Case report

Renal allograft failure due to emphysematous pyelonephritis: successful non-operative management and proposed new classification scheme based on literature review


Abstract: Emphysematous pyelonephritis (EPN) is a rare necrotizing infection of the kidney caused by gas-forming organisms, usually occurs in diabetic patients, and often requires nephrectomy for effective therapy. EPN is rarely reported in renal allografts, with only 20 cases found in the English literature. We report herein a case of EPN in a transplanted kidney resulting in acute renal failure and sepsis. The patient was managed non-operatively with subsequent recovery of renal allograft function. Based on this experience and a review of the literature, we suggest an amended classification system for EPN in kidney transplantation to plan and guide treatment options accordingly. However, the scarcity of this disease process, coupled with the lack of prospective validation of the new classification scheme, prevents drawing definitive conclusions regarding optimal management strategies including the role and timing of allograft nephrectomy.

Emphysematous pyelonephritis (EPN) is a rare necrotizing infection of the kidney caused by gas-forming organisms, usually occurs in diabetic patients, and often requires nephrectomy for effective therapy. EPN is rarely reported in renal allografts, with only 20 cases found in the English literature. We report herein a case of EPN in a transplanted kidney resulting in acute renal failure and sepsis. The patient was managed non-operatively with subsequent recovery of renal allograft function. Based on this experience and a review of the literature, we suggest an amended classification system for EPN in kidney transplantation to plan and guide treatment options accordingly. However, the scarcity of this disease process, coupled with the lack of prospective validation of the new classification scheme, prevents drawing definitive conclusions regarding optimal management strategies including the role and timing of allograft nephrectomy.

Case report

A 58-year-old Hispanic woman with a history of insulin-requiring type 2 diabetes mellitus developed end-stage renal disease secondary to diabetes, hypertension, and hyperfiltration; a right native nephrectomy had been performed 12 years previously for urolithiasis. She received
maintenance hemodialysis through a left forearm arteriovenous fistula for 3 years before undergoing expanded-criteria deceased donor kidney transplantation in January 2008. She received single-dose alemtuzumab induction in combination with tacrolimus, mycophenolate mofetil, and tapered steroids. The donor kidney was a zero human leukocyte antigen (HLA) mismatch with the recipient, who had a panel reactive antibody level of 63% at the time of transplant. She experienced immediate graft function and was discharged on the 4th postoperative day. Her initial post-transplant course was uncomplicated except for anemia, difficult-to-control diabetes, and 2 uncomplicated *Escherichia coli* urinary tract infections. She did not require any early hospital readmissions and exhibited excellent renal allograft function with a baseline serum creatinine level of 1.0 mg/dL.

At 15 months after transplantation, the patient presented to the Emergency Department with fever, hypotension, nausea, and vomiting. She appeared acutely ill but denied any lower urinary tract symptoms, abdominal or flank pain, or localizing symptoms. Her vital signs included a blood pressure of 95/50 mmHg, heart rate 119/min, temperature 39.3°C (102.7°F), respiratory rate 30/min, and a room air oxygen saturation of 84%. She was noted to have altered mental status and was subsequently found to have metabolic and lactic acidosis (pH 7.24, bicarbonate level 9 mmol/L, lactate 8.1 mmol/L) as well as acute renal failure (blood urea nitrogen level 68 mg/dL, serum creatinine level 5.7 mg/dL), and hyponatremia (serum sodium level 115 mmol/L). Her complete blood count demonstrated thrombocytopenia with a platelet count of 58,000 but no leukocytosis (total white blood cell count 6100/mm³ with 16% bands). Urinalysis revealed 50 white blood cells per high power field.

She was admitted to the Medical Intensive Care Unit, started on intravenous (IV) cefepime, and given a single dose of vancomycin for a provisional diagnosis of urosepsis, septic shock, and acute renal failure. An indwelling urethral catheter was placed and the patient was started on IV fluid resuscitation including sodium bicarbonate replacement. Her maintenance immunosuppressants were discontinued and the patient was started on stress-dose steroids (hydrocortisone 100 mg IV every 8 h). Unfortunately, she continued to decompensate from a respiratory standpoint and required intubation for tachypnea 24 h after admission. She then underwent urgent hemodialysis through her functioning arteriovenous fistula. She did not require vasopressor support to maintain adequate hemodynamic parameters but did develop oligoanuria.

A kidney transplant ultrasound performed the night of admission demonstrated allograft edema, with echogenic foci along the lower pole of the allograft that were suspicious for gas in the renal parenchyma (Fig. 1). Non-contrast computerized tomography (CT) scan later that first night of admission revealed gas in the parenchyma of the lower pole of the transplanted kidney, with a small fluid collection along the lower pole, and perinephric stranding (Fig. 2). Because of the onset of acute renal allograft failure, IV contrast was not administered for any CT scans. Her urine and blood cultures subsequently grew *Klebsiella pneumoniae* and she was switched to IV piperacillin–tazobactam that was dosed according to renal function.

**Fig. 1.** Ultrasound of renal allograft at presentation (day 0) demonstrating echogenic foci and perinephric fluid along the lower pole of the kidney.

**Fig. 2.** Non-contrast computed tomography scan of renal allograft at presentation (day 0) showing gas in the renal parenchyma.
The patient was transferred to the care of the transplant team with the request to perform urgent allograft nephrectomy. She was administered IV immune globulin (10 g IV, with another dose 5 days later). Interventional Radiology placed a CT-guided percutaneous drain (PCD) in the perinephric fluid collection on the first day after admission; another PCD was placed directly into the gas-containing abscess in the kidney 2 days later. The perinephric fluid appeared bland and was culture negative in the setting of broad-spectrum antibiotic therapy, whereas the renal parenchymal fluid was turbid and subsequently grew *K. pneumoniae*.

The patient began to improve clinically and was extubated after 4 days of ventilatory support. She continued to receive scheduled dialysis treatments even though her urine output improved. Follow-up non-contrast CT scans at 24, 48, 72, and 144 h following PCD showed significant radiographic improvement in the EPN (Figs. 3 and 4). Her immunosuppression regimen was gradually resumed once it became apparent that her clinical condition was improving.

She received a 2-week course of IV piperacillin–tazobactam and then was switched to oral ciprofloxacin for an additional 4 weeks. The PCDs were removed after 2 weeks, and she was transferred to a rehabilitation center for an additional week to receive physical therapy and observation because of deconditioning related to her acute illness. Hemodialysis was slowly weaned over the ensuing weeks and the patient became dialysis free after 6 weeks.

Follow-up CT scan 2 weeks after discharge (1 month after initial PCD) showed complete resolution of the gas with evidence of residual fluid accumulation in the affected areas of the lower pole of the kidney allograft (Fig. 5). However, the patient was completely asymptomatic and

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**Fig. 3.** Non-contrast computed tomography scan after placement of drain in the gas-containing area of the renal allograft (day 3). Another drain was placed in the perinephric fluid collection (on day 1), which was subsequently culture negative in the setting of empiric antibiotic therapy.

**Fig. 4.** Follow-up non-contrast computed tomography scan 3 days after placement of intrarenal drain showing interval partial resolution of the abscess.

**Fig. 5.** Non-contrast computed tomography scan 2 weeks after discharge from hospital (1 month after initial drain placement) demonstrating complete resolution of the gas with residual fluid in the renal parenchyma.
Discussion

EPN is a necrotizing infection of the kidney and its surroundings defined by the presence of gas in the renal parenchyma, collecting system, or perinephric space (1). EPN is most commonly encountered in diabetics, with >80% of reported cases occurring in diabetic patients (2, 3). Urinary tract obstruction is clearly a risk factor for EPN, and women are more commonly affected than men in a ratio of 4:1 (4). Gas-forming organisms, especially E. coli, and then K. pneumoniae, are most commonly seen in EPN. It is believed that with severe infection, areas of ischemic injury develop. The presence of necrotic tissue with high glucose concentration provides the ideal environment for such organisms to ferment glucose to lactose, carbon dioxide, and hydrogen, resulting in the clinical entity known as EPN (5).

The clinical presentation of EPN is usually that of severe pyelonephritis that rapidly progresses to sepsis with multiple organ failure. Although evidence of EPN can be seen on plain radiographs and 2-dimensional B mode ultrasound, the gold standard for the diagnosis and staging of EPN is CT scanning (6). A staging system for native kidney EPN has been described by Huang and Tseng (6) (Table 1). In their study, risk factors associated with poor outcome included shock on admission, thrombocytopenia, acute renal dysfunction, and mental status changes. Unfortunately, no cases of EPN after kidney transplantation were included in their series. Consequently, this staging system is not really applicable to the management of EPN in transplanted kidneys, because all cases of EPN in renal allografts would be categorized as stage 4, which might mandate a more aggressive surgical approach than is necessary. In addition, this classification system does not address the proportion of renal parenchyma involved by infection, which may be particularly important in the management of a solitary kidney, as is the case in most renal allografts. Renal allografts are also unique in that they lack an investing Gerota’s fascia, which may act as a strong barrier to the spread of infection in native kidneys.

The incidence of EPN in renal allografts is very rare, with only 20 reported cases in the English literature. Data from previously published studies are summarized in Table 2 (1, 3, 4, 7–22). In these reported cases, 90% of patients were diabetic and the timing of EPN was quite variable, ranging from 2 weeks to 11 years after transplantation. Surprisingly, 15 of the 20 patients were male, which differs from the epidemiology of EPN in native kidneys. As expected, E. coli was the most commonly identified organism, accounting for 55% of cases, followed by K. pneumoniae in 15%, and then other bacteria such as Salmonella, Enterobacter, Staphylococcus, and Bacteroides. Allograft nephrectomy was performed in 55% of cases, whereas medical therapy with antibiotics with or without drainage was utilized in the remaining patients. In these reported cases, the mortality rate was 15%. However, we suspect that the incidence of EPN in renal allografts is underreported, especially in patients with poor outcomes, so the above mortality rate may underestimate the actual lethality of this condition.

No real consensus exists on the optimal management of EPN in kidney transplant recipients. It is notable that medical therapy alone in non-transplant patients carries a poor prognosis with a mortality rate as high as 75% (5, 23). Historically, nephrectomy has been the standard treatment for EPN in the non-transplant population. However, with the advent of CT scanning, aggressive medical management including PCD, which was first described in 1986 by Hudson et al. (24), has become an integral part of the management algorithm. CT scanning allows for early diagnosis and monitoring, and facilitates aggressive PCD which, when used with modern antibiotics, may alleviate the need for emergency nephrectomy. In kidney transplantation, EPN is confounded by the role of immunosuppression and the fact that nephrectomy results in end-stage renal disease and an immediate return to dialysis for the patient. It is apparent that not all transplant patients with EPN are best
Summary of previously published cases of emphysematous pyelonephritis (EPN) in renal allografts, including classification of these cases according to our new proposed staging system (shown in Table 3).

<table>
<thead>
<tr>
<th>Author</th>
<th>Age in years/sex</th>
<th>Time of EPN post transplant</th>
<th>Diabetes</th>
<th>Presentation</th>
<th>Bacteria</th>
<th>Treatment</th>
<th>Result</th>
<th>Staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameswaran and Feest (7)</td>
<td>53/F</td>
<td>2 months</td>
<td>Yes</td>
<td>Palpable mass and sepsis</td>
<td>Gram-negative bacilli</td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>NA</td>
</tr>
<tr>
<td>Brenbridge et al. (8)</td>
<td>33/M</td>
<td>2 weeks</td>
<td>Yes</td>
<td>Fever</td>
<td><em>Escherichia coli</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>NA</td>
</tr>
<tr>
<td>Potter et al. (9)</td>
<td>31/F</td>
<td>20 months</td>
<td>Yes</td>
<td>Pain, anuria</td>
<td><em>E. coli</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Potter et al. (9)</td>
<td>39/M</td>
<td>8 weeks</td>
<td>Yes</td>
<td>Sepsis</td>
<td><em>E. coli</em></td>
<td>Nephrectomy</td>
<td>Died</td>
<td>3</td>
</tr>
<tr>
<td>Balsara et al. (10)</td>
<td>32/M</td>
<td>1.5 months</td>
<td>Yes</td>
<td>Fever, lethargy</td>
<td><em>E. coli</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>NA</td>
</tr>
<tr>
<td>O’Donnell et al. (11)</td>
<td>27/M</td>
<td>5 years</td>
<td>Yes</td>
<td>Fever, tenderness</td>
<td><em>Enterobacter</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Glen et al. (12)</td>
<td>66/M</td>
<td>–</td>
<td>Yes</td>
<td>Fever, lethargy</td>
<td><em>E. coli</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Kaira et al. (13)</td>
<td>35/M</td>
<td>3 months</td>
<td>No</td>
<td>LUTS</td>
<td><em>Klebsiella pneumoniae</em></td>
<td>Nephrectomy</td>
<td>Died</td>
<td>NA</td>
</tr>
<tr>
<td>Akalin et al. (14)</td>
<td>62/M</td>
<td>5 years</td>
<td>Yes</td>
<td>Lethargy</td>
<td><em>K. pneumoniae</em></td>
<td>Antibiotics</td>
<td>Recovered</td>
<td>1</td>
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<tr>
<td>Goral and Stone (15)</td>
<td>55/F</td>
<td>5 years</td>
<td>Yes</td>
<td>Lethargy, tenderness</td>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Cheng et al. (16)</td>
<td>55/M</td>
<td>7 years</td>
<td>Yes</td>
<td>Pain, fever</td>
<td><em>E. coli</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Fujita et al. (4)</td>
<td>49/M</td>
<td>15 months</td>
<td>Yes</td>
<td>Hematuria, reduced consciousness</td>
<td><em>Salmonella</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Schmidt et al. (3)</td>
<td>55/M</td>
<td>10 month</td>
<td>Yes</td>
<td>Fever, anuria</td>
<td><em>E. coli</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Debnath et al. (22)</td>
<td>52/F</td>
<td>3 years</td>
<td>Yes</td>
<td>Septic shock</td>
<td>–</td>
<td>Antibiotics</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Bolton et al. (17)</td>
<td>76/M</td>
<td>10 years</td>
<td>Yes</td>
<td>Fever, nosocomial</td>
<td><em>K. pneumoniae</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Al-Makadma and Al-Akash (18)</td>
<td>12/M</td>
<td>5 months</td>
<td>No</td>
<td>Fever, pain</td>
<td><em>E. coli</em></td>
<td>Antibiotics</td>
<td>Recovered</td>
<td>1</td>
</tr>
<tr>
<td>Sejji et al. (19)</td>
<td>61/M</td>
<td>2 years</td>
<td>Yes</td>
<td>Anuria, pain</td>
<td><em>E. coli</em></td>
<td>Nephrectomy</td>
<td>Died</td>
<td>3</td>
</tr>
<tr>
<td>Chuang et al. (1)</td>
<td>51/M</td>
<td>12 years</td>
<td>Yes</td>
<td>Fever, LUTS</td>
<td><em>E. coli</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Ballga et al. (20)</td>
<td>52/F</td>
<td>4 years</td>
<td>Yes</td>
<td>Fever, pain</td>
<td><em>E. coli</em></td>
<td>Antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
<tr>
<td>Ortiz et al. (21)</td>
<td>40/M</td>
<td>11 years</td>
<td>No</td>
<td>Fever, sepsis</td>
<td><em>Bacteroides capillosus</em></td>
<td>Nephrectomy</td>
<td>Recovered</td>
<td>3</td>
</tr>
<tr>
<td>Al-Gelwazi et al. (current report)</td>
<td>58/F</td>
<td>15 months</td>
<td>Yes</td>
<td>Fever, vomiting, sepsis</td>
<td><em>K. pneumoniae</em></td>
<td>Drainage, antibiotics</td>
<td>Recovered</td>
<td>2</td>
</tr>
</tbody>
</table>

F, female; M, male; NA, not available; LUTS, lower urinary tract symptoms.

Table 2
served by immediate nephrectomy of the solitary functioning transplanted kidney. A review of the non-transplant literature by Somani et al. (2) demonstrated a 25% mortality rate associated with emergency native nephrectomy for EPN, whereas the mortality from medical management alone was 50%. In comparison, the mortality with PCD and/or percutaneous nephrostomy combined with medical management was only 13%. In patients managed with PCD, 70% maintained sufficient renal function to remain dialysis independent; 9 out of 46 patients (20%) eventually required native nephrectomy within 3–6 weeks of PCD placement. The authors suggested that there may be additional benefit from placement of multiple drains and changing drain sites, with follow-up CT scanning and repositioning of drains as needed within 4–7 days (25). The higher mortality rate with surgery compared with PCD might, in part, be attributed to selection bias, because patients who had more severe infections were more likely to have been treated with nephrectomy.

In the case described herein, we attempted to preserve the renal allograft, bearing in mind the high annual mortality of diabetic patients on dialysis, which might approach 10%. Moreover, the patient was known to have excellent and stable renal allograft function before this acute event and had received a 0 HLA mismatch donor kidney in the setting of being sensitized. Therefore, we opted for PCD of the perinephric fluid collection surrounding the lower pole of the kidney as well as the parenchymal abscess. The patient was managed with ventilator and dialysis support, immediate withdrawal of immunosuppression other than stress-dose steroids, broad-spectrum antibiotics, aggressive fluid resuscitation and electrolyte replacement, and tight glucose control with an insulin infusion. Serial imaging with non-contrast CT scans was performed daily for the first several days and then at 1 week. Fortunately, the patient showed steady clinical and radiographic improvement. Even though she was dialysis dependent at the time of hospital discharge, her renal function slowly recovered and she was taken off of dialysis 3 weeks after discharge (6 weeks after her initial presentation).

Although the incidence of EPN in renal allografts is quite low, we believe that a dedicated staging system specifically for EPN in transplanted kidneys would be of great value in guiding management of patients with this unusual, life-threatening condition, particularly as the current staging system for EPN (Table 1) is not really applicable to renal allografts. We propose a new staging system (Table 3) that addresses the lack of an investing Gerota’s fascia around a transplanted kidney, as well as the proportion of renal parenchyma involved in the necrotizing process to determine whether the remaining renal parenchyma will be sufficient either to keep the patient off dialysis or with reversible dialysis requirements. Moreover, the severity of sepsis, the development of multiple system organ failure, and the lack of clinical improvement after withdrawing immunosuppression all play a crucial role in determining the indications for and timing of allograft nephrectomy in the setting of EPN. In our classification system we include the estimated percentage of renal involvement, the extent of perinephric involvement, and controlled sepsis in Stage 2, whereas uncontrolled sepsis is part of Stage 3.

Interestingly, in our case, the patient manifested all 4 risk factors for poor outcome, notably shock, thrombocytopenia, acute renal dysfunction, and mental status changes, as proposed by Huang and Tseng (6). However, the reversibility of sepsis, as opposed to the initial severity, differentiates between our proposed new Stages 2 and 3. Consequently, the patient presented herein may have started as Stage 3 but shifted to Stage 2 disease with improved controlled sepsis in Stage 2, whereas uncontrolled sepsis is part of Stage 3.

According to our proposed staging system, we recommend aggressive medical management (fluid and electrolyte correction, targeted antibiotic therapy, strict glycemic control, reduction in immunosuppression) initially in Stage 1 disease, in combination with placement of an indwelling urethral catheter and either a percutaneous nephrostomy or ureteral stent in cases of urinary obstruction. For Stage 2 disease, we recommend aggressive medical management as for Stage 1, with placement of 1 or more PCDs, as well as early and frequent follow-up imaging (either ultrasound or non-contrast CT scans) to determine the need for more drains or repositioning/changing of drains. It is generally believed that 40–50% of functioning renal parenchyma is needed to maintain acceptable renal function in the setting of a solitary kidney transplant. For Stage 3 disease, and in
patients who progress in the course of management to Stage 3, allograft nephrectomy is warranted.

In an attempt to validate our proposed staging system for EPN in renal allografts, we classified the previously reported cases in the literature according to our new staging system (Table 2). We were unable to categorize 4 cases, either because of incomplete data on the severity of infection or absence of CT scan findings. In the remaining 16 cases, the management strategy employed correlated with our staging system in 13 cases, although 2 patients with Stage 3 disease died after allograft nephrectomy. In a case reported by Potter et al. (9), allograft nephrectomy was delayed for 9 days after the diagnosis of EPN and the patient died 5 days postoperatively. In another case reported by Seiji et al. (19), allograft nephrectomy was performed 4 days after the diagnosis of EPN in a hepatitis B-positive patient, but the patient died 25 days later from fulminant hepatic failure. In the 3 cases in which the management strategy employed was discordant with our staging system, Potter et al. (9) treated a patient with Stage 2 disease with allograft nephrectomy and the patient subsequently recovered; Baliga et al. (20) reported a patient with Stage 2 disease who responded to antibiotic therapy alone without the need for drainage; and Deb Nath et al. (22) reported a patient with Stage 3 disease who was treated successfully with antibiotic therapy alone, without the need for either drainage or nephrectomy. Although these latter 2 cases demonstrate that patients may be treated successfully with antibiotic therapy alone in either Stage 2 or Stage 3 EPN, it is also important to emphasize that a delay in PCD or surgical therapy in this setting may lead to mortality.

In conclusion, the present case demonstrates successful non-operative therapy of EPN with PCD in combination with aggressive medical management in a kidney transplant recipient who presented with urosepsis, shock, and acute renal failure, and highlights the crucial role of serial imaging studies to determine the extent of infection and response to therapy. We discuss limitations of applying the current system used to stage EPN in native kidneys to EPN in renal allografts, and propose a new classification system that addresses the unique aspects of kidney transplantation and management strategies, according to the revised staging scheme. In general, it may be possible to safely and successfully treat many cases of EPN in renal allografts without allograft nephrectomy. The rarity of this condition and the lack of prospective validation of the new staging system prevent definitive conclusions from being reached via controlled prospective studies. However, keeping in mind the limitations of the proposed classification, the new staging system should be helpful to clinicians making the decision to try to save the allograft in renal transplant patients with EPN.

References


