

## Case of emphysematous pyelonephritis in kidney allograft: Conservative treatment

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### Abstract

Emphysematous pyelonephritis is an acute necrotizing infection with gas in the kidney and perinephric space that carries a bad prognosis. Apart from its predisposing clinical entities, diabetes mellitus and immune-incompetence are quite common in patients with this infection. We report a case of a 53-year-old kidney transplant recipient diabetic male, suffering from recurrent fever, abdominal pain and nausea episodes. Immediate broad-spectrum antibiotics were administered and percutaneous drainage was performed after the diagnosis. The bacteria involved were *Staphylococcus epidermidis* and *Escherichia coli*. After 4 weeks of antibiotic treatment and abscesses drainage, the case was resolved. Consecutive urine cultures and ultrasonographies confirm the complete resolution of the disease. We discuss the predisposing factors, clinical presentation and management.

### Introduction

Emphysematous pyelonephritis is a severe necrotizing infection of the renal parenchyma. The main causal agent is gas-forming bacteria like *Escherichia coli*, *Klebsiella pneumoniae* or *Proteus mirabilis*.<sup>1-3</sup> The disease may induce fever, pain, acute renal failure, septic shock or even death.<sup>4</sup> It is a rare disease, with a high mortality rate.<sup>3,5</sup> Few cases in kidney allograft have been reported.<sup>6,7</sup> The risk factors are poor controlled diabetes, immunosuppression and urinary obstruction.<sup>5</sup>

Treatment for this infection is debatable.<sup>1,8</sup> At first, nephrectomy combined with intravenous antibiotics was considered the preferred treatment.<sup>8</sup> Currently, a percutaneous drainage combined with intravenous antibiotics has been proposed as a possible successful treatment. Over time, the condition could worsen and treatment, even surgery, would be too late to consider.<sup>1</sup>

Several classifications with the treatment options have been proposed, with no clear conclusion. Therefore, individual assessments yield better results.<sup>2,4,5,7,8</sup>

We report a case of emphysematous pyelonephritis in a renal transplant recipient. We also review the other reported cases.

### Case report

A 53-year-old male with end-stage renal disease secondary to insulin-dependent diabetes mellitus suffers recurrent fever episodes. He received kidney transplantation 9 years ago. His current immunosuppression regimen was sirolimus 4 mg, mycophenolate mofetil (MM), 500 mg in the morning and 250 mg in the evening, and insulin therapy. He had a baseline serum creatinine of 1.1 mg/dL after kidney transplantation and poorly controlled blood glucose with glycosylated hemoglobin 8.3%. A percutaneous transluminal coronary angioplasty (PTCA) was performed 10 years ago due to a 90% ischaemic injury requiring a coronary stenting. He is a smoker, suffers hypertension and diabetes mellitus. On follow-up by a cardiologist none relevant findings were highlighted.

He developed an episode of graft pyelonephritis in January 2012, from which he recovered after a 2-week course of intravenous antibiotics (amikacin and linezolid) to a serum creatinine (SCr) of 1.7 mg/dL. No instrumentation of the urinary tract had been performed prior to this episode. A graft ultrasound has been done yearly, with no evidence of stones or obstruction in the urinary system. The urine culture showed *Staphylococcus epidermidis* and *E. coli* growth. The repeat urine culture done 2 weeks later did not reveal any growth.

Four months later, the patient request medical assessment. He had episodic fever with recent nausea and vomiting. No urinary symptoms were reported. He had deteriorating general health and weight loss was evident. At examination, tender graft was observed at palpation. No rise of tempera-

ture was measured, his heart rate and blood pressure were within normal range (70 bpm, 130/85 mmHg). The laboratory analysis showed elevated serum creatinine of 3.2 mg/dL, a hemoglobin level of 7.5 mg/mL, an elevated C-reactive protein which reach a maximum of 6.7 mg/L and a total leukocyte count of 12000/ $\mu$ L. Although his blood sugar was 100 mg/dL at this time, glycosylated hemoglobin was increased which implied poorly controlled diabetes mellitus. His immunosuppression regimen was not modified and he complied with it. His sirolimus levels were desirable (10 ngr/mL).

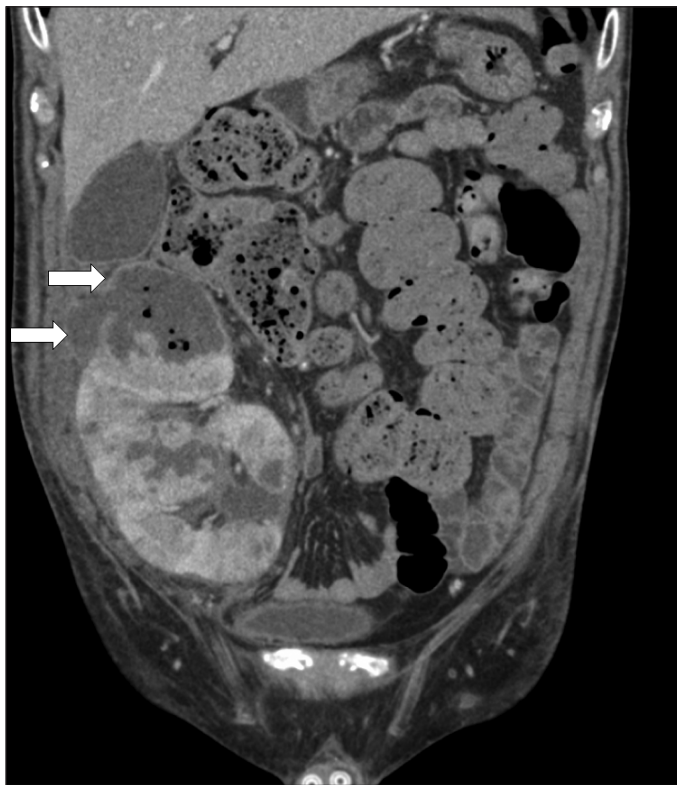
He was admitted to hospital so that we can begin investigations and to start antibiotic treatment. Two packed erythrocytes were transfused and broad-spectrum intravenous antibiotics were initiated. We performed an abdomen computed tomography (CT) scan, which revealed multiple abscesses, gas in parenchyma and collecting system (Fig. 1, Fig. 2), with no signs of obstruction or stones. We diagnosed the patient with emphysematous pyelonephritis. An ultrasound-guided percutaneous aspiration was performed and found purulent material with *Staphylococcus epidermidis* isolated on culture. We placed a drainage catheter of 6 cm over the bigger abscess for 25 days.

The intravenous antibiotic treatment was linezolid (600 mg) twice a day for 1 week and ertapenem 1 g per day for 1 month, according to the sensitivity of the micro-

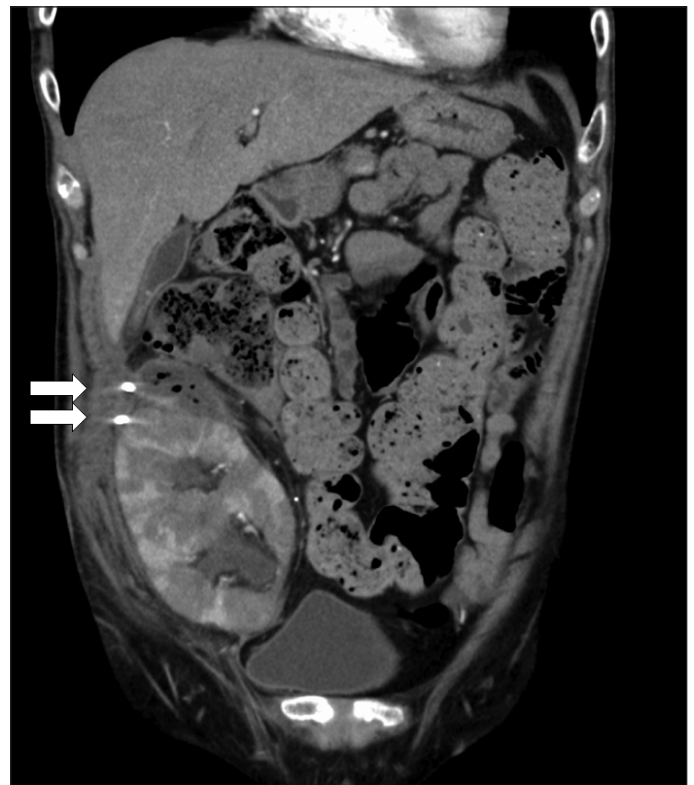
organism. Two consecutive urine cultures were positive for *Escherichia coli*. Although the patient had hypertension, his blood pressure remained well-controlled. It was difficult, however, to keep his blood sugar under control; it went from 100 to 244 mg/dL with isolated levels of 300 to 400 mg/dL in 3 days. Immunosuppression therapy was modified, decreasing the sirolimus to 3 mg. Sirolimus levels slightly fluctuated between 11.8 and 6.16 ng/mL.

Hematogenous spread was not suspicious due to recent tests and uncontrolled blood glucose. The cardiologist performed electrocardiograms which were normal and echocardiogram yearly, which showed a left ventricular hypertrophy with an ejection fraction of 0.6 and which remained stable for years. No more episodes of fever were measured after admission. Since the disease started, the patient suffered a weight loss of 10 kg and reactive arthritis in his left wrist. The patient was discharged after 11 days.

Antibiotic treatment with sulfamethoxazole/trimethoprim (800/160 mg) 3 times a day was maintained for another week after the 1-month of ertapenem treatment. Ultrasonography tests were performed weekly. A decrease in the abscess size (from 6 to 4 cm) was observed until its disappearance 3 weeks later. Another smaller abscess of 2.8 cm was observed without variation in its size. Urine cultures were taken weekly for 4 weeks and 3 months later without positive result.



**Fig. 1.** A computed tomography scan shows the kidney allograft in the right iliac fossa with two abscesses on upper pole and gas in parenchyma.



**Fig. 2.** An early follow-up computed tomography scan shows a decrease of abscesses and two drainage tubes.

After 9 months, with regular follow-up every 3 months, the patient did not report any fever. His serum creatinine was stable at 1.5 mg/dL, his urine cultures were negative and the graft ultrasound performed did not show residual abscesses.

## Discussion

Emphysematous pyelonephritis is an extremely rare disease in kidney allografts. It is an acute suppurative infection due to a gas-forming bacteria.<sup>5</sup> Patients with high tissue glucose levels, impaired tissue perfusion and defective immune response are more likely to suffer a renal parenchyma and perirenal tissue infection.<sup>4,5</sup> Tissue necrosis is observed and could lead to a life-threatening situation.<sup>1,8</sup>

Emphysematous pyelonephritis should be suspected in immunosuppressed patients or in patients with abnormal immune response, inadequate tissue perfusion, or poorly controlled diabetics.<sup>2,4,5</sup> Females are more likely to suffer a emphysematous pyelonephritis; although in renal transplantation, males are more likely to suffer.<sup>3,6</sup>

Another issue to consider is the urinary tract. Patients with obstructive uropathy are more readily to have this infection, and a more severe one. This is due to increased tissue pressure and compromised local perfusion.<sup>8</sup> Anatomic abnormalities must be dismissed too.<sup>4</sup>

The most important pathogenic micro-organisms related to emphysematous pyelonephritis are gas-forming bacteria and those with anaerobic metabolism. More than half of pathogens are *Escherichia coli* (50%<sup>8</sup> or 60%-70%),<sup>4</sup> *Klebsiella pneumoniae* (17%<sup>8</sup> and 20%-30%<sup>4</sup>). In our case, *Staphylococcus epidermidis* was isolated in the urine culture together with *Escherichia coli*.

The typical presentation of emphysematous pyelonephritis includes fever in 80% of cases with flank or abdominal or back pain in 70%, and acute renal failure or defined septic shock appear in one-third of cases.<sup>4</sup> Urine test and culture and blood test usually show at least leukocytosis, increased c-reactive protein and pyuria.<sup>1</sup> Although transplanted patients may cloud, reduce or confuse some symptoms, an imaging test would guide our diagnosis. The first approach is ultrasonography, showing gas in renal or perinephric tissue with dirty shadowing,<sup>5</sup> but the definitive diagnosis test is an abdomen CT.<sup>3</sup> It allows us to assess the extent of renal parenchymal involvement and to determine the patient's response to therapy.<sup>9</sup>

The most controversial point of this pathological entity is its management. Early nephrectomy and joint antibiotic therapy were the standard treatment.<sup>5,8</sup> Now there is a trend to maintain a conservative treatment regimen by percutaneous techniques. A percutaneous drainage proposed in critical patients or in patients with a solitary kidney or severe chronic renal insufficiency showed a successful rate of 18%

to 80%.<sup>8</sup> Early nephrectomy is associated with higher mortality rates than initial conservative treatment. A 25% mortality rate was observed in patients undergoing an emergency nephrectomy, 50% in medical management, and only 13% in percutaneous nephrostomy and medical management.<sup>6</sup> Imaging follow-up is mandatory and especially useful if the patient's condition worsens or deteriorates.

To simplify the management of emphysematous pyelonephritis, a few options have been proposed. The one most used was made by Huang and Tseng.<sup>10</sup> It is based on CT findings and 4 classes, in which a kidney transplantation patient will always be in class 4 and would require a nephrectomy.<sup>5</sup> Wan and colleagues propose another classification divided into 2 types. It is more simple and the real challenge is to achieve a conservative management in patients in the type 2 classification (with collections on renal/perirenal tissue with gas in the collecting system).<sup>7</sup> Three classification stages were proposed by Al-Geizawi and colleagues and depend on the percentage of gas replacing renal parenchyma, and specially focus on renal allograft cases.<sup>6</sup>

## Conclusion

Emphysematous pyelonephritis is a life-threatening condition mostly associated with poorly controlled glucose levels. A high index of suspicion is required in those patients not responding to the routine management of pyelonephritis. It is a radiological diagnosis and CT is the best investigation. The general status of the patient, a prompt response to antibiotic treatment and a proper derivation or no signs of obstruction in the urinary tract would indicate the prognosis. The condition is currently managed with percutaneous drainage, while there is still a possible high mortality rate.

**Competing interests:** Dr. Tienza, Dr. Hevia, Dr. Merino, Dr. Velis, Dr. Algarra, Dr. Pascual, Dr. Zudaire, and Dr. Robles all declare no competing financial or personal interests.

This paper has been peer-reviewed.

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