adjacent tissues, resulting in the formation of gas (nitrogen (60%), hydrogen (15%), carbon dioxide (5%), and oxygen (8%)) in the renal parenchyma, perinephric tissue, and collecting system. It has a grave prognosis and commonly affects individuals with uncontrolled diabetes mellitus (DM); however, it may be observed in individuals without DM, particularly when associated with obstruction of the renoureteral unit [1]. This acute necrotizing infection involving the kidney demonstrates a high death rate of 42% [2, 3]. EPN is characterized by the presence of gas within the renal parenchyma, collecting ducts, or both [4]. The gas is produced by gram-negative bacteria, particularly Klebsiella pneumoniae (22%) and E. coli (56%), following the fermentation of glucose. This gas results in the aggregation of carbon dioxide within renal tissue, which leads to a further cascade of sepsis [5, 6]. Here, we report a case series of four cases of EPN in COVID-19 patients.

Case presentations

Case 1

A 45-year-old diabetic female presented to the emergency room (ER) with complaints of right flank pain, fever, and dysuria for four days with minimal respiratory symptoms. On examination, tenderness at the right renal angle was observed. CT KUB findings suggested right moderate hydroureteronephrosis (HUN) with a bulky kidney with multiple air pockets in the right renal parenchyma, suggestive of Grade 2 EPN according to the Huang and Tseng classifi-

https://doi.org/10.62347/SHWR9606

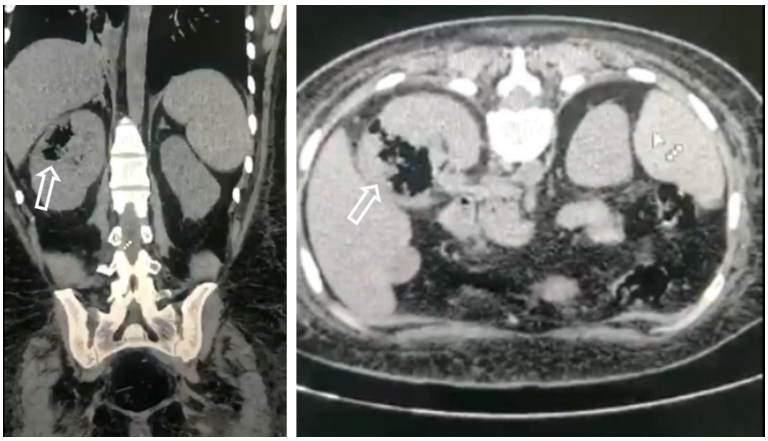

Figure 1. CT scan images showing bulky right kidney with multiple air pockets in the renal parenchyma.

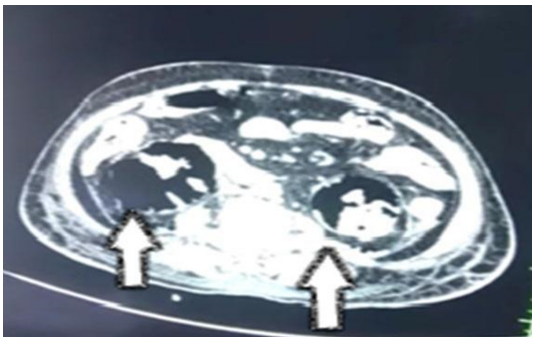

Figure 2. CT scan image showing hypoechoic area within the cortex of right kidney measuring 2×3×1.5 cm, with renal abscess.

cation (**Figure 1**). Laboratory investigations showed a serum creatinine was 2.4 mg/dl, total leukocytes count (TLC) of 22,800/ml, hemoglobin (Hb) of 11 g/dl, random blood sugar (RBS) level of 236 mg/dl, and HbA1c of 11%. The COVID-19 RT-PCR test results were positive. Urine culture showed polymicrobial growth. The patient was admitted to the intensive care unit (ICU) and started on dual inotropes. The patient was initially managed with percutaneous drainage (PCD) and broad-spectrum antibiotics (carbapenem). However, the patient's condition worsened; hence, open nephrectomy was performed. The postoperative period was uneventful and was discharged after the COVID test was negative.

Case 2

A 70-year-old female patient reported to the ER with complaints of bilateral flank pain, fever, and nausea for 3 days. Upon examination, bilateral renal angle tenderness was observed. The patient was a known case of hypertension (HTN). Laboratory investigations revealed a serum creatinine level of 6.2 mg/dl, TLC of 13,200/μL, RBS of 142 mg/dl, and positive COVID-19 RT-PCR test. CT scan showed right moderate HUN with left mild HUN and a bulky kidney with multiple air pockets extending into the perinephric space. The right kidney also showed a hypoechoic area within the cortex measuring 2×3×1.5 cm, suggestive of bilateral grade 4 EPN with a right renal abscess (**Figure 2**). Urine culture showed Klebsiella growth that was sensitive to all antibiotics. The patient was diagnosed with severe acute acute ARDS with EPN Grade 4. Bilateral pigtail insertion was performed, and pus was drained. Pus drainage from the pcn was not improving so bilateral dj stent was performed, which helped in improving the condition of the patient. Later, serum creatinine was reduced to 4.2 mg/dl, the COVID test was negative, and the patient was discharged with bilateral pigtail and stent in situ. The patient's follow-up was uneventful. The pigtail was removed after six weeks and the stent was removed ten weeks after the follow-up scan.

Case 3

A 74-year-old female presented to the ER with complaints of fever, dysuria, and left flank pain for six days. On examination, tenderness in the left renal angle was observed. The patient was a known case of DM and HTN. ARDS was also observed in the patient. Laboratory investigations showed that the TLC was 22,300/microliters; Hb was 10.2 g/dl; RBS, 309 mg/dl; HbA1c, 7.8%; and serum creatinine, 1.6 mg/dl. The COVID-19 RT-PCR test results were positive. Urine culture showed growth of meropenem-sensitive E. Coli. CT findings showed left mild HUN, bulky kidney with multiple air pockets in the left renal parenchyma, suggestive of Grade 2 EPN (**Figure 3**). The patient responded to conservative treatment and recovered uneventfully during subsequent follow-up.

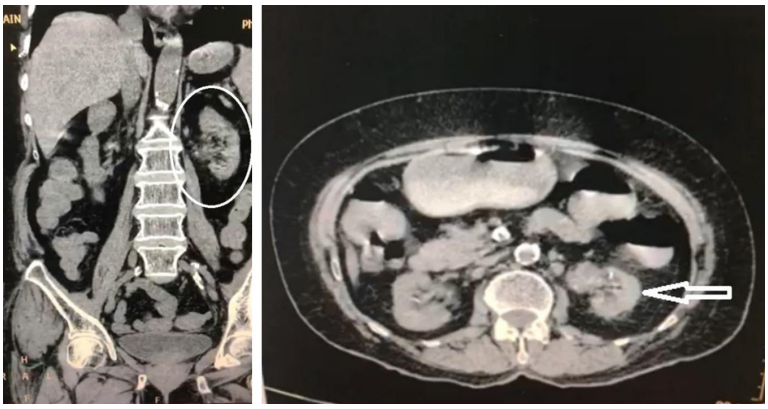

Figure 3. CT scan image showing left bulky kidney with multiple air pockets in the renal parenchyma.

Case 4

A 35-year-old diabetic female presented to the emergency department with complaints of fever and right flank pain for 5 days. On examination, she was hypoxic with moderate ARDS in Septic Shock with right renal angle tenderness. Laboratory investigations revealed leukocytosis with thrombocytopenia (TLC, 17,800/µL; Platelets, 32,000/microliters); serum creatinine, 2.1 mg/dl; Hb was 7.3 g/dl; RBS, 292 mg/dl; HbA1c, 11.2%; D-dimer, 6345 mg/L; serum sodium, 142 mg/dl; serum potassium, 3.7 mg/dl; and COVID-19 RT-PCR, positive. Urine culture were sterile. Computed tomography showed right moderate HUN with bulky kidney and multiple air pockets in the right renal parenchyma with extension into the para-renal and perinephric spaces with moderate fat stranding. The right kidney showed a hypoechoic area within the cortex and perinephric space measuring 6×8×4.5 cm suggestive of grade 3 EPN with renal abscess (**Figure 4**). The patient was started on broad-spectrum antibiotics with stabilization of vital signs in the ICU. The patient underwent CT-guided PCN after platelet transfusion for source contral and rising leucocyte counts. The post-procedure patient started improving and was discharged after the COVID-19 negative result with stable vitals, and the follow-up remained uneventful. The pigtail was removed at 6 weeks of follow-up.

Discussion

EPN is an infectious disease that affects the renal and perirenal tissues, with significant mortality and morbidity rates. Gas formation occurs in the renal parenchyma, perinephric tissues, and collecting system [1, 3]. In 1898, Kelly and MacCullum described the first case of renal illness associated with gas accumulation within renal tissues. The term 'EPN' was coined by Schultz and Klorfein [7] in 1962. Since then, several types of renal infections accompanied by gas build-up within the renal tissues have been reported in the literature. EPN is more commonly observed in patients with DM [8]. In our cases, three out of four patients were diabetic. Moreover, all of our patients were COVID-positive. In addition to DM, other conditions that may serve as risk factors for EPN include urinary tract blockage due to urinary tract stones or a sloughed papilla, gaint fecaloma, severe uterine prolapse, and an immunocompromised state [9, 10]. To date, all cases of EPN have been reported in adults, and the majority of them were females [1], which was also observed in our cases, where all patients were female. However, only a few cases have been reported in infants and young children [11, 12]. Moreover, according to available literature, EPN is more commonly observed in the left kidney [1]. However, in our cases, the right kidney was affected in two patients, the left kidney was affected in one patient, and bilateral kidneys were affected in one patient.

E. coli is the most commonly isolated pathogen in EPN patients, *E. coli* has been linked to approximately 62.7% of previously reported cases [1]. In addition to this, other pathogens associated with EPN infection include *Proteus mirabilis*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *Bacteroides fragilis*, *Enterobacter cloacae*, *Aspergillus fumigatus*, *Clostridium septicum*, *Enterococcus*, *Entamoeba histolytica*, and *Candida* [1, 13, 14]. In our study, E. Coli was present in one case, Klebsiella was present in one case, and polymicrobial growth was observed in one patient.

In a meta-analysis, a mortality rate of 25% was reported in patients with EPN [2]. As per this meta-analysis, factors associated with fatal outcomes include radiological type I according to the Wan classification, conservative treat-

Figure 4. CT scan images showing hypoechoic area within the cortex of the right kidney and perinephric space with renal abscess.

ment alone, thrombocytopenia, and bilateral EPN. Increased serum glucose at the time of hospital admission and the EPN radiological CT class, according to both the Wan and Huang and Tseng systems, are considered predictors of mortality [15]. In our cases, three of the four patients had hyperglycemia at the time of presentation to the hospital. Moreover, confusion, shock, thrombocytopenia, and acute kidney failure are associated with an undesirable prognosis [16]. Thrombocytopenia was observed in one of our cases. Leukocytosis, low serum sodium and albumin levels, and high HbA1c levels are associated with poor prognosis [8]. In our case series, the commonly observed presenting complaints were fever, flank pain, and dysuria, with mild to moderate upper respiratory tract symptoms. In addition, we discovered that all patients had elevated absolute leukocyte counts and AKI. Apart from this, three patients had ARDS with septic shock, and all four were COVID positive. Despite being critically ill, all four patients recovered uneventfully.

The various management strategies utilised in patients with EPN include antibiotic administration, fluid resuscitation, surgery or PCD/DJ stenting, strict glucose control, and nephrectomy. Early initiation of aggressive surgical treatment yields successful outcomes compared to medical management alone [13]. EPN patients have been categorised into three risk groups by Kuzgunbay *et al.* [17]: mild (No septicemia; CT: Emphysematous lesion <1 cm^2 in the kidney, solitary or multiple; Percutaneous drainage is necessary/inapplicable); moderate (No septicemia; CT: Emphysematous lesion involving equal or less than half of the kidney; Amenable to percutaneous drainage); and severe (Septicemia; CT: Emphysematous lesion involving more than half of the kidney and/or perinephric extension).

Nephrectomy saves lives in patients with severe EPN and signs of sepsis and kidney involvement. In patients with mild or moderate EPN and septicemia, the recommended management strategies involve broad-spectrum antibiotics and PCD. Monotherapy with broad-spectrum antibiotics can be useful for lesions that are small and difficult to drain [1]. In our cases, three patients needed surgical intervention in

terms of drainage of pus and source control (nephrectomy), and only one patient was managed conservatively without any sequelae. In our observation, it is a new finding that all patients were associated with COVID-19, which has not been reported in previous literature. COVID-19 may be a risk/predisposing factor, but larger data are needed to support this observation. Furthermore, early intervention with higher antibiotics and critical care in the ICU play a crucial role in the treatment of EPN. Due to the COVID-19 pandemic, all cases being COVID-19 positive with urological emergencies were initially managed conservatively with a high threshold for intervention.

Conclusion

Due to the rarity of the lesion and variations in the clinical spectrum, the diagnosis of EPN is challenging. EPN requires early diagnosis and prompt management. The interventional technique depends on the clinical status of the patient and the severity of the lesion. Both the COVID and DM causes weakened immunity of the body which may have led to the body being predisposed to EPN. Necessary interventional procedures should not be postponed, and in patients showing no improvement, therapeutic modifications should be considered for adequate management. However, as these cases were presented during the COVID pandemic, there was a high threshold for intervention in these EPN cases. EPN cases with moderate to high severity can also be managed with minimal intervention but with close intensive care monitoring.

Disclosure of conflict of interest

None.

Address correspondence to: Drs. Sajal Gupta and Abheesh Varma Hegde, Department of Urology and Renal Transplantation, Father Muller Medical College, Mangalore, Karnataka-575002, India. Tel: +91-9560765429; ORCID: 0000-0001-7246-4515; E-mail: sajal.dare@gmail.com (SG); Tel: +91-990-0924015; ORCID: 0000-0002-2524-6889; E-mail: abhi.vhegde@gmail.com (AVH)

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