‘Case of the Month’ from University of Michigan, Ann Arbor, MI, USA:

Emphysematous Pyelonephritis Following Ureteroscopy in a Solitary Kidney

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Case Presentation

A 46-year-old man with diabetes mellitus and morbid obesity (BMI 38) was referred to our clinic with asymptomatic right hydronephrosis. Five months previously he presented with chronic urinary retention and renal impairment (GFR 59). Past history included bilateral megaureter with tapering and reimplantation in childhood. CT demonstrated right hydroureteronephrosis and non-obstructing small renal calculi. The left kidney was atrophic resulting in functionally solitary right kidney. Cystoscopy and retrograde access to the right ureter was attempted by his local urologist and failed.

Urodynamic studies at our center revealed an atonic bladder. He was managed with regular intermittent catheterization. A dynamic renogram demonstrated right renal obstruction despite the patient making adequate urine and stable GFR. A percutaneous nephrostomy (PCN) was organized to allow for evaluation of the ureter. However, due to the COVID-19 pandemic this was delayed. He then developed left flank pain. A CT demonstrated right distal ureteral calculi (largest 8 mm). A right PCN was placed followed by a right antegrade ureteroscopy and laser lithotripsy four weeks later. Multiple stones proximal to a ureteral orifice stricture in a megaureter were fragmented and a 7F DJ stent placed. A second look retrograde ureteroscopy was performed six weeks later. The patient was treated with pre-operative antibiotics for bacteriuria, per our institutional protocol. Small fragments in the distal ureter were treated and a
persistent stricture was confirmed. An 8F Silhouette stent was placed (Applied Medical, CA). The patient was discharged the same day, with plan for reconstructive ureteral surgery.

The following day (POD #1), the patient presented to his local hospital with a fever, dyspnea and in septic shock. After negative SARS-CoV-2 testing, he was transferred to our institution. CT showed an appropriately positioned DJ stent, mild right hydronephrosis and a small focus of gas in the collecting system thought to be from recent instrumentation (Figure 1a). He was in septic shock with multi-organ dysfunction and required ICU admission; ICU care included systemic antibiotics (piperacillin-tazobactam), vasopressors, mechanical ventilation and continuous renal replacement therapy. He improved and was extubated on POD #4. Blood cultures grew *Klebsiella aerogenes*, resistant to pipercillin-tazobactam. Renal ultrasound was performed on POD #6 due to persistently positive blood cultures. This demonstrated possible emphysematous pyelonephritis (EPN) which was confirmed on non-contrast CT (Figure 1b).

**Management Considerations**

All treatment options including medical management, PCN or percutaneous drain (PCD) placement, and emergent nephrectomy in case of clinical deterioration were discussed. At the time of EPN diagnosis, despite the striking CT findings, he had no flank pain or tenderness which would be expected of pyelonephritis and was off vasopressors and extubated. He required renal replacement therapy for acute kidney injury. Antibiotic therapy was changed to cefepime due to the resistance profile of the *Klebsiella* isolate.

The dilemma we had was whether to place a PCD or PCN (or both) into the right kidney. He had a functionally solitary kidney which allowed for accurate assessment of urine formation and excretion. There was good urinary drainage via the DJ stent and minimal hydronephrosis. The parenchyma had multiple foci of gas but no fluid collection. The risk of a severe bleeding complication from PCD placement in an improving patient with morbid obesity and solitary kidney had to be carefully considered.
After multi-disciplinary consultation, the consensus was to continue management with systemic antibiotics and DJ stent, and place a PCD if the clinical condition changed. An open surgery team was coordinated in case of need to perform salvage nephrectomy.

**Treatment Course**
The patient was transferred out of ICU on POD #9. Additional CTs were obtained to assess gas appearance, especially since the patient complained of no pain or flank tenderness. These showed minimal change (Figure 2). Just prior to discharge, on POD #22, he developed anemia and melena, requiring blood transfusion. Gastroscopy revealed a duodenal ulcer and *H. pylori* which was managed medically. Hemodialysis was discontinued on POD #23. The GFR stabilized at 17. He was ultimately discharged on POD #30 on a long-term course of IV ertapenem with plan for serial scans to assess EPN resolution. On POD #43 he had right flank pain for the first time. A CT on POD #47 demonstrated concern for developing 6.2 cm right upper pole abscess. He underwent uncomplicated PCD placement on POD #48 with drainage of purulent material (*Klebsiella aerogenes*). The drain was removed 14 days later. He recovered well thereafter, returning back to work. On POD #89 he underwent a ureteral stent exchange without complication.

**Discussion**
Sepsis following ureteroscopy for urinary stones is uncommon, but can be fatal. In 1737 patients undergoing ureteroscopy in 11 practices from the Michigan Urological Surgery Improvement Collaborative, the hospitalization rate for infection-related complications was 2.4%, and the mortality rate was 0.2%\(^1\). Risk factors included comorbidity, large stone size, and history of recurrent UTI. EPN specifically following ureteroscopy has not been well documented. Our patient had risk factors of morbid obesity, diabetes, obstructive uropathy and bacteriuria. Despite ureteroscopy mitigated with pre-operative antibiotics, the patient developed sepsis.

EPN is a rare but potentially life-threatening necrotizing infection of the renal parenchyma characterized by imaging findings of gas in the renal collecting system,
parenchyma, or perinephric tissue. Clinical presentation is variable but typically includes fever, flank pain, and vomiting. A significant number of patients will present with sepsis and bacteremia. Risk factors include female gender, diabetes, and urinary obstruction. Huang and Tseng developed a classification system for the severity of EPN: Class I - gas in the collecting system only, Class II - parenchymal gas only, Class IIIA - extension of gas into perinephric space, Class IIIB - extension of gas into pararenal space, Class IV - EPN in a solitary kidney, or bilateral disease.

Management of EPN has evolved. Parenteral antibiotics targeting gram-negative organisms should be initiated in all cases, as these are the most common organisms to cause EPN. Appropriate empiric therapy includes a β-lactam/β-lactamase inhibitor or a 3rd-4th generation cephalosporin. However, some Enterobacteriaceae (including Klebsiella aerogenes) may produce an AmpC β-lactamase, which can lead to development of β-lactam resistance; this was suspected in this case. Cefepime or a carbapenem are preferred therapy in the setting of a known AmpC-producing organism. A switch to a carbapenem or fluoroquinolone may be required in this situation and infectious diseases consultation is encouraged. Because EPN is a deep infection, prolonged therapy (4-6 weeks) is required. Our patient was treated with 6 weeks of ertapenem and transitioned to prophylactic ciprofloxacin until stent exchange.

Historically, EPN was managed with emergent nephrectomy and antibiotic therapy. Ahlering et al reported on 13 patients, of which 12 (92%) underwent emergent nephrectomy. The mortality rate was 42%, and the authors suggested early nephrectomy to reduce mortality. However contemporary data has shown that EPN can be managed successfully with antibiotics and endourologic or percutaneous drainage without nephrectomy in the majority of cases (Table 1). Lu et al demonstrated an overall survival of 90% in 51 patients. PCD was needed in 73%. One patient with EPN after ureteroscopy with DJ stent was treated successfully with antibiotic therapy. Sokhal and colleagues reported on 71 patients with a survival of 92%; 38% were managed with a DJ stent. In their assessment, DJ stenting or PCD was based on clinical and
radiological extent of disease. Presence of internal echoes in the collecting system with obstruction was an indication for PCD.

Our case highlights the challenge of managing a patient who developed EPN during the course of treatment for septic shock following ureteroscopy. Initial therapy must take into consideration the patient’s clinical status, and emergent nephrectomy may be required in critically ill patients as a life-saving strategy. Our patient had a DJ stent with good urinary drainage established, therefore PCN was not thought to add benefit. PCD was strongly considered but not performed initially due to improving clinical condition with appropriate antibiotics and supportive care, and lack of localizing collection on imaging. The occurrence of GI bleeding highlights the cascade of events which can occur in patients who develop complications. Nephrectomy was not favored as it would have rendered the patient functionally anephric. Nonetheless, an open surgical team was coordinated in case of need for salvage nephrectomy, as this is an operation with high mortality. We found that with antibiotic therapy and DJ stent, the emphysematous appearance improved minimally over time. Eventually the phlegmon coalesced into a collection suitable for drainage.

Conclusion
The management dogma of EPN has changed from emergent nephrectomy to a kidney-sparing approach with antibiotic therapy and percutaneous and/or endourologic drainage depending on clinical and radiological features. Our patient was managed in a multi-disciplinary manner with medical therapy and DJ stent. Serial CTs showed minimal resolution of the emphysematous changes which eventually progressed to abscess formation which was successfully drained. Recent studies demonstrate the overall survival of EPN is as high as 92%, but nephrectomy is needed in those who do not respond. PCD in a solitary kidney has risks, and in patients who are clinically improving with a stent, can be forestalled. If there is any deterioration, drainage must be promptly provided.
References


<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>N</th>
<th>Antibiotics alone (%)</th>
<th>Percutaneous drainage (%)</th>
<th>DJ stent (%)</th>
<th>DJ and drain (%)</th>
<th>Open drainage (%)</th>
<th>Salvage nephrectomy (%)</th>
<th>Emergent nephrectomy (%)</th>
<th>Survival (%)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huang &amp; Tseng 2000¹</td>
<td>Taiwan</td>
<td>48</td>
<td>5 (10%)</td>
<td>41 (56%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>8 (16%)</td>
<td>2 (4%)</td>
<td>39 (81%)</td>
<td>In class 1 and 2 EPN, all patients treated with a PCD or DJ stent survived</td>
</tr>
<tr>
<td>Lu, et al. 2016⁴</td>
<td>Taiwan</td>
<td>51</td>
<td>10 (20%)</td>
<td>39 (76%)</td>
<td>1 (2%)</td>
<td>-</td>
<td>1 (2%)</td>
<td>5 (9.8%)</td>
<td>1 (2%)</td>
<td>46 (90%)</td>
<td>If Class 2-4 EPN and risk factors, carbapenem was recommended as initial therapy</td>
</tr>
<tr>
<td>Sokhal, et al. 2017⁵</td>
<td>India</td>
<td>74</td>
<td>12 (16%)</td>
<td>44 (59%)</td>
<td>28 (38%)</td>
<td>10 (14%)</td>
<td>2 (3%)</td>
<td>18 (24%)</td>
<td>4 (5%)</td>
<td>68 (92%)</td>
<td>16% had ureteral calculi; 24% had renal calculi</td>
</tr>
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</table>

Table 1. Summary of three large case series of EPN management and outcomes.