Case Report

Left Emphysematous Pyelonephritis in a 44-year-old Female with Diabetic Nephropathy from a Tertiary Healthcare Facility in Southern Nigeria: A Case Report

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Article history: Received 06 February 2023, Reviewed 13 February 2023, Accepted for publication 25 February 2023, Published 07 March 2023

Abstract

This is a case of a 44-year-old lady living with type 2 diabetes mellitus for 7 years with poor adherence to therapy and complicating diabetic nephropathy presenting with a 2 weeks' history of high-grade continuous fever and left flank pain with associated nausea, vomiting and frothiness of urine. She denies previous urological disease. Physical examination revealed a moderately dehydrated, febrile (T=39.2°C) and pale young lady with tachycardia and tachypnea. Her left kidney was ballotable, tender with a positive punch sign on the left renal angle. Her urinalysis revealed numerous pus cells and leucocytes, her abdominal ultrasound revealed an enlarged left kidney measuring 15x7.58cm with irregular outline and areas of hyper-echogenicity within the cortical region casting dirty acoustic shadows in keeping with left Class 3A emphysematous pyelonephritis. Her abdominal CT further confirmed this diagnosis. She was managed conservatively with intravenous ceftazidime and Tinidazole with adequate fluid therapy. She was discharged home after 2 weeks of hospitalization. She is being followed up in the Nephrology clinic of our hospital.

Keywords: Diabetic nephropathy, fever, left emphysematous pyelonephritis

Introduction

This case highlights an uncommon clinical presentation of pyelonephritis complicating diabetic nephropathy in a 44-year-old lady with type 2 diabetes mellitus and poor adherence to therapy. Emphysematous pyelonephritis is a severe, yet uncommon presentation in our environment and a high index of suspicion as well as prompt intervention is critical for its management.

Patients' concerns and important clinical findings

Our patient presented with a 2 weeks' history of continuous high-grade fever, left flank pain with associated nausea, vomiting and frothiness of urine. She denies previous urological disease. Physical examination revealed a moderately dehydrated, febrile (T=39.2°C) and pale young lady with tachycardia and tachypnea. Her left kidney was ballotable, tender with a positive punch sign on the left renal angle. Her urinalysis revealed numerous pus cells and leucocytes, her abdominal ultrasound revealed an enlarged left kidney measuring 15x7.58cm with irregular outline and areas of hyper-echogenicity within the cortical region casting dirty acoustic shadows in keeping with left Class 3A emphysematous pyelonephritis. Her abdominal CT further confirmed this diagnosis.

Diagnosis/Interventions/Outcomes

A diagnosis of Left Emphysematous Pyelonephritis complicating Diabetic nephropathy was made. She was however managed conservatively with intravenous ceftazidime and Tinidazole with adequate fluid therapy. She was discharged home in good clinical state after 2 weeks of hospitalization. She is being followed up in the Nephrology clinic of our hospital.

Case Presentation

Mrs. N.J a 44-year-old business woman, living with diabetes for the past 7 years with poor adherence to therapy and recently diagnosed with diabetic nephropathy. She presented with a 2 weeks' history of high grade continuous fever and left flank pain. Fever

Print ISSN: 0189-9287

was associated with chills, nausea and non-projectile vomiting. Her left flank pain was of insidious onset but progressively worsened to be described as "excruciating" but not radiating. She had associated dysuria, increased urinary frequency, polyuria, nocturia with increased frothiness of urine. There was no facial puffiness or leg edema.

She is not a known hypertensive but was diagnosed with diabetic nephropathy in the index illness. She has a family history of diabetes mellitus and hypertension; she is currently separated from her spouse. She volunteered a history of unprotected multiple sexual partners and also admits to a significant alcohol (36 units/week) and tobacco history (six pack years).

Examination revealed a drowsy, moderately dehydrated young. She was febrile, pale anicteric and not cyanosed. She had no palpable lymphadenopathy and no pedal edema. She had tachycardia with a pulse rate of 118beats per minute, her blood pressure was 110/60 mmHg left arm supine and 100/56mmHg left arm erect position; other cardiovascular examination findings were normal. She had tachypnea of 28 cycles per minute but there was no other respiratory system abnormality noted. Her abdominal findings revealed subcutaneous crepitus over the left lumbar area anteriorly. Her left kidney was ballotable, tender with a positive punch sign. Her liver and spleen were not palpable. There was no ascites and no renal bruit. She had no focal neurological deficits.

Her presenting random blood sugar was 32.7mmol/L, bedside urinalysis was positive to glucose (+++), protein (+), nitrites (++), and ketones (+) with an acidic pH.

A working diagnosis of hyper-osmolar hyperglycemic state (HHS) precipitated by left acute pyelonephritis on background diabetic nephropathy was made. Differential diagnosis entertained included (1) Left hydronephrosis secondary to obstructive uropathy with superimposed pyelonephritis presenting in HHS and (2) Left emphysematous pyelonephritis on background diabetic nephropathy presenting in HHS.

She was referred for a urinalysis, microscopy, culture and sensitivity test, urine albumin creatinine ratio, serum electrolyte, urea and creatinine assessment, fasting lipid profile, fasting plasma glucose, HbA1c, urgent abdominal ultrasound scan with renal bias, plain abdominal x-ray (KUB), abdominal computed tomography scan and electrocardiogram assessment. She was however indigent and could not afford some of her investigations.

Her urinalysis showed a cloudy urine with a pH of 5.0, specific gravity of 1.020, glucose of 3+, protein (+), Nitrite was negative, ketones +, blood 2+ and leucocytes 2+. There were numerous pus cells, and red blood cells of 3-5/hpf with cellular casts. There was no bacterial growth after 48 hours of incubation.

Her hematological and biochemical results obtained are outlined in table 1. She was seronegative to HIV I& II, HBsAg, HCV antibodies and had a non-reactive venereal disease research laboratory (VDRL) test. Result of her abdominal ultrasound are shown below in Figure 1

Her abdominal ultrasound revealed an enlarged right kidney 13.53x 5.21cm and a left kidney measuring 15x7.58cm that displayed an irregular outline with areas of hyper-echogenicity within the cortical region casting dirty acoustic shadows in keeping with left emphysematous pyelonephritis. Her unenhanced abdominal CT demonstrated pockets of gas within the left renal parenchyma which is also enlarged, while the contrast CT revealed patchy enhancement of the left kidney.

Table 1: Showing haematology and biochemical parameters

INVESTIGATIONS	RESULTS	REFERENCE RANGE	REMARKS
HAEMATOLOGY			
Haemoglobin (g/dl)	9.3*	12-16	Anaemia
White blood cells (L^{-1})	16.3 x 10^{9} *	4-11 x 10^{9}	Leukocytosis
Platelets (L^{-1})	408 x 10^{9}	140-400 x 10^{9}	Thrombocytosis
Neutrophils (%)	77*	40-75	Neutrophilia
Lymphocytes (%)	11*	20-45	Lymphocytopenia
Monocytes	10	2-10	Normal
Eosinophils (%)	2	1-6	Normal
ESR (mm/hr)	78*	5-7	Elevated
BIOCHEMISTRY			
Serum urea	15*	2.4 -6.0	Elevated
Serum creatinine	180*	60 -120	Elevated

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INVESTIGATIONS	RESULTS	REFERENCE RANGE	REMARKS
Sodium	110*	135 -145	Low
Potassium	5.1*	3.5 -5.0	Elevated
Bicarbonate	20*	24 -30	Reduced
eGFR	34.2ml/min/1.73		CKD 3b
Serum calcium	2.4	2.2 -2.6	Normal
Phosphate	1.2	1.1 -1.7	Normal
Uric acid	441*	120- 420	Elevated
Total protein	70	62-80	Normal
Serum albumin	32*	36-50	Reduced
Total cholesterol	5.16	<5.2	Normal
Triglycerides	1.79*	0.3-1.7	Elevated
HDL	1.2	>1.12	Normal
LDL	3.15*	<2.6	Elevated
RBS	32.7*	3.3-5.5	Elevated

ESR- Erythrocyte sedimentation rate, eGFR- estimated Glomerular filtration rate, HDL- High density lipoprotein, LDL- Low density lipoprotein, RBS- Random blood sugar

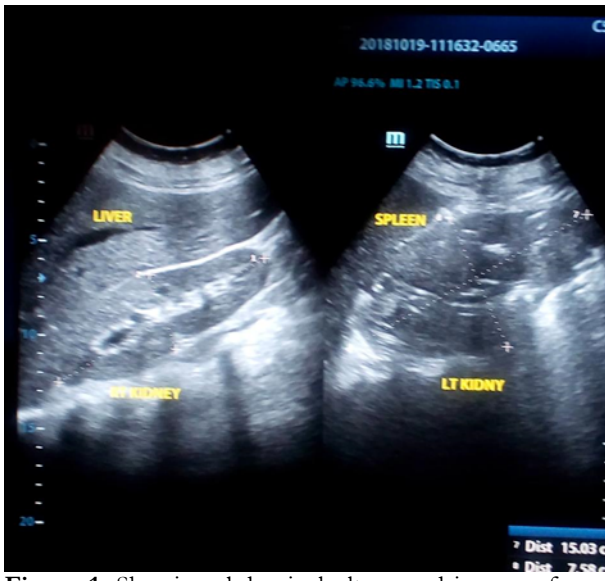

Figure 1: Showing abdominal ultrasound images of the right and left kidneys with the left enlarged with hyper echoic features suggestive of emphysematous pyelonephritis.

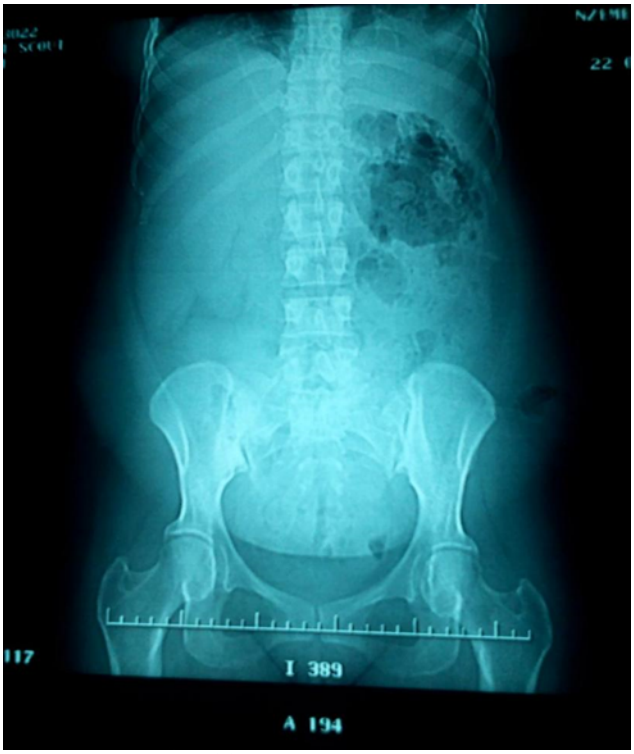

Figure 2: Erect CT image showing multiple gas shadows within the left renal fossa.

Print ISSN: 0189-9287

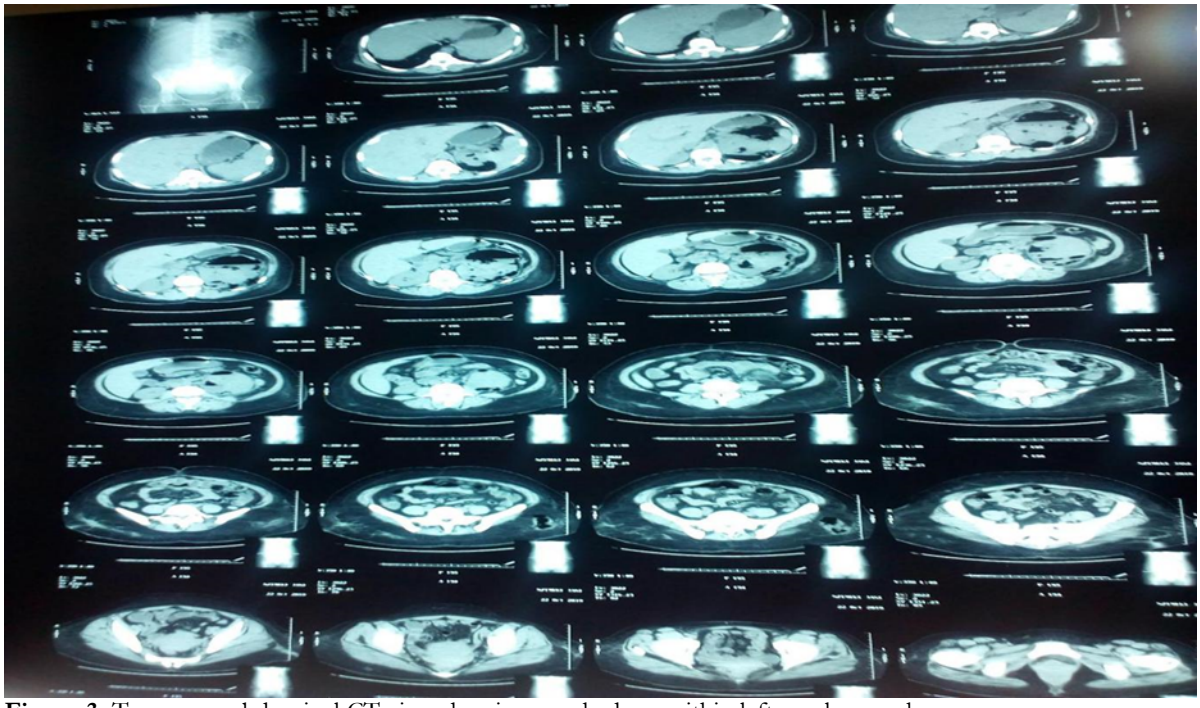

Figure 3: Transverse abdominal CT view showing gas shadows within left renal parenchyma.

She was admitted into the intensive care unit where acute resuscitative measures were instituted. She was reviewed by the urology and endocrinology units of our hospital. She received intravenous 0.9% normal saline and Insulin therapy for blood glucose control, while empirical antibiotics therapy with intravenous ceftazidime 1 gram BD and tinidazole 800mg daily was commenced whilst awaiting urine culture and sensitivity results.

She was counseled on her clinical diagnosis and the possible treatment strategies and prognosis. Two weeks after hospitalization, she made significant clinical improvement, her blood glucose stabilized at 5.6mmol/L and renal functions had improved. Her medications at discharge included tablets Metformin 1gm BD, tablets Glimepiride 2mg daily, tablets Lisinopril 2.5 mg daily, tablets Clopidogrel 75mg daily and tablets Rosuvastatin 10mg daily in line with her elevated lipid profile and cardiovascular risk assessment.

At her first follow up visit, she was in good clinical condition and a repeat abdominal ultrasound reported enlarged left kidney measuring 13cm x 6.4 cm, with increased echogenicity and poor corticomedullary differentiation without features of emphysematous pyelonephritis. She is currently being followed up in the nephrology clinic of our hospital.
Results of her serial E/U/Cr are shown in table 2.

Table 2: Showing baseline renal functions of the patient from admission to discharge.

Investigation	Day 1	Day 6	Day 11
Sodium (mmol /L)	110	138	142
Potassium (mmol/L)	5.1	4.6	4.2
Bicarbonate (mmol/L)	20	22	23
Urea (mmol/L)	15	8.6	6.3
Creatinine (mmol/L)	180	147	100
eGFR ml/min/1.73m^2	34.2	43.1	67.3

eGFR- estimated glomerular filtration rate

Print ISSN: 0189-9287

Case Discussion

Emphysematous pyelonephritis (EPN) is a urological emergency of great concern to the Nephrologist as well as a rare complication of diabetes mellitus in recent times. It is a severe necrotizing infection of the renal parenchyma that results in gas accumulation in the renal parenchyma, collecting system, or perinephric tissues and can be fatal if not identified and treated promptly.[1] It was first reported in 1671 as a case of 'pneumaturia' and later as 'gas forming' renal infection in 1898. Other descriptive terms used for this condition also included 'renal emphysema' and 'pneumonephritis', however in 1962, Shultz and Klorfein recommended the nomenclature 'emphysematous pyelonephritis' (EPN).[1]

Although cases of EPN have been reported worldwide, it appears more common in Asia. About 1-2 cases are seen per year and reported to be 6 times more common in women than in men with a mean age reportedly 55 years.[1] Increased susceptibility to UTI seems to be the reason for the higher incidence in females. It affects the left kidney more often than the right however, less than 10% of cases involve both kidneys. [2] 95% of affected individuals are poorly controlled diabetics with an HbA1c level far exceeding recommended values.[1] Our index patient meets this epidemiologic criteria for the development of EPN.

This risk of EPN further increases in urinary tract obstruction to about 25-40%. [1]EPN may also be seen in patients with renal stones, polycystic kidney disease, end stage renal disease, drug abuse, malnourishment, neurogenic bladder, alcoholism, diabetic ketoacidosis and anatomic anomaly. A few cases have been reported in transplanted kidneys.[3] Overall mortality rate is reported at 21% and a cure rate following nephrectomy being 90%, while success rate with conservative management is 66%. Mortality from EPN is primarily attributable to septic complications however, improvement in management techniques has reduced the mortality rate.[1]

Enteric gram negative facultative anaerobes such as Escherichia coli species have been implicated in 70% of cases.[1]Other organisms found in EPN may include *Pseudomonas, Proteus mirabilis, Klebsiella pneumoniae*, Group D *Steptococcus* and coagulase-negative *Staphylococcus*. There have been reports of mixed organisms in about 10% of cases with a blood culture identical to a urine culture in 54% of cases. Our patient had a urine culture that was sterile however we could not have a comparative blood culture result for reasons of financial constraint. Rarely, anaerobic micro-organisms including *Clostridium septicum*, *Pneumocystis jiroveci* , fungi such as *Candida albicans, Cryptococcus neoformans* , *Aspergillus fumigatus* as well as protozoa (*Entamoeba histolytica*) have been isolated in samples.[1]

The proposed mechanism of EPN is thought to be mixed acid fermentation of glucose with carbon dioxide production by these pathogens, however analysis of the gas content in EPN is found to contain Nitrogen (60%), Hydrogen (15%), Carbon dioxide (5%) and oxygen (8%).[4] Diabetic patients are particularly predisposed to EPN due to factors such as uncontrolled diabetes, high levels of glycosylated hemoglobin and impaired host immune mechanism.[2] In addition, diabetic nephropathy with associated microvascular disease may potentiate the growth of gas-forming microbes and delayed removal of these waste products of catabolism promoting gas formation and accumulation in renal tissues.[2]

Classification of EPN is based on radiological findings. The more recent classification by Huang and Tseng published in 2000,[5] was based on the CT findings. They classified EPN as follows: Class 1: gas in the collecting system only; Class 2: gas in the renal parenchyma without extension to extra-renal space; Class 3A: extension of gas or abscess to perinephric space; Class 3B: extension of gas or abscess to para-renal space; and Class 4: bilateral EPN or solitary kidney with EPN. The index patient may be classified as class 3A.[5]

As observed in the index case, patients with EPN usually present with nonspecific signs and symptoms such as fever, rigors, nausea and vomiting, pain in the flanks, abdomen or back, dysuria, changes in mental status, and even shock. Loin tenderness is the most common physical sign with crepitus around the renal area and the scrotum in advanced cases.[1] More unusual presentations include pneumomediastinum and subcutaneous emphysema, multiple septic emboli to the brain, lungs, and liver.[2]

Print ISSN: 0189-9287

Laboratory data will indicate sepsis with evidence of leucocytosis in 70–80% of cases, thrombocytopenia in 46% of cases[1] however our patient had thrombocytosis. Other laboratory findings will include microscopic or macroscopic haematuria and severe proteinuria, acute renal dysfunction and acid-base disturbances.[1] Emphysematous pyelonephritis is a radiological diagnosis. A plain radiograph shows an abnormal gas shadow in the renal bed in 65% of cases whereas an ultrasonography will diagnose in 69% of cases.[1] Abdominal CT is more sensitive and will confirm the presence of intrarenal gas. CT defines the extent of EPN by identifying features of parenchymal destruction which supports the early diagnosis and further management of EPN.

Differential diagnosis for EPN will include xanthogranulomatous pyelonephritis, autosomal dominant polycystic kidney disease, multicystic dysplastic kidneys, renal cell carcinoma etc.
The treatment strategies include medical management alone, Percutaneous drainage (PCD) plus medical management, emergency nephrectomy plus medical management, and PCD plus medical management plus emergency nephrectomy. Although emergency nephrectomy has been the preferred treatment for EPN, a nephron-sparing approach is increasingly favored. Generally, antibiotics, percutaneous drainage of abscesses, fluid resuscitation, and tight control of glucose are the mainstays of treatment. Successful treatment with medical management alone has been reported even in the severe forms of bilateral emphysematous pyelonephritis.[2]

Basic resuscitative measures of oxygen and acid base balance correction are necessary for outcome.[2,5] Choice of antibiotics should be tailored towards gram-negative bacteria, and so initial regimen should deploy the use of any of the Aminoglycosides, β-lactamase inhibitors, cephalosporins or quinolones. Once the culture report is available, the antibiotics can be changed according their individual sensitivities. Our patient was commenced on the cephalosporins and she responded well to the treatment despite the culture negative urinalysis.

Percutaneous drainage (PCD) as a treatment option for EPN,[6] have shown benefits when used in addition to medical management, with significant reduction in the mortality rates. PCD helps to preserve the function of the affected kidney in about 70% of cases.[7] PCD is performed under CT guidance and conservative treatment using PCD with antibiotics is indicated for patients with compromised renal function, early cases associated with gas in the collecting system alone. Multiple abscesses can be drained with more than one catheter. The drainage tubes are allowed to stay until follow-up abdominal CT at 4 to 7weeks shows resolution of the EPN features such as non-communicating air/fluid collections.[1]

Nephrectomy is the treatment of choice for most patients especially when there is no access to percutaneous drainage or internal stenting or if there is the presence of gas in the renal parenchyma or "dry-type" EPN. It is also indicated in patients with bilateral EPN, as well as Class 3 and class 4 EPN with two or more risk factors (e.g. thrombocytopenia, elevated serum creatinine, altered sensorium, shock).[1]

EPN mortality rate is about 18.7 - 50% depending on the class of EPN,[2] significant treatment success rates with percutaneous drainage and antibiotics is reported at 66% and 90% with nephrectomy.[5] Although our patient had class 3A EPN and two of the risk factors associated with poor prognosis, emergency nephrectomy was not attempted and an attempt at percutaneous drainage of perinephric abscesses was planned but not done, nevertheless, she responded well to antibiotic therapy and was able to be discharged to rehabilitate at home.

Limitations of the case report: There is paucity of data of emphysematous pyelonephritis among diabetic patients in our environment with which we could have compared clinical presentation and management challenges to that of our index patient. Percutaneous drainage of perinephric abscesses with concomitant antibiotic therapy could have been a better treatment option if there were available resources for the procedure. This would invariably enhance better long-term treatment outcomes and strengthen already established treatment guideline.

Conflict of interest: No conflict of interest

Funding: No funding

Conclusion

Emphysematous pyelonephritis is a rare presentation of pyelonephritis, also its severity and patient outcome

Print ISSN: 0189-9287

is worse with coexisting diabetes mellitus. Prompt and appropriate treatment therefore must be instituted to prevent mortality.

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Print ISSN: 0189-9287