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Nephrectomy for emphysematous pyelonephritis in a nonfunctional renal allograft due to rejection after kidney transplantation

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Abstract

Background Emphysematous pyelonephritis represents an acute and necrotizing infection characterized by the accumulation of gas within the kidney. This condition poses a swift progression toward sepsis, leading to a poor prognosis. We experienced a rare case of emphysematous pyelonephritis in a nonfunctioning renal allograft attributed to antibody-mediated rejection after kidney transplantation.

Case presentation A 71-year-old man with diabetes had undergone living-donor renal transplantation from his wife. Unfortunately, the transplanted kidney's function declined due to antibody-mediated rejection, necessitating the introduction of hemodialysis 12 months post-transplantation. Subsequently, 4 months after initiating hemodialysis, the patient presented with pain and swelling in the right lower abdomen. A computed tomography scan revealed the enlargement of the transplanted kidney and gas formation. This constellation of symptoms led to the diagnosis of emphysematous pyelonephritis, resulting in his hospitalization. Further contrast-enhanced computed tomography scans demonstrated an absence of arterial flow and ischemia within the renal allograft. Despite antibiotic treatment and percutaneous drainage, both the gas and fluid in the renal parenchyma and surrounding tissue displayed minimal reduction. Given these compelling findings, an allograft nephrectomy was performed 20 days into his hospital stay. Pathological examination confirmed complete allograft necrosis, revealing nonviable renal parenchyma. The patient's postoperative recovery progressed favorably.

Conclusions Instances of emphysematous pyelonephritis within transplanted kidneys are infrequently documented. Among these cases, emphysematous pyelonephritis in a nonfunctioning renal allograft is very rare and may be associated with graft ischemia and the presence of injured tissue. The determination of an immediate diagnosis and surgery is important.

Keywords Emphysematous pyelonephritis, Kidney transplantation, Nephrectomy, Case report

1 Background

Emphysematous pyelonephritis (EPN) is a rare acute necrotizing infection characterized by the accumulation of gas within the renal parenchyma, adjacent tissues, and/or the urinary collecting system [1, 2]. It predominantly affects diabetic patients, progresses rapidly to septic shock, and frequently necessitates nephrectomy as an effective treatment approach [3]. EPN occurring after kidney transplantation is infrequent in functioning renal allografts and exceptional in nonfunctioning renal allografts [4]. As a result, determining the optimal

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management strategy, including the timing of allograft nephrectomy, poses challenges. In this report, we present a case of EPN following thrombotic ischemia in a renal allograft, which was a consequence of antibody-mediated rejection in a nonfunctioning renal allograft. Our discussion encompasses the management of EPN, supplemented by a comprehensive review of the literature, and considers the strategies to prevent EPN in renal allografts.

2 Case presentation

A 71-year-old male with type 2 diabetes underwent ABO incompatible preemptive genetically unrelated living kidney transplantation from his wife, involving a donor with blood type A and a recipient with blood type O. The donor had four human leukocyte antigen (HLA) mismatches with the recipient. Pre-transplant T-cell crossmatch, conducted through both complement-dependent cytotoxic and flow cytometric methods, showed a negative result. Despite a measured panel reactive antibody (PRA) value of 7.8% for HLA class 2, donor-specific antibody (DSA) was not detected using single-antigen beads. The patient received intravenous rituximab at a dosage of 200 mg/m^2 and was commenced on oral mycophenolate mofetil (MMF), cyclosporine, and methylprednisolone 2 weeks before the transplantation for induction immunosuppression. Prior to the transplantation, the patient underwent two rounds of plasma exchange (PE). Following the transplantation, his initial postoperative course was uneventful, exhibiting excellent renal allograft function with a baseline serum creatinine level of 1.0 mg/dL.

Three months after transplantation, his renal function deteriorated, and a renal allograft biopsy revealed acute T-cell-mediated rejection. Despite treatment with methylprednisolone pulse therapy, deoxyspergualin, and everolimus induction, his renal function gradually worsened. Eight months after transplantation, another renal allograft biopsy was performed. Although flow PRA and de novo DSA were negative, antibody-mediated rejection and plasma cell-rich acute rejection were diagnosed. His renal function failed to improve after three courses of PE, leading to the initiation of hemodialysis 12 months after transplantation. MMF and everolimus were discontinued upon the commencement of hemodialysis. Subsequently, cyclosporine was halted 14 months after transplantation due to a febrile urinary tract infection, and low-dose methylprednisolone was continued.

Four months after the introduction of hemodialysis, the patient experienced right lower abdominal pain. A non-contrast computerized tomography (CT) scan revealed an enlarged renal allograft containing parenchymal gas and fluid collections (Fig. 1). Additionally, fluid collections were identified in the perirenal and subcutaneous tissue. His complete blood count demonstrated leukocytosis with a total white blood cell count of 10,240/mm^3, and his C-reactive protein level was elevated to 5.09 mg/dL. Urinalysis revealed 100 white blood cells per high-power field, and subsequent urine culture grew *Enterococcus faecium*. He was admitted with a diagnosis of EPN of a renal graft, initiated on intravenous meropenem, and underwent placement of an ultrasound-guided percutaneous drain into the gas-containing abscess in the renal allograft. Subsequently, the fluid within the renal parenchyma grew *Bacteroides fragilis*. Follow-up contrast-enhanced CT scans conducted 2 weeks after drainage showed no radiographic improvement in the EPN and confirmed the complete occlusion of the renal artery (Fig. 2A, B). Due to the reaccumulation of fluid indicated by ultrasonography after drain removal, it was determined that an allograft nephrectomy was imperative. Allograft nephrectomy was performed 20 days after admission. During the laparotomy, the graft was found to be completely necrotic, with the renal capsule adhering to the perinephric tissue and peritoneum (Fig. 3). The renal capsule was excised wherever feasible, and the necrotic renal parenchyma was detached from its pedicle. The remaining renal vein and artery were closed via suturing. Histological examination revealed nonviable kidney parenchyma and the presence of multiple abscesses resulting from renal infarction and ischemic necrosis (Fig. 4). Following the nephrectomy, the patient was discharged in stable condition and transitioned to chronic hemodialysis. Immunosuppression was gradually reduced over the course of 1 month post-nephrectomy.

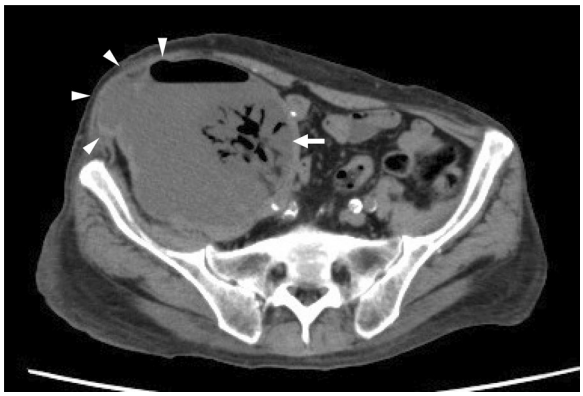

Fig. 1 Non-contrast CT of renal allograft at presentation showing an enlarged renal allograft whose parenchyma has been replaced by gas and fluid collections (arrow) with fluid collection in perirenal and subcutaneous tissue (arrowhead)

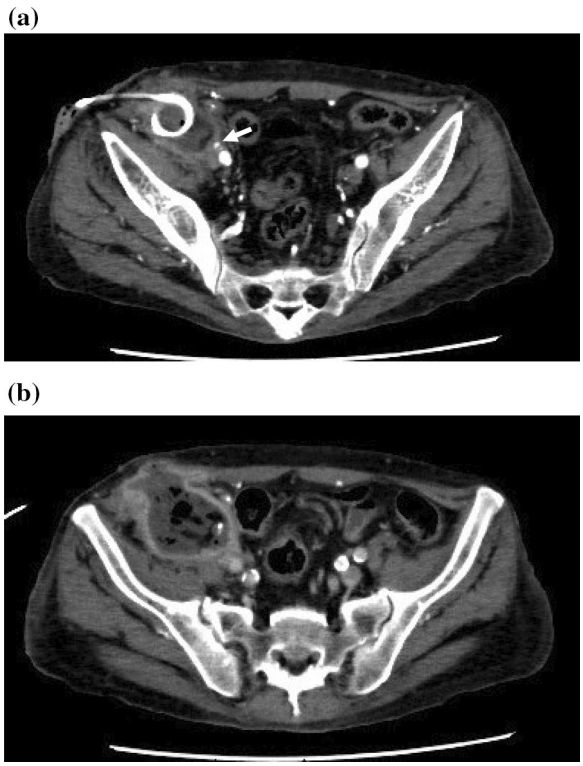

Fig. 2 Contrast CT after placement of a drain in the gas-containing area of the renal allograft. **A** CT showing renal allograft without arterial blood flow due to complete occlusion of the renal artery (arrow). **B** CT showing residual gas and fluid collection in the renal parenchyma

Fig. 3 Intraoperative findings of allograft nephrectomy. The allograft capsule was destructed (arrow), and the parenchyma of the renal allograft was completely necrotic with abscess formation (arrowhead)

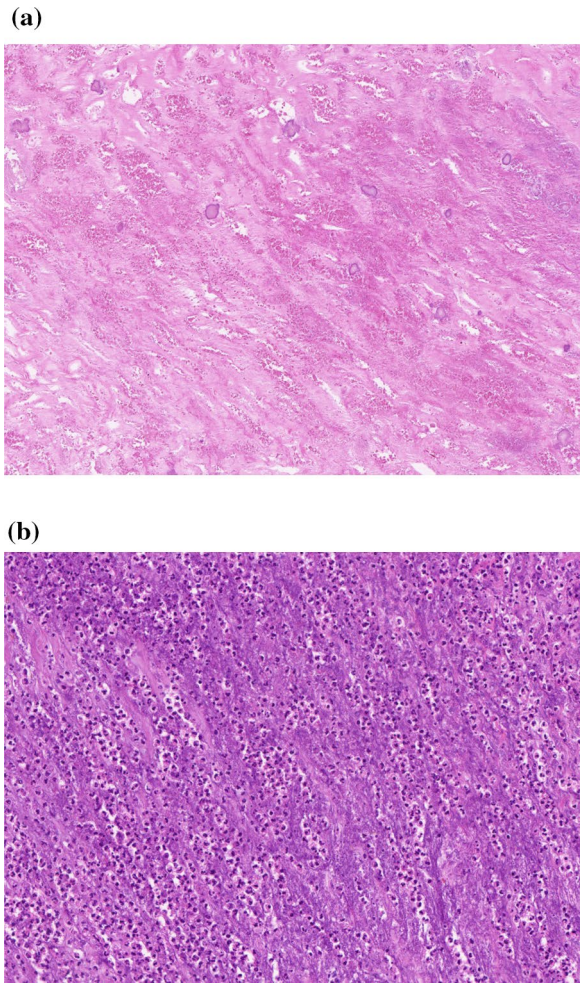

Fig. 4 Histological findings of resected renal allograft (hematoxylin and eosin staining). **A** Hemorrhage and necrosis were seen in most of the renal parenchyma, and normal renal structures such as glomeruli and tubules were not visible (magnification, × 100). **B** Severe interstitial neutrophilic inflammation of the renal parenchyma (magnification, ×200)

3 Discussion

EPN is an acute necrotizing infection of the kidney and is defined by the presence of gas within the renal parenchyma, collecting system, or perinephric tissue [1]. EPN is strongly associated with diabetes, with approximately 80% of reported cases occurring in diabetic patients [3]. Immunosuppression and urinary tract obstruction are also encompassed within the risk factors for EPN. The visualization of gas within the renal parenchyma is essential for diagnosing EPN, and CT is a suitable method for confirming the presence of renal gas [5]. The gas is produced because of glucose fermentation by Gram-negative bacteria, particularly *Escherichia coli* and *Klebsiella pneumoniae* [2]. The presence of necrotic tissue within a

high glucose concentration provides an optimal environment for such organisms, leading to the accumulation of carbon dioxide within the kidney tissue [2].

EPN in transplanted kidneys is a rare occurrence, with only 43 cases reported in the literature, including our case [4, 6, 7]. In the previous reports, 80% of the patients had diabetes, and the most frequently isolated organisms from the specimens were *Escherichia coli* (44%) and *Klebsiella pneumoniae* (23%). The overall mortality rate was 21%. Most cases occurred in functioning allografts, whereas EPN in nonfunctioning allografts is notably infrequent due to reduced or discontinued immunosuppression therapy. Our case is one of only four instances of EPN in nonfunctioning allografts reported, with two cases occurring after allograft embolization for the treatment of graft intolerance syndrome [8–10]. These findings suggest that EPN in nonfunctioning allografts may be particularly prevalent following graft ischemia and the presence of injured tissue. In our case, the patient had a nonfunctioning allograft with complete occlusion of the renal artery caused by antibody-mediated rejection. The causative organisms differed from those in patients with functioning allografts, as evidenced by two of the four patients with nonfunctioning allografts isolating coagulase-negative *Staphylococcus* and *Bacteroides capillosus*, respectively [9, 10]. In our case, the causative agent was identified as *Bacteroides fragilis*, a type of anaerobic bacteria and endemic to the gastrointestinal tract. Although *Bacteroides fragilis* infections are often intraperitoneal and urinary tract infection is rare, diabetes, urinary tract obstruction, transurethral procedure, and immunosuppressed state may be risks of developing urinary tract infection by *Bacteroides fragilis* [11].

EPN in the native kidney can be classified into four classes based on the severity of the disease, as described by Huang and Tseng. Class 1 disease involves gas within the collecting system only, class 2 affects the renal parenchyma, class 3A extends into the perinephric space, and class 3B extends into the paranephric spaces. Class 4 disease involves bilateral kidneys or a solitary kidney [5]. However, because all cases of EPN in renal allografts would be categorized as stage 4 due to the functional solitary kidney scenario, this staging system is not applicable to the management of EPN in transplanted kidneys. Moreover, since the absence of investing Gerota's fascia which acts as a strong barrier to the spread of infection, a more aggressive surgical approach may be necessary in comparison with the native kidney.

Al-Geizawi et al. proposed a novel classification system for EPN specific to transplanted kidney allografts [12]. According to this classification, stage 1 involves gas in the collecting system, stage 2 entails gas replacing < 50% of renal parenchyma with limited extension to the surrounding tissues and controlled sepsis, and stage 3 signified gas replacing > 50% of renal parenchyma, an extensive infection spread in the perinephric area, a patient exhibiting multiple organ failure, uncontrolled sepsis, or unresponsive shock. For stage 1, they recommended medical management involving antibiotic therapy and a reduction in immunosuppression. For stage 2, they suggested medical management as in stage 1, along with percutaneous drainage. Stage 3 necessitates allograft nephrectomy. In the previous reports of EPN in renal allografts, nephrectomy was performed in 21 out of 43 cases (49%) [4, 6, 7]. Among these 43 cases, 19 (44%) aligned with Al-Geizawi's stage 3 classification, and nephrectomy was performed in 13 out of these 19 cases (68%). Additionally, 12 cases (28%) aligned with stage 2, with nephrectomy being performed in 3 out of these 12 cases (25%). Cases classified as stage 2 or 3 that did not undergo nephrectomy opted for percutaneous drainage in 12 cases. According to this classification, our patient corresponds to stage 3, given the extensive infection spread with gas replacing > 50% of renal parenchyma and perinephric involvement. Therefore, considering nephrectomy as a management approach for EPN seems appropriate. However, owing to the relatively low incidence of EPN in renal allografts, a consensus on the optimal management of EPN in kidney transplant recipients remains lacking. Moreover, the applicability of this staging system designed for EPN in transplanted kidneys to renal allografts remains uncertain. Furthermore, the management strategy differs based on the functionality of the affected renal allograft, whether it is functioning or nonfunctioning, and the potential implications of surgery on the need for permanent dialysis.

4 Conclusion

We have presented a rare case of EPN in a nonfunctioning renal allograft. Initially, this patient received conservative treatment involving antibiotics and drainage but subsequently required a nephrectomy. Although EPN in a nonfunctioning renal allograft is rare, EPN should be especially noted as a possibility in patients with graft ischemia and the presence of injured tissue. In addition to early diagnosis and management, making a judicious decision regarding the necessity for surgical intervention is pivotal in EPN cases. Further studies are warranted to comprehensively characterize the incidence and optimal management of EPN in transplanted kidneys.

Abbreviations

EPN	Emphysematous pyelonephritis
HLA	Human leukocyte antigen
PRA	Panel reactive antibody
DSA	Donor-specific antibody
MMF	Mycophenolate mofetil
PE	Plasma exchange
CT	Computerized tomography

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Not applicable.

Author contributions
KK performed project development, data management, data analysis, and manuscript writing. TW performed data collection and data management. FK performed data collection and data management. YK performed project development and manuscript editing. IH performed project development, data management, and manuscript editing.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

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Not applicable.

Consent for publication
We obtained consent from the patients for publication.

Competing interests
The authors declare that they have no competing interests.

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