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Original Research Article

Emphysematous Pyelonepheritis– Clinico-Radiological Correlation

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Abstract

Emphysematous pyelonephritis (EPN) is an uncommon necrotizing infection characterized by gas in the renal parenchyma and surrounding tissues. It is rapidly progressive and life endangering condition, requiring strong suspicion and appropriate therapy to salvage the infected kidney. We have delineated clinical, laboratory and imaging characteristics outcomes of patients with EPN admitted in hospital.

Methodology: This prospective observational study was carried out in medicine wards of rural tertiary care hospital and medical college named DR. RPGMC Kangra at Tanda Himachal Pradesh. They presented with a clinical, laboratory and radiologic diagnosis of EPN. Each patient had a unique predisposing factor for developing EPN.

Result: We studied 32 patients (mean age 48.6 years; females 71.87%). Risk factors for EPN were diabetes mellitus (in 93%) and renal stones (in 9%). Fever, loin pain, vomiting and dysuria were common. Complications included acute kidney injury, 74%; mostly stage 1, (77.5%), hyponatraemia (54%) and bacteraemia (28%). Escherichia coli was the most common (66%) urinary isolate. Most patients (78%) had class 2 EPN, with 12% class 3B and 10 % class 3A. Besides medical management, one (3.12%) required surgery (nephrectomy). Nephrectomised patient had a higher radiological class and one death occurred. Early goal directed therapy with intravenous fluids and antibiotics was given. This was followed by less invasive urologic interventions in an attempt to avoid nephrectomy and thereby salvage the infected kidney. Out of 32 patients, 30 patients were discharged in clinically stable conditions. One patient was referred to higher centre PGIMER Chandigarh for further management. Where he was managed conservatively initially, but condition kept on deteriorating, subsequently nephrectomy was done and he was discharged after 21 days of admission on oral antibiotics.

Discussion and Conclusion: This study provides practice-based support to available literature for managing EPN. Early goal directed medical therapy for sepsis coupled with interventional urologic procedures is a useful alternative to avoid forthcoming emergent nephrectomy except in cases where a fulminant infection may be present at the time of admission or develop later on in the course of the illness despite conservative line of therapy. It also high points the importance of considering a diagnosis of EPN in patients with urinary infections who have certain predisposing factors like diabetes mellitus.

Keywords: emphysematous pyelonephritis (EPN), Urinary tract infection (UTI), hyperglycemia

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Introduction

Emphysematous pyelonephritis (EPN) is a severe, acute necrotizing infection with formation of gas in the collecting system, renal parenchyma and perirenal tissues[1]. It is a life-threatening condition with a high mortality rate. It predominantly affects females who are diabetics[2,3]. Rare cases have been reported in non-diabetics who have other predisposing factors such as immunosuppression, urinary tract obstruction secondary to stones, tumor or sloughed papilla. The factors that predispose to EPN in diabetics may include uncontrolled diabetes mellitus, high levels of glycosylated hemoglobin and impaired host immune mechanism[3]. Emphysematous pyelonephritis should be strongly suspected in patients with flank pain and fever who have history of diabetes mellitus and stone disease[3]. It is caused by gas forming organisms like Escherichia coli (commonest), Klebsiella, Clostridium, Candida, Aspergillus, Cryptococcus[4,5]. Although renal or perirenal gas can be diagnosed on plain x-ray KUB film and on ultrasound, CT scan is the modality of choice in the diagnosis and staging of the disease[6]. Classification of EPN on the basis of CT scan are: class 1- gas in the collecting system only; class 2- gas in the renal parenchyma without extension to the extrarenal space; class 3A- extension of gas or abscess to the perinephric space; class 3B- extension of gas or abscess to the pararenal space; class 4- bilateral EPN or a solitary kidney with EPN.[1,3]

The aim of this study is to add to current literature by delivering information regarding our experience in diagnosing and successfully treating the patients who were diagnosed with EPN in this institution.[1,3] Outcomes for patients with EPN are variable and depend on status at presentation, radiological class and quality of care.[1,2]

Material and Method

This was a hospital based prospective observational study, conducted in a tertiary care hospital Dr.RPGMC Tanda, from January 2019 to march 2022 for demographic data, clinical and laboratory profile, and outcome assessment. The presence and duration of diabetes mellitus (DM) and the level of glycemic control were noted. The hemodynamic status and the level of consciousness at initial presentation, renal function, and other biochemical parameters were recorded. Initial diagnosis was recorded as acute pyelonephritis (APN), urosepsis, or multi-organ dysfunction syndrome. APN was diagnosed by the triad of fever, dysuria, and loin pain. Urosepsis was defined as bacteriological evidence of urinary tract infection, pyuria with markers of sepsis syndrome and MODS was defined as clinical or biochemical markers of dysfunction of two or more organ systems in the presence of sepsis syndrome. Acute renal function impairment was defined as persistent elevation of the serum creatinine level of more than 0.3 mg/dl from the baseline or first serum level at the time of admission, after volume resuscitation and excluding significant obstruction. Blood and urine were collected for microbiology culture sensitivity. The diagnosis of EPN was initially suspected on abdominal X-ray and ultrasonography of the abdomen which was later confirmed by computed tomography (CT) scan of abdomen shown in (Figures 1to 6b respectively). Cases were classified into four classes based on CT findings, as described by Huang and Tseng. We used Statistical Package for the Social Sciences (SPSS), version 16 for Windows, for data analysis. Results expressed as frequency and as mean ± SD. The study was approved by the Institutional Ethical Committee.

Results: A total of 32 patients were recruited in this study from 24 years to 70

years of age. Mean age (±sd) was 48.6 ± 12.3 years. All the patients were diabetics and 23 patients (71.87%) were females. The co-morbidities included hypertension in 14 patients (43.75%), chronic kidney disease in 5 patients (15.63%), enlarged prostate in 3 patients (15%) and renal stones in 3 patients (9.37%). (Table 1)

Table 1: Baseline characteristics of patients

Characteristic	Mean*/ number (%)
Age (years)*	48.6 ± 12.3
Females	24
Diabetics	32
Duration of Diabetes mellitus (years)*	7.8 ± 2.4
DKA	3 (9.4)
NKHS	3 (9.4)
Diabetic neuropathy	25 (78.1)
Diabetic nephropathy	14 (43.8)
Diabetic retinopathy	10 (31.3)
Renal stones	2 (6.2)

*mean age/ duration ± standard deviation

Fever was the commonest presenting clinical feature present in all the 32 patients (100%). Other clinical features present were loin pain and/or renal- angle tenderness in 18 patients (56.25%), vomiting in 27 patients (84.37%), dysuria in 14 patients (43.75%), increased urinary frequency in 4 patients (12.50%) and dehydration in 6 patients (18.75%). 7 patients (21.85%) presented with altered sensorium and 6 (18.75%) patients with hypotension.(table 2)

Table 2: Clinical characteristics of patients

Variable (Clinical features)	N (%)
Fever/ chills	32 (100)
Flank pain	28 (87.5)
Vomiting	27 (84.4)
Dysurea	14 (43.8)
Renal angle tenderness	24 (75)
Palpable kidney(s)	05 (15.6)
Altered sensorium	07 (21.9)
Hypotension (systolic BP<90mmHg)	06 (18.8)

The patients had experienced these symptoms for 3–14 days before presenting at our hospital. Neutrophilic leucocytosis was common and eleven patients had thrombocytopaenia. All had high erythrocyte sedimentation rates (ESR) and C-reactive protein (CRP) levels. Overall, glycaemic status was poor (Table 2). Other features were pyuria in 27 patients (84.37%), glycosuria in 28 patients (87.50%) and microscopic haematuria in 11 patients (34.37%). 23 patients (74%) were having acute kidney injury (AKI)[8] mostly at stage 1 (77.56%) and 17 (54%) had hyponatraemia. (table 3)

Table 3: Laboratory findings of patients

Variable (biochemical features)	N (%)
Pyuria	27 (84.4)
Haematuria	11 (34.4)
Glucosuria	28 (87.5)
Leucocytosis (leucocytes>11,000/mm^3)	29 (90.6)
Thrombocytopenia (platelet<150,000/mm^3)	11 (34.4)
Serum creatinine (>1.2mg/dl)	23 (71.9)
Hypoalbuminia (<3.7gm/dl)	19(59.4)
Hyponatraemia (<135mmol/l)	18 (56.3)
Hypokalaemia (<3.5mmol/l)	6 (18.8)

The average HbA1c was 10.7% and average random blood sugar level was 350 mg/dl among the study participants at the time of admission

The diagnosis of EPN was confirmed by abdominal CT scan. The right kidney was involved in 10 patients (31.25%) and the left in 14 patients (43.75%) while 8 patients (25%) had evidence of pyelonephritis in contralateral kidneys along with EPN. (Table 4)

Table 4: Side involvement of EPN

Side involved	N (%)
Left	14 (43.8)
Right	10 (31.2)
Bilateral	08 (25)

According to the Huang and Tseng classification Four patients (12%) had class 3B EPN, Three (10%) had class 3A, and 25 (78%) had class 2 EPN (Figure 1- 6b). Micro-biochemical analysis of data for microbiologic profile reveals that Escherichia coli (E.coli) was the most commonly isolated organism and was isolated in a total of 17 patients (in urine in 9, in blood in 2 and in both i.e. blood and urine in 6). Proteus mirabilis was isolated from urine in three patients. In two patients, we isolated candida species from urine. Polymicrobial infection was documented in four patients (Klebsiella pneumoniae was isolated from urine and Pseudomonas aeruginosa from blood). Acinetobacter was isolated from urine in three patients. No organism was isolated from any sample in 3 (26.9%) patients. All patients were treated with intravenous antibiotics and other supportive measures including fluid resuscitation. Out of 32 patients, 30 patients were discharged in clinically stable conditions. One patient was referred to higher centre PGIMER Chandigarh for further management. Where he was managed conservatively initially but the condition kept on deteriorating, subsequently nephrectomy was done and he was discharged after 21 days of admission on oral antibiotics. One death was reported involving a 58 year old female who, in addition to bilateral EPN, had comorbidities including renal stone with hydronephrosis, T2DM and septic shock with MODS.

Figure 1: Ultrasonography of right kidney showing multiple air foci throughout renal parenchyma.

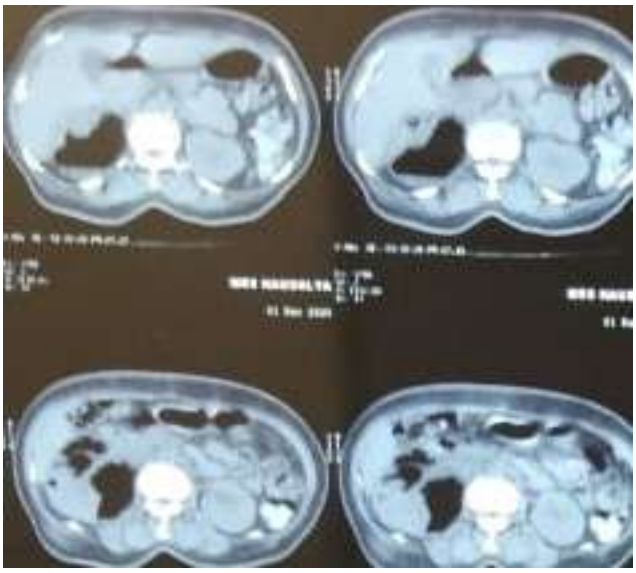

Figure 2: Right enlarged kidney with large air density in parenchyma and pelvicalyceal system with fluid level in emphysematous cavity and perirenal area wirh air in adjoining psoas muscle.

Figure 3: longitudinal section showing multiple air level in right kidney and in right psoas muscle.

Figure 4: X-RAYS abdomen s/o multiple calculi in left kidney with multiple air.

Figure (5a): Left kidney with multiseptated thick-walled collection and multiple large calculi with multiple air foci with extension to perinephric spaces and trans abdominal wall.

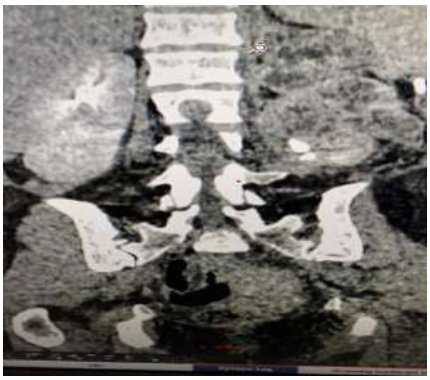

Figure (5b): Coronal section abdomen s/o emphysematous pyelonephritis with multiple perinephric strands.

Figure (6a): Showing left Emphasymarous pyelonephritis with large intra and perinephric collection with decreased enhancement of residual parenchyma.

Figure (6b): Coronal section abdomen s/o left emphysematous pyelonephritis with intra-perinephric collection with air in kidney, perinephric space inferior to kidney with air extending to ureter into bladder.

Discussion

EPN is an uncommon necrotizing infection predominantly seen in patients with diabetes. All our patients were diabetic. EPN is a disease in women with a female: male ratio of 4:1.[7] The increased occurrence in women is presumably because of their increased susceptibility to urinary tract infection.[8] The only exception to this female predominance is that males undergoing renal transplantation are more likely to suffer.[9] The most common clinical features in our series and reported by others include fever/chills, flank pain, renal angle tenderness, vomiting, and dysuria. These symptoms and signs are nonspecific and cannot differentiate EPN from the usual pyelonephritis. Crepitus in the lumbar region are rare but can provide an important clue regarding underlying EPN. In The absence of any signs or symptoms specific to this condition, and poor response to antibiotics in a patient with DM thought to have uncomplicated pyelonephritis should immediately arouse suspicion of this life-threatening infection and prompt an early CT abdomen to clinch the diagnosis and plan treatment. The factors believed to underlie the pathogenesis of EPN include gas forming bacteria, high tissue glucose concentrations, impaired tissue perfusion, and defective immune response which occurs in DM.[10] The high tissue glucose level acts as a substrate for the microorganisms such as Enterobacteriaceae to produce hydrogen (H2) and carbon dioxide (CO2) by mixed acid fermentation of glucose. In a study by Huang et al., five of the six gas samples contained H2 and all the gas samples contained CO2.[8] Our patients had poor glycemic control before getting EPN as reflected by high average HbA1c. In our study, renal stones were present only in10% cases. E. coli is by far the most common causative organism for EPN isolated in 47–90% of the patients; the other commonly involved organisms include P. mirabilis, K. pneumoniae, Enterococcus species, and P. aeruginosa.[11] In keeping with the literature, we also found that E. coli to be involved in 66% of our cases and P. mirabilis to be the second most frequently isolated pathogen. In our study, Candida albicans was the causative organism in two patients. C. albicans has been occasionally identified as a pathogen in EPN.[12] Acinetobacter was isolated from urine in one patient. In our study, seven patients (26.9%) were culture negative in both urine and blood. In EPN, left kidney is more frequently involved than the right. A recent meta-analysis has reported that 52% of patients had left sided, 37.70% right sided, and 10.2% bilateral EPN . Huang et al[10]

have reported that 67, 25, and 8% of the 48 patients with EPN had left sided, right sided, and bilateral disease, respectively.[8] In our study, the left kidney was involved in 38.5% patients and the right kidney was involved in 30.8% patients. In the literature, bilateral EPN is reported to occur in up to 10% of patients.[13] In our cases, a much larger proportion of patients (30.8%) had bilateral EPN. To the best of our knowledge, this is the highest reported percentage of bilateral involvement in patients with EPN. Some studies have focused on the factors that are associated with poor outcome in EPN. Wan and Rullard reported that thrombocytopenia, azotemia, and hematuria were predictors of poor outcome in EPN.[7] Huang et al. have reported that initial presentations of thrombocytopenia, altered consciousness, severe proteinuria, shock (systolic BP <90 mmHg), and extension of infection to the perinephric space are significantly associated with mortality.[8] A recent meta-analysis has reported that in patients with EPN, shock is associated with high mortality rate.[10] Another recent study has reported that need for emergency hemodialysis, severe hypoalbuminemia (serum albumin <3 g/dl), and polymicrobial infections are bad prognostic factors in patients with EPN.[11] In a study of 21 patients with EPN, it was reported that only hematuria is associated with bad prognosis.[3] An Indian study by Kapoor et al. reported that altered mental status, thrombocytopenia, renal failure, and severe hyponatremia at presentation are associated with higher mortality rates whereas extensive of our 32 patients, 20 (76.9%) had 2 or more bad prognostic factors. In our series, 16 patients had extensive EPN (class 3 or 4) and all these patients had ≥2 bad prognostic factors shown in Table 3. Of these 16 patients, conservative treatment was successful in 13 patients and unsuccessful in 2 patients (1 needed nephrectomy and 1 died). Huang et al. in a study of 48 cases concluded that nephrectomy can provide the best management and should be promptly attempted for extensive EPN with a fulminant course (≥2 bad prognostic factors).[8] Our findings seriously question this radical approach as 13 of our 16 patients with extensive (class 3 or 4) EPN responded to conservative treatment. Similar results have been reported by Lu et al.[11] It is supposed that high tissue glucose levels may cause a fulminant course in patients with DM because it can provide gas forming microbes with a microenvironment more favorable for growth and catabolism.[14] In our series, glycemic control had no prognostic significance as all but one of our patients despite having poor glycemic control as reflected by their high mean HbA1c of 10.7 ± 2.4% recovered. Similarly, other studies have concluded that glycemic control is not a prognostic factor in patients with EPN. Renal parenchymal destruction is associated with a need for nephrectomy.[15] The treatment of EPN is controversial. Traditionally, early nephrectomy has been considered the treatment of choice in EPN with few reports suggesting increased mortality with medical therapy as compared to surgery.[16,17] However, surgery is often poorly tolerated in EPN due to poor hemodynamic status; the mortality rate in a series y Ahlering et al. advocating emergency nephrectomy was 42%.[18] Kapoor et al. have also reported that early nephrectomy is associated with higher mortality rates than an initial conservative approach.[15] In 1996, Chen et al. reported that antibiotic therapy combined with CT-guided percutaneous drainage was an acceptable alternative to nephrectomy.[19] In that study, most patients received medical and percutaneous therapy and only two patients required nephrectomy. The treatment of EPN has evolved over the years from invasive surgery to more conservative approaches due to the availability of better imaging modalities, potent antibiotics and image guided drainage.

Over the last two decades, improvements in management techniques have drastically reduced the mortality rate of EPN to 21%.[20,21] A recent meta-analysis has shown that compared to emergency nephrectomy, percutaneous drainage and medical management alone are associated with a significantly lower mortality rate.[10] Our results also reflect the evolving trends in the management of EPN as the success rate of conservative treatment in our series was 88.5%. About a fourth (8/32) of our patients had bilateral EPN. Nephrectomy in such patients would obviously necessitate lifelong renal replacement therapy. Successful nonsurgical management of bilateral EPN has been reported by us and others.[22-23] Seven of our 8 patients with bilateral EPN responded combination of medical treatment and percutaneous catheter drainage, while one patient expired. The likely reasons for the remarkably low mortality (<4%) in our series are rapid glycemic control, early and aggressive fluid resuscitation, use of a combination of two potent antibiotics, and in the vast majority, absence of additional risk factors other than DM for the development of EPN.

Conclusions

Our clinical experience and data suggest the importance of considering the possibility of EPN in patients, particularly those with diabetes, who present with symptoms of pyelonephritis. Early goal directed therapy with IV antibiotics and fluid resuscitation together with less invasive interventions such as nephrostomy tubes provide viable alternatives to nephrectomies in early stages of EPN, thereby attempting to salvage kidneys. Nephrectomies could be reserved for the more fulminant cases of EPN presenting with hemodynamic compromise or progressive infections despite percutaneous drainage and medical therapy. These case series show the EPN requires a radiological diagnosis and the prompt diagnosis is fundamental to improve the outcome. Computed tomography is the imaging procedure of choice to confirm the presence and extent of parenchymal gas.

However, the management of EPN still remains a controversial issue. These case series are of value because supports the evidence of a successful treatment with combined Medical and PCD.

References

1. Michaeli J, Mogle P, Perlberg S, et al. Emphysematous pyelonephritis. J Urol 1984;131:203-8.
2. Falagas ME, Alexiou VG, Giannopoulou FP, Siempos II. Risk factors for mortality in patients with emphysematous pyelonephritis: a meta-analysis. J Urol 2007; 178:880-5.
3. J. J. Huang and C. C. Tseng, Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis, Archives of Internal Medicine. 2000;160(6):797–805.
4. Tsitouridis, M. Michaelides, D. Sidiropoulos, and M. Arvanity, Renal emphysema in diabetic patients: CT evaluation, Diagnostic and Interventional Radiology, 2010; 16(3): 221–226.
5. M. Nayeemuddin, O. J. Wiseman, and A. G. Turner, Emphysematous pyelonephritis, Nature Clinical Practice Urology, 2005;2(2):108–112.
6. Wan YL, Lee TY, Bullard MJ, Tsai CC. Acute gas-producing bacterial renal infection: correlation between imaging findings and clinical outcome. Radiology 1996;198:433-8.
7. R. Kapoor, K. Muruganandham, A. K. Gulia et al., Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis, BJU International, 2010;105(7):986–989.
8. Shokeir AA, El-Azab M, Mohsen T, El-Diasty T. Emphysematous pyelonephritis: A 15-year experience with 20 cases. Urology 1997;49:343-6.

9. Tienza A, Hevia M, Merino I, Velis JM, Algarra R, Pascual JI, et al. Case of emphysematous pyelonephritis in kidney allograft: Conservative treatment. Can Urol Assoc J 2014; 8:E256-9
10. Huang JJ, Chen KW, Ruaan MK. Mixed acid fermentation of glucose as a mechanism of emphysematous urinary tract infection. J Urol1991;146:148-51.
11. Lu YC, Chiang BJ, Pong YH, Huang KH, Hsueh PR, Huang CY, et al. Predictors of failure of conservative treatment among patients with emphysematous pyelonephritis. BMC Infect Dis 2014;14:418.
12. Johnson JR, Ireton RC, Lipsky BA. Emphysematous pyelonephritis caused by Candida albicans. J Urol 1986;136:80-2.
13. Zabbo A, Montie JE, Popowniak KL, Weinstein AJ. Bilateral emphysematous pyelonephritis. Urology. 1985; 25:293-6.
14. Chen KW, Huang JJ, Wu MH, Lin XZ, Chen CY, Ruaan MK. Gas in hepatic veins: A rare and critical presentation of emphysematous pyelonephritis. J Urol 1994;151: 125-6.
15. Kapoor R, Muruganandham K, Gulia AK, Singla M, Agrawal S, Mandhani A, et al. Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis. BJU Int 2010;105:986-9.
16. Dunn SR, Dewolf WC, Gonzalez R. Emphysematous pyelonephritis: Report of 3 cases treated by nephrectomy. J Urol 1975;114:348-50.
17. Cook DJ, Achong MR, Dobranowski J. Emphysematous pyelonephritis. Complicated urinary tract infection in diabetes. Diabetes Care 1989;12: 229-32.
18. Ahlering TE, Boyd SD, Hamilton CL, Bragin SD, Chandrasoma PT, Lieskovsky G, et al. Emphysematous pyelonephritis: A 5-year experience with 13 patients. J Urol 1985; 134: 1086-8.
19. Chen MT, Huang CN, Chou YH, Huang CH, Chiang CP, Liu GC. Percutaneous drainage in the treatment of emphysematous pyelonephritis: 10-year experience. J Urol 1997;157:1569-73.
20. Somani BK, Nabi G, Thorpe P, Hussey J, Cook J, N'Dow J; ABACUS Research Group. Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis? Evidence from a systematic review. J Urol 2008; 179: 1844-9.
21. Ubee SS, McGlynn L, Fordham M. Emphysematous pyelonephritis. BJU Int 2011;107:1474-8.
22. Kuchay MS, Laway BA, Bhat MA, Mir SA. Medical therapy alone can be sufficient for bilateral emphysematous pyelonephritis: Report of a new case and review of previous experiences. Int Urol Nephrol 2014;46:223-7.
23. Misgar RA, Wani AI, Bashir MI, Pala NA, Mubarik I, Lateef M, et al. Successful medical management of severe bilateral emphysematous pyelonephritis: Case studies. Clin Diabetes 2015;33:76-9.