ORIGINAL ARTICLE

EMPHYSEMATOUS PYELONEPHRITIS: A REVIEW OF SIX CASES

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Background: Emphysematous pyelonephritis is a severe life threatening necrotising infection of the renal parenchyma. The infection most commonly occurs in the diabetic population, often associated with the organism *E. coli*. Emphysematous pyelonephritis differs from standard pyelonephritis by the bacterial liberation and accumulation of gas in the surrounding tissues. The condition is rarely encountered in clinical practice and since the first description by Kelly *et al* in 1898, approximately 200 cases have been reported in the literature. **Methods:** The case series examines our experience with six diagnosed cases of emphysematous pyelonephritis over a one year period. **Results:** All patients were female, the mean age of presentation being 53 years. Of the six patients, five were diabetics with hypertension, the one exception being a non-diabetic patient who had undergone renal exploration in the past. Computed tomography confirmed the diagnosis in all patients except one which was confirmed during renal exploration. Urine culture was positive for E. coli in two patients. **Conclusion:** Emphysematous pyelonephritis which used to be a rare disease is now being more readily diagnosed. The cases were diagnosed at a late stage making its conservative management not feasible

Keywords: Emphysematous pyelonephritis, renal infections, nephrectomy, renal parenchyma

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INTRODUCTION

Emphysematous pyelonephritis (EPN) is a severe, necrotizing, intra-parenchymal gas forming renal infection.[1] Gas formation commonly occurs in the collecting system, renal parenchyma and perirenal tissues. The first reported case of a gas forming renal infection was presented by Kelly and McCullum in 1898. Since then, approximately 200 cases have been described in the literature.

The majority of Emphysematous pyelonephritis cases occur in the diabetic population, often associated with poor glycaemic control.[3] EPN is also prevalent in patients with urinary tract obstruction[2], and in immuno-compromised individuals.[3,4]

Emphysematous pyelonephritis commonly presents with fever, altered mental status, loin/flank pain, dysuria, lethargy and confusion. In severe cases, toxic encephalopathy and/or septic shock are seen.[1,5] The most common causative organisms cultured from urine or pus collections are E. Coli.[6–8] *Proteus* spp., *Klebsiella* spp., Anaerobic *Streptococci* and *Pseudomonas* spp.[3]

Computed tomography is the preferred imaging modality, providing direct visualization of gas in the renal parenchyma and assisting with staging of the disease process.[1]

Nephrectomy is treatment of choice in extensive EPN, however, early diagnosis with aggressive medical management and percutaneous stenting can diminish the need for a nephrectomy.[3–12]

We present six cases of diagnosed EPN over a one year period from January 2012, to January 2013.

CASE-1

A 60 year old female presented to the outpatient department with symptoms of bilateral flank pain which radiated to the back, intermittent vomiting and fever since 2 weeks. She was a known diabetic and had been put on oral hypoglycaemic agents with good patient compliance. She had undergone dialysis five days previously due to declining renal function and abnormal blood chemistry. The patient also had a CVA 2 years previously.

On physical examination, the patient appeared pale and distinctly ill looking. She seemed confused and was not orientated in space or time. Systemic examination was unremarkable with the exception of some limb power loss. Laboratory tests included a complete blood count which showed no derangement, renal function tests which showed a BUN of 56mg/dl and a Creatinine of 1.95 mg/dl. A random blood glucose test showed good glycaemic control (112 mg/dl). Urinalysis revealed numerous pus cells and RBCs (10-12/HPF).

A CT scan of the abdomen revealed the presence of air in renal pelvis with perinephric pus. Surgical renal exploration was performed and a nephrostomy tube was inserted, evacuating 1,500ml of pus. She was put on a 3rd generation cephalosporin following surgery

Post-operative wound examination showed a healthy wound margins with no evidence of infection. During her stay her blood sugar was

closely monitored and she was put on a insulin sliding scale regimen. She was put on oral hypoglycaemics on 6th post op day. On 7th post op day she was discharged without a drain and put on diuretics and metronidazole. The patient made a full recovery and was followed up after 1 month.

CASE-2

A 55 year old paraplegic female presented to the outpatient department with symptoms of suprapubic and bilateral flank pain radiating to the back, burning micturition and fever since 10 days. The patient was a diagnosed diabetic with no glycaemic control and had a history of hypertension. On general examination, the patient had a temperature of (101F) and an elevated blood pressure (160/90). Systemic examination was unremarkable apart from exquisite flank tenderness.

A complete blood count was performed showing an elevated WBC count (15.3). Serum electrolytes showed elevated potassium and chloride levels. Renal function tests revealed a BUN of 180 mg/dl, Uric acid 13.6 mg/dl and a Creatinine of 5.06 mg/dl. Urine microscopy showed numerous pus cells, 4-6/HPF RBCs and epithelial cells were seen on microscopic examination Albumin +++.

A plain KUB radiograph showed a left renal stone. An Ultrasound was performed which showed a perinephric abscess. CT abdomen showed a small left radio-opaque shadow with a hypodensity at the perirenal space.

The patient underwent dialysis prior to surgery and had a left kidney exploration performed, nephrolithiasis .The patient was discharged on 6th post op day with good health and renal chemistry (urea 49 mg/dl, Creatinine 1.49 mg/dl) with follow up planned in two weeks.

The patient presented after 11 days with history of confusion, fever and chills as well as suprapubic pain, bodyaches, loss of appetite, nausea, non-productive cough and surgical site pain. The patient was deemed to have renal sepsis and was admitted into the SICU. Despite critical care the patient expired on 3rd day of admission.

CASE-3

A 60 years old diabetic and hypertensive female presented to the neurology outpatient department with a 15 day history of right flank pain, fever and a one day history of urinary retention. General examination revealed a temperature of 98º F, a heart rate of 117 bpm and a blood pressure of 140/70. She was anxious and confused with tenderness at the right flank.

Laboratory tests revealed a Hb of 11.2g/dl, WBC count of 22×10^9/L with 90% neutrophils. A Random blood sugar test showed poor glycaemic control (225mg/dl). Renal function tests showed an elevated BUN (42 mg/dl).

Urine microscopy showed numerous (+++) leukocytes. E.coli was cultured from the urine. An Ultrasound study showed right ureteric and renal stones. CT Abdomen showed right renal calculi with moderate hydronephrosis and a focal right perinephric collection likely to be a urinoma communicating with the mid pole calyx (Figure-1).

Pre-operative ECG revealed ST elevation deemed to be low risk by cardiologists. The patient underwent right URSF with right pyelolithotomy. 1,700ml of pus was drained and gases evacuated. The wound was left open and packs were placed in the wound. She was put on IV Cefoperozone/Sulbactam 2 gm BD and IV piperacillin 4.5 gm BD, with 2 Red blood Cell packs transfused. The patient had an uneventful postoperative course and discharged home in stable condition with Angiography advice. She came again after 3 months having no complaints; a repeated CT KUB shows no evidence of air in kidney and DJ stent removed.

CASE-4

A 60 year old known diabetic and hypertensive female presented to the outpatient department with 6 month history of intermittent fever, epigastric pain radiating to the flank, burning micturition, hematuria and foul smelling urine.

She had undergone a lithotripsy for a renal stone in the past. A general examination was unremarkable except for an elevated blood pressure (150/90). Systemic examination revealed a tender right flank with abdominal striae on both flanks.

Laboratory tests showed a Haemoglobin 13.8 g/dl, TLC 11.7×10^9/L, triglycerides 419 mg/dl, RBS 114 mg/dl with HBA1c 11.6%, urea 38mg/dl, Creatinine 0.92 mg/dl Urine Analysis shows +++, Leukocytes with 10–12 red cells, 20–25/HFF pus cells with no ketone bodies.

An abdominal ultrasound was performed which showed a small scarred right kidney. CT excretory urograph showed a right renal calculus with hydronephrosis and air within pelvicalyceal system (Figure-2). Echocardiography showed a mitral regurgitation with concentric left ventricular hypertrophy. A DPTA scan was done which revealed markedly reduced right kidney function and adequate left kidney. A Blood culture showed no growth of microorganisms.

The patient underwent a right total nephrectomy. She was put on IV ceftriaxone, omeprazole and analgesics. The patient had an uneventful postoperative course except for two

fever spikes which were managed with a paracetamol infusion. The patient was discharged in a stable condition.

CASE-5

A 35 year old female presented to A&E with one day history of nystagmus, generalized seizures, tongue biting and fever. She had previously been operated on for a left kidney stone two years ago. Physical examination was unremarkable except for bilateral constricted pupils. Laboratory investigation revealed a Hb of 15.5 gm/dl, TLC 10.6 $x10^9$/L, urea 26mg/dl, creatinine 0.79 mg dl and RBS 86 mg/dl, urine analysis shows numerous leukocytes (++), albumin+ and epithelial cells with no ketones bodies.

A CT KUB showed bilateral renal calculi causing obstruction, hydronephrosis bilaterally with suspicion of pyonephrosis on right side, bilateral pleural effusion with a uterine fibroid and pelvic ascites. (Figure-3) She underwent right sided kidney exploration with nephrostomy and bilateral stenting and was discharged home in a stable condition.

CASE-6

A 50 year old known diabetic and hypertensive female presented to the outpatient department with a fifteen day history of intermittent fever, chills and right flank pain. She had previous history of having undergone a hysterectomy.

Physical examination showed pallor and pedal oedema with a Blood pressure of 140/90. Systemic examination revealed tender right flank with no visceromegaly. Chest examination shows bilateral basal crackles.

Laboratory investigation results were as follows: Haemoglobin 9.39 g/dl, TLC 10.5×10^9/L with 65% Neutrophils, RBS 394 mg/dl with HBA1c 10.6%, urea 71 mg/dl, Creatinine 2.32 mg/dl. Urine Analysis showed +++ Leucocytes with++ Albumin, numerous pus cells with no ketone bodies. A urine culture revealed the presence of E.Coli (cephalosporin producing) sensitive to imipenem, meropenem and nitrofurantoin.

CT KUB showed air in urinary bladder, perivesical space and right pelvicalyceal system. The patient was empirically put on ceftriaxone and switched to meropenem after a C/S report. The patient has also received one session of haemodialysis.

Patient discharged home in stable condition on antibiotics, oral hypoglycaemic. The patient is followed up after 1 month repeatedly 3 times with 10 days gape and her renal function (creatinine 1.5 mg/dl) and clinical status was improving. Her CT KUB repeated showing no air in renal pelvis/parenchyma except right swollen kidney with mild par aortic lymphadenopathy. The patient again presented to urology OPD after 2 months of stable condition with 10 days history of back pain, right flank pain, persistence vomiting, and numbness in lower limbs.

She has 2 episodes of bubbles passing in urine (pnematuria).Physical examination shows pallor looking; peripheral oedema .Systematic Examination shows tenderness in right hypochondrium, Rest of examination was unremarkable. Her Fresh investigations shows 11.2 g/dl Hb,16700/cmm TLC,RBS 299mg/dl, urea 112 mg/dl and creatinine 2.93 mg/dl. Urine analysis shows +++ albumin as well as leucocyte, loaded pus cells with no ketone bodies. Fresh CT KUB done shows air within pelvicalyceal system, right ureter, lumen and wall of bladder, suggestive of Right side pyelonephritis with Emphysematous pyelitis and cystitis (Figure-4).

Patient was put on meropenem and ceftriaxone, she had again subsiding symptoms and discharged home in stable condition having no symptoms.

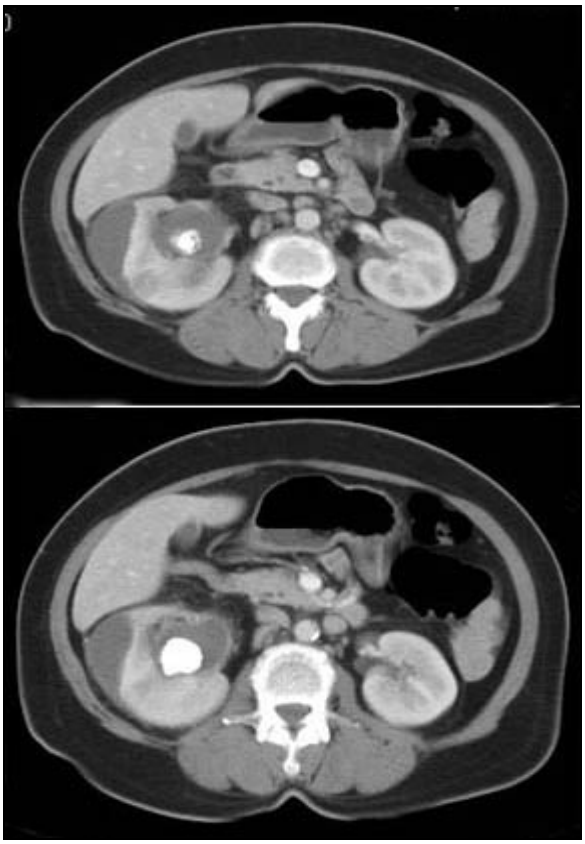

Figure-1: CT Abdomen shows right renal calculi with moderate hydronephrosis, focal right perinephric collection, right distal ureteric stone with paraortic lymphadenopathy

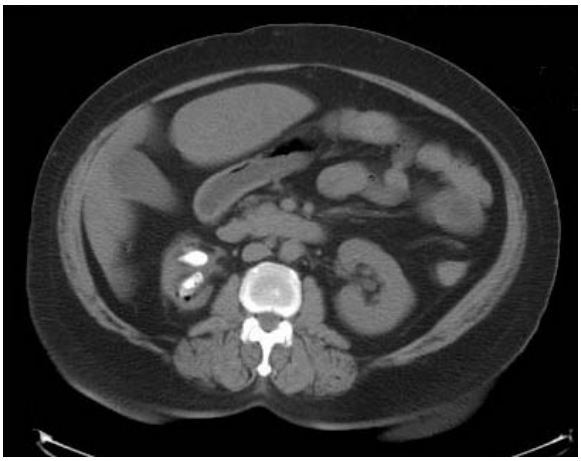

Figure-2: CT Excertory urography shows right renal calculi with hydronephrosis, contain air in pelvicalyceal system, small echogenic kidney on right side

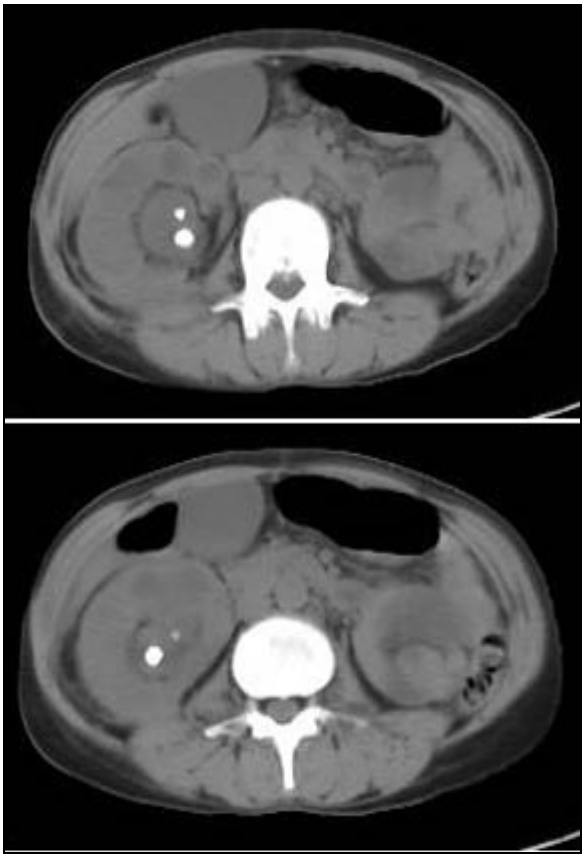

Figure-3: Biateral renal calculi causing obstruction, hydronephrosis bilaterally with suspicion of pyonephrosis on right side.

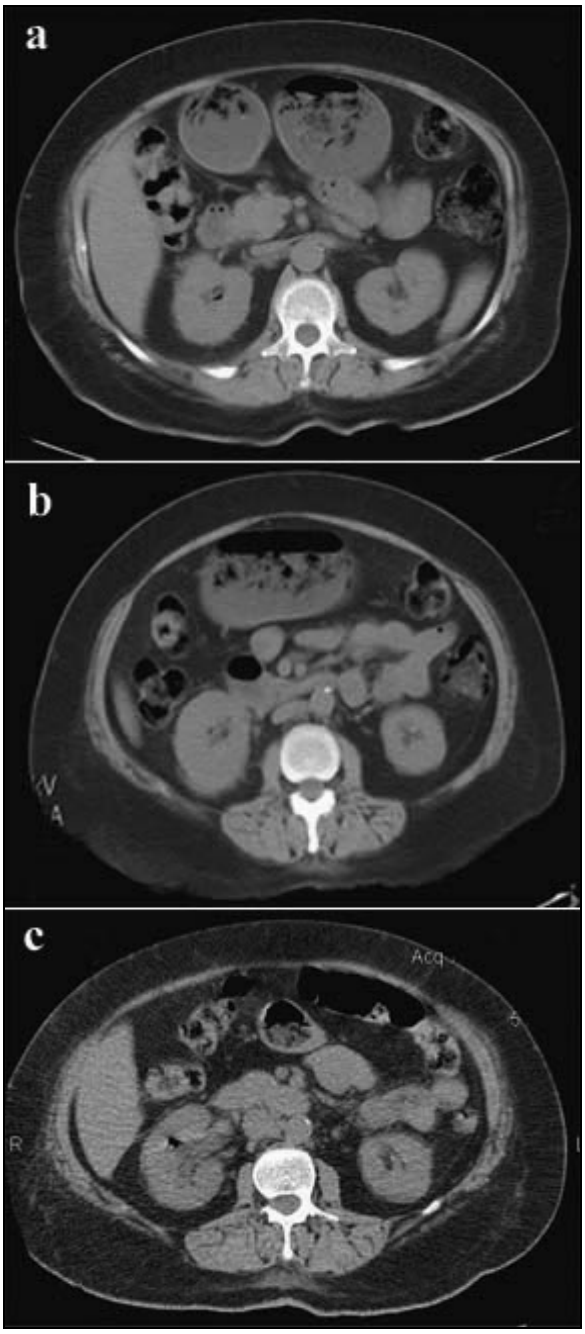

Figure-4.a) Swollen right kidney with air in the urinary bladder, perivesical space and right pelvicalyceal system(before treatment).
b) Enlarged swollen kidney with mild paraortic lymphadenopathy(after medical treatment).
c) Air within pelvicalyceal system, right ureter, lumen and wall of bladder (recurrent infection)

Table: Summary of demographic characteristics and clinical features of cases

		Demographic And Clinical Charactiristic Of Patient And OutCome					
Patient		Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age		60 y	55 y	60 y	60 y	35 y	50 y
Gender		Female	Female	Female	Female	Female	Female
Co-Morbid		DM,HTN	DM,HTN	DM,HTN	DM,HTN	Epilipsey	DM,HTN
Past Histroy		CVA	paraplagia after fall	Urolithiasis,ST elevatated MI	heamoridectomy,lithrotripsy	Left kidney stone being operated	NA
Clinical Feature		bilateral flank pain,vomitting,intermittent fever	suprapubic and flank pain with burning micturation, readmitted with confusion,fever and chills after 11 days .	Right flank pain,fever and1 day of urinary retentation	fever off/on,epigastric pain,pnemuturia,foul smelling urine	nystegmus,seziure,tongue biting,fever	Fever,chills,right flank pain and uncontrolled sugar, readmitted with pnemuturia,vomitting,numbness in limbs and back pain
Clinical Finding		pale,anoxious,slurred speech,tender flank,power 2/5 left side	pale looking,febrile,tender flank, readmiited with	anoxious,tender right flank pain	pale,anoxious,tender right flank,bilateral abdominal striea	bilateral constricted pupil	pale looking,afebrile,pedal edema present,right tender flank,bilateral basal crackels
SymptomDuration		10 days	10 days	15 days	6 months	1 day	15 days
Class		IIIA	IIIA	IIIA	I	I	II
Blood Test							
	TLC	13.8 x 109/L	15.3x109/L ,28x109/L	22x109/L	11.7x109/L	10.6x109/L	10.5x109/L
	RBS	112 mg/dl	75mg/dl	225mg/dl	114mg/dl	86mg/dl	394mg/dl
	CREAT	1.95mg/dl	5.06mg/dl,2.68	1.02mg/dl	0.92 mg/dl	0.79mg/dl	2.32mg/dl
	UREA	56mg/dl	180 mg/dl,94mg/dl	42mg/dl	NA	26mg/dl	71mg/dl
	BLOOD C/S	NA	NA	NA	No growth	NA	NA
URINE Exam							
	Leucocyte	present +++	present +++	present ++	present +++	present ++	present +++
	Albumin	NIL	present +	Nil	Nil	present +	present ++
	Puse Cells	10-12/HPF	numerous	Nil	20-25/HPF	Nil	Numerous
	Culture	NA	NA	No growth	NA	NA	E.coli
pus culture		No growth	NA	E.coli	NA	NA	NA
Dialysis		1 session	1 session	NA	NA	4 session	1 session
Intervention		Right side Renal exploration with nephrostomy tube insertion and 1500 ml pus drained	Left kidney exploration,nephrolithiasis,abscess drainage confirm EP	Right URSF,Phyleolithotomy,Lot of pus drained,wound left open	Right total nephrectomy	Right side kidney exploration with nephrostomy and bilateral stenting	medical treatment with ceftriaxone ,imepenem and sliding scale
Outcome		Recovered	Died	Recovered	Recovered	Recovered	Recuurent infection

DISCUSSION

Emphysematous pyelonephritis is a severe gas forming renal parenchymal infection, rarely occurring, having bad prognosis.[14] Several authors recommended that EPN is a gas in renal parenchyma but defines it as the presence of gas in collecting system, renal parenchyma and perirenal space.[18] Two of our cases have gas in pelvicayceal system with one of case had gas as well in bladder and perirenal space. All other cases of emphysematous pyelonephrities had gas in minimal amount along with pus in large amount at perinephric area.

Emphysematous pyelonephritis occurred in about 90% of Diabetic patient.[18,19] EPN with immunological impairment had been reported in 10% of patient, while some authors had reported EPN with urinary tract obstruction in 20% of patients.[19] All of our patients were Diabetic and hypertensive with one had lithrotripsy in past, except one who was non Diabetic but epileptic, however she had been done left nephrolithotomy for renal stone. One of Diabetic and Hypertensive patient had urinary tract obstruction with a stone in ureter which was most likely cause of EPN.

A case of EPN by Yayi He had been reported with congenital hypospadias in China in 2012.[19] Renal transplant recipient and polycystic kidney disease patients with EPN had also been reported.[12] Morioka et al reported one case of splenic abscess in Japan having hypotension diagnosed as EPN, showing association of disease with splenic abscess.[10] None of our cases were renal transplant recipient and had polycystic kidney disease. Congenital hypospadias and hypotension was not found in any of cases however except one all others were hypertensive.

Drug abuse, alcoholism and anatomic anomaly are other co factors associated with EPN reported so far.[17] Our cases were from developing countries where alcoholism is not so common like developed countries, however drug abuse is more common but history regarding drug abuse were not asked.

Most common organism in EPN patients is *E. Coli* (70%)[18], isolated in urine or pus of about 70% of cases reported so far [17].K.pnemonia (24%), *Proteus mirbalus* (5%) and mixed or other form (1%) had also been isolated from urine/blood in most of patients.[18]

Our cases were from developing countries ,due to financial problem Culture and sensitivity of majority of patients were not sent, however one blood culture showing no growth, and two pus as well as urine specimen were sent for Culture and sensitivity. E.coli growth was reported from one pus and one urine specimen of different patients while others specimen show no growth.

EPN presented most commonly with fever, abdominal pain, nausea, vomiting, lethargy, confusion, dyspnea and shock.[3] Pnemuturia is a less common feature.[12] All of our cases were presented with fever some have chills associated with it, flank pain in four patients, pnemuturia and vomiting in two patients. These clinical features of EPN are consistent with features reported in different literatures.

One patient with urolithiasis also presented with urinary retention, Epileptic patient only presented with signs of epileptic seizure such as nystagmus and tongue biting. None of our patients were presented with shock except one who had been operated and readmitted with shock possibly may be because of sepsis. When EPN extends outside the perirenal space crepitus may be palpated over the underlying tissue of kidney.[1] In our patients there were no crepitus palpated as some of them had infection extending to perirenal space. However one patient with lithotripsy and haemorrhoidectomy done in past had abdominal striea, which were not reported in EPN patients in literatures so far, however other causes of abdominal striea were not found.

High blood sugar, increased leukocyte count and thrombocytopenia are present in laboratory investigations. Most of EPN patient have pyuria.[3] All of our patient had normal glycosylated blood because they were controlled with medication except one who had high blood sugar level because she had presented with uncontrolled sugar level and so had recurrent EPN. Except two all other patients have pyuria which is more significant with literature search.

Abdominal radiography allow easy detection of air with less than 33% of sensitivity in case of EPN[18], Renal ultrasound can confirm presence of EPN in 80% of cases.[15]

However CT scan is 100% sensitive[15] which not only help in diagnosis but also help in staging of disease.[18] In our patients X-ray KUB shows stones with streak of slight radiolucent shadow however ultrasound helps in diagnosis a lot by showing pyonephrosis in most of patients. Diagnosis of EPN was confirmed by CT KUB in all patients except one which only show stone in kidney; however EPN in that patient was confirmed by surgery showing lot of pus.

Immediate resuscitation, broad spectrum antibiotic and percutaneous JJ stenting is a best way of treating EPN.[17] Huang *et al* concluded that class-1 and class-2 should be treated with percutaneous drainage and antibiotic. Class-3 and 4 with fewer than 2 risk factors treated with percutaneous drainage and antibiotic having less than 64% success rate.[5] Subsequent studies have shown that EPN treated with PCD along with medical management have been successfully treated and had shown reduction in mortality rate.[17]

Aswathan *et al* reported a review on 41 patients of EPN in 2008 showed that 80% of these patients were successfully treated with PCD along with antibiotic.[14] A case of EPN with renal allograft treated successfully with PCD and antibiotic was reported by Alexander et al in 2012 in India.[6]

In our cases half of patients were treated successfully with broad spectrum antibiotic along with nephrostomy tube insertion as well as pus drainage; however one patient had done bilateral stenting. All of them were followed of having no complication and repeated scan was negative for presence of gas. One patient who had also backache history with numbness was treated with imipenem successfully.

She was brought again by having flank pain, repeated scan was negative and so no intervention done .But after a month she had again presented with air bubbles in urine so repeated scan was done suggesting EPN. Her blood sugar level was high and uncontrolled so that's why she had recurrent infection but again treated with ceftriaxone and imipenem and within two days her symptoms subsides. All our cases treated medically without requiring nephrectomy were of class-I and class-IIIA having no other risk factors such as thrombocytopenia. Patient treated with only broad spectrum antibiotic was of class-II.

Haemodialysis may be lifesaving therapy (empirical) while awaiting normal kidney function[16], In case of bilateral renal disease it may require long term dialysis.[1] All our patients who were treated medically were dialyzed once, Except one who had epilepsy, she had received 4 sessions of dialysis to normalize her renal biochemistry because she was at acute renal failure.

A study conducted by Huang JJ *et al* in 2000 in china on 48 cases of Emphysematous pyelonephritis have shown overall 90% success rate of nephrectomy.[5] Bilateral nephrectomy done in a patient of bilateral EPN with autosomal dominant kidney, putting her on long term dialysis and planed renal transplant later, case reported by Lakshminarayana G *et al*.[9] Class-III and Class-IV with more than 3 risk factors is better option to be treated by nephrectomy.[5] A case of EPN Class-III A with shock, renal impairment, conscious loss and thrombocytopenia reported by He Y in China in 2012 treated with nephrectomy as elective procedure.[19] One of our patient of class I was undergone total right nephrectomy who has no other

significant history except surgical history of haemorrhoidectomy and lithotripsy, she was planned for nephrectomy because she had small echogenic kidney which was non function and her left kidney was good functioning adequately. The patient biopsy was positive for pyelonephritis and she was recovered successfully without any complication.

A study conducted by Huang JJ in 2000 in china on 48 cases of Emphysematous pyelonephritis who were treated by doing nephrectomy with mortality rate of 18.8%.[5] EPN carries 40% of mortality rate with medical management alone.[15] Our cases were recovered fully after doing intervention, with one having recurrent infection.

Only one patient expired who has undergone nephrostomy tube insertion. She died because of sepsis which may be produced due to no care of infection and antibiotic proper doing at home. Although she was given option of mechanical ventilation but her attendant refused due to some financial reason, if she would been intubated, properly she would have recovered.

CONCLUSION

Emphysematous pyelonephritis is not uncommon; most commonly occur in Diabetic & hypertensive patients and with age above 50 years. Renal stone causing obstruction, Urinary tract infection and immuno-suppression as such or due to other co-morbid disease such as Diabetes, Hypertension, convulsion disorder is one of major risk factor for Emphysematous pyelonephritis.

Flank pain, fever and tender flank are some of the common signs and symptoms of Emphysematous pyelonephritis; however some of patient may be asymptomatic. Early diagnose and medical management as well as renal exploration with stenting can prevent nephrectomy carrying good prognosis.

RECOMMENDATION

Research on large scale needed to be done on Emphysematous pyelonephritis because its an emerging disease and some specific clinical feature and physical finding should be sought out.

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