Renal Replacement Therapy Case 1

The nephrology team was asked to provide dialysis support for a 45-year-old man with end stage kidney disease treated with maintenance hemodialysis who presented to the hospital with a swollen right knee. He was in his usual state of health until about 1 week before, when he started experiencing progressively worsening pain and swelling of the knee. The pain gradually worsened until he was unable to ambulate. He denied having similar symptoms in the past, involvement of any other joint, or a history of trauma. He also did not have any other associated symptoms. Given the degree of pain, swelling, and erythema, the Emergency Department physician performed an arthrocentesis before calling. The aspirate appeared yellow-green, and the synovial white blood cell count was 72,000/µl, of which 95% were polymorphonuclear cells. The synovial red cell count was 20,000/µl. All other studies were pending at the time of initial consultation.

He had been asymptomatic and apparently in otherwise good health until about 1 year ago, when he noticed anorexia and declining energy level, and he was diagnosed with end stage kidney disease. He was undergoing three times per week in-center hemodialysis through a cuffed tunneled right internal jugular central venous catheter, and his wife was being evaluated as a potential donor for kidney transplantation. His last hemodialysis treatment 1 day earlier was uneventful. The only other significant medical problem was atrial fibrillation for the last 6 months. His dialysis treatments had been uncomplicated, and his last measured single pool Kt/Vurea was 1.64. His other relevant laboratory data, obtained from the dialysis facility, included a serum phosphorus level of 8.4 mg/dl and a serum parathyroid hormone level of 775 pg/ml. His medications included atenolol, amlodipine, sevelamer, a multivitamin for dialysis patients, and warfarin.

On examination, temperature was 99.4°F, heart rate was 98/min, BP was 145/80 mmHg, and respiratory rate was 20/min. The right knee was erythematosus and visibly swollen. The knee was markedly tender, with substantially limited range of motion because of pain. The central venous catheter exit site was clean and dry, and the rest of the physical examination was unremarkable.

Selected initial laboratory data included a peripheral blood white cell count of 13,000/mm³ (85% polymorphonuclear white blood cells), hemoglobin of 11.3 g/dl, serum calcium of 10.1 mg/dl, phosphorus of 7.9 mg/dl, uric acid of 9.6 mg/dl, and international normalized ratio for prothrombin time of 2.8.

Question 1 (Figure 1 has responses of program directors and attendees): which one of the following is most likely to be necessary for the complete, effective management of this patient?

A. Antibiotic catheter lock  B. Fresh frozen plasma  C. Removal of the central venous catheter  D. Systemic glucocorticoids  E. Daily hemodialysis

Discussion of Question 1

In summary, this 45-year-old individual, who is undergoing maintenance hemodialysis through a central
venous catheter while awaiting living donor kidney transplantation, presented with a low-grade fever and local signs and symptoms consistent with mono-articular arthritis. The most likely diagnosis is septic arthritis and the most effective management, in addition to antibiotic therapy, would be removal of the central venous catheter (choice C is correct).

A large number of clinical conditions can present with mono-articular arthritis, including infections (gonococcal and nongonococcal infections, including Lyme disease), crystal deposition (gout and pseudogout), trauma, hemarthrosis, sickle cell disease, autoimmune disorders (rheumatoid arthritis and systemic lupus erythematosus), and osteoarthritis (1). The presence of a joint effusion in this patient who has presented with severe pain, tenderness, and limited range of motion suggests that the mono-articular arthritis is inflammatory in origin. Whether inflammatory arthritis in a patient is infectious in origin can be definitively determined only through the acquisition of a gram stain and fluid culture. However, a presumptive diagnosis can often be made by a constellation of findings on laboratory testing in the presence of a consistent clinical picture (1). The change in likelihood of this in

Figure 1. | Answer for case 1, question 1: which one of the following is most likely to be necessary for the complete, effective management of this patient? Correct answer is C.

### Table 1. Likelihood ratios for selected laboratory test results for the diagnosis of septic arthritis in a patient with mono-articular arthritis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive Likelihood Ratio</th>
<th>Negative Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal blood white blood cell count</td>
<td>1.4 (1.1–1.8)</td>
<td>0.28 (0.07–1.10)</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate&gt;30 mm</td>
<td>1.3 (1.1–1.8)</td>
<td>0.17 (0.20–1.30)</td>
</tr>
<tr>
<td>Elevated serum C-reactive levels</td>
<td>1.6 (1.1–2.5)</td>
<td>0.44 (0.24–0.82)</td>
</tr>
<tr>
<td>Synovial fluid (/mm³)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;100,000</td>
<td>28.0 (12.0–66.0)</td>
<td>0.71 (0.64–0.79)</td>
</tr>
<tr>
<td>&gt;50,000</td>
<td>7.7 (5.7–11.0)</td>
<td>0.42 (0.34–0.51)</td>
</tr>
<tr>
<td>&gt;25,000</td>
<td>2.9 (2.5–3.4)</td>
<td>0.32 (0.23–0.43)</td>
</tr>
<tr>
<td>Polymorphonuclear cells≥90%</td>
<td>3.4 (2.8–4.2)</td>
<td>0.34 (0.23–0.43)</td>
</tr>
<tr>
<td>Low glucose</td>
<td>3.4 (2.2–5.1)</td>
<td>0.58 (0.44–0.76)</td>
</tr>
<tr>
<td>High protein</td>
<td>0.90 (0.61–1.30)</td>
<td>1.10 (0.76–1.60)</td>
</tr>
<tr>
<td>Lactate dehydrogenase&gt;250 IU/L</td>
<td>1.9 (1.5–2.5)</td>
<td>0.10 (0.00–1.60)</td>
</tr>
</tbody>
</table>

Modified from reference 1, with permission.

with positive or negative results of different tests commonly used in clinical practice is summarized in Table 1 (1). Of all the tests that are used to empirically diagnose septic arthritis while awaiting the results of synovial fluid culture, the initial results of the arthrocentesis have the greatest diagnostic value. The higher the total synovial white blood cell count, the higher the probability of septic arthritis. Individuals with a synovial cell count>100,000/µL have a 28-fold higher likelihood of having septic arthritis (Table 1) (1). The diagnostic certitude also increases significantly if the synovial pleocytosis is predominantly polymorphonuclear and associated with a low-fluid glucose concentration (1). In contrast to these tests, the synovial protein or lactate dehydrogenase and an abnormal blood white blood cell count, serum C-reactive protein, or erythrocyte sedimentation rate have limited value in ruling in or out the diagnosis of septic arthritis (Table 1) (1). Thus, in this patient with joint pain, swelling, erythema, low-grade fever, an abnormal blood white blood cell count, and a synovial white blood cell count of 72,000 cells/µL (92% polymorphonuclear), the likely cause of this inflammatory mono-arthritis is, indeed, septic arthritis. Therefore, most effective management for this patient would be the removal of the central venous catheter (choice C is correct).

Two small case series of septic arthritis in patients undergoing maintenance hemodialysis suggest that the joint infection in this setting invariably occurs from hematogenous seeding from bacteremia (Table 2) (2,3). In this patient who is undergoing hemodialysis with a central venous catheter with no other localizing symptoms and signs, bacteremia is highly likely to be resulting from a catheter-related bloodstream infection. The Infectious Disease Society of America has published clinical practice guidelines for the diagnosis of catheter-related bloodstream infection, and they include the presence of one of the following criteria: (1) isolation of the same organism from at least one percutaneous blood culture and the tip of the catheter; (2) two cultures, one from the catheter hub and one from a peripheral vein, meeting the criteria for quantitative cultures (colony count from catheter hub more than threefold higher than peripheral vein) or differential time to positivity (bacterial growth in sample from
the catheter hub first detected at least 2 hours before it is detected in the sample from the peripheral vein; or (3) two cultures—one from each catheter hub—where the colony count from one hub is threefold higher than the other (4).

For patients undergoing hemodialysis, samples obtained from the blood lines connected to the central venous catheter during the hemodialysis procedure can be used in lieu of samples obtained from peripheral veins (4,5).

Working under the assumption that this patient has a very high likelihood of having septic arthritis secondary to a catheter-related bloodstream infection, what steps other than antimicrobial therapy will be necessary for a complete cure of the infection in this patient? Clinical practice guidelines from the Infectious Disease Society of America and European Renal Best Practice guidelines identify four absolute indications for the removal of a central venous catheter in the setting of catheter-related bloodstream infection: (1) infections with Staphylococcus aureus, Pseudomonas aeruginosa, or candida species; (2) metastatic infections (endocarditis, osteomyelitis, or septic arthritis); (3) systemic sepsis; or (4) tunnel infection with fever (4–6). These guidelines are consistent with findings of high rates of treatment failure and mortality in individuals with catheter-associated bloodstream infection when attempts are made to salvage the catheter (7). Thus, in the setting of catheter-related bloodstream infection, the presence of septic arthritis constitutes an absolute indication for the removal of central venous catheter and will be necessary for complete and effective management of this patient.

Renal Replacement Therapy Case 2

A 27-year-old man with end stage kidney disease secondary to congenital renal hypoplasia treated with peritoneal dialysis (PD) is being seen in the clinic for his routine monthly visit. He was generally doing well but now reports that, for the last 3 months, he is frequently nauseated and occasionally vomits 3–4 hours after meals. His appetite has decreased, and he lost about 8 pounds over the preceding 3 months. He denies abdominal pain or discomfort, bloating, or change in bowel habits.

He was diagnosed with end stage kidney disease at age 9 years and initially treated with PD. He received a living donor transplant from his stepfather at 10 years of age. The allograft failed after 10 years, and he restarted PD at age 20 years. He is currently listed for a deceased donor transplant but is highly sensitized. A peritoneal equilibration test done when he restarted PD showed a 4-hour dialysate–plasma creatinine of 0.72. Currently, he is anuric, and his automated PD prescription consists of four exchanges over 9 hours nightly with 3 L fill volume using 2.5% dextrose and 3 L last bag fill with 7.5% icodextrin for the 15-hour day dwell. His last measured total weekly Kt/Vurea was 1.76. His PD treatment history has been largely uncomplicated, except for two episodes of peritonitis in the last 7 years; the last episode was 6 months ago. His medications included metoprolol, clonidine, lisinopril, sevelamer carbonate, calcitriol, cinacalcet, erythropoietin, a multivitamin indicated for dialysis patients, and when needed, metoclopropamide. Except for the metoclopropamide, the medications had been unchanged for the last 3 years.

On examination, his temperature is 97.8°F, heart rate is 84/min, BP is 153/84 mmHg, and respiratory rate is 18/min. He has basilar rales, mild epigastric tenderness, and bilateral lower extremity pitting edema. The rest of the physical examination is unremarkable.

His most recently measured serum albumin was 3.1 g/dl, and a repeat peritoneal equilibration test (4.25% dextrose), done 1 month before clinic visit, showed a 4-hour drain volume of 2200 ml and 4-hour dialysate-to-plasma creatinine of 0.89.

Question 2 (Figure 2): which one of the following represents the best next step for evaluation of his gastrointestinal symptoms?

A. Echocardiography
B. Contrast-enhanced computed tomography of the abdomen
C. Esophagogastroduodenoscopy
D. Gastric emptying study
E. Serum amylase and lipase determination

![Figure 2. | Answer for case 2, question 2: which one of the following represents the best next step for evaluation of his gastrointestinal symptoms? Correct answer is B.](image)
Discussion of Question 2

In summary, this 27-year-old man treated with PD cumulatively for 8 years has new onset of gastrointestinal symptoms, clinical evidence of volume overload, increase in peritoneal solute transport rate, decrease in peritoneal ultrafiltration capacity, and low serum albumin. This constellation of clinical and laboratory findings in a patient treated with PD for a long time is highly concerning for encapsulating peritoneal sclerosis (EPS). The most appropriate test for diagnosis of EPS would be a computed tomography scan (choice B is correct).

EPS is a rare but potentially devastating complication of PD (8). Recent large prospective cohort studies from Australia, New Zealand, and Scotland suggest that the 8-year cumulative incidence in patients undergoing PD ranges from 4% to 8% (9,10). Although peritoneal fibrosis is common in patients treated with PD, a diagnosis of EPS requires the clinical or radiologic/anatomic evidence for both peritoneal sclerosis and intestinal encapsulation (9). EPS should be diagnosed only in patients with suggestive clinical features with consistent radiologic or anatomic (intraoperative) findings. The clinical findings that have been most commonly described in patients with EPS include symptoms/signs of bowel obstruction, nausea, vomiting, anorexia, failure to thrive, and protein-energy wasting. Peritoneal fibrosis is invariably associated with neovascularization and hence, an increase in peritoneal solute transport rate (commonly measured as 4-hour dialysate-to-plasma creatinine ratio on peritoneal equilibration testing) and a decrease in peritoneal ultrafiltration capacity.

The radiologic findings in patients with an eventual diagnosis of EPS have been described using ultrasonography, contrast-enhanced computed tomography, and cine magnetic resonance imaging (11–14). An overarching conclusion that can be reached from all these reports is that no one single radiologic finding is pathognomonic for the diagnosis of EPS. Of the different imaging methods described to diagnose EPS, contrast-enhanced computed tomography is the preferred method; the diagnostic value of ultrasonography is dependent on the expertise of the technician, and cine magnetic resonance imaging is neither widely available nor widely used. At least two studies have attempted to develop scoring systems or criteria for the diagnosis of EPS (Table 3) (11,12). Although these criteria have not been validated in independent cohorts, they are still useful for clinical application. Thus, in the presence of high level of clinical suspicion for EPS, a contrast-enhanced computed tomography scan is the best next step for diagnostic evaluation of this patient.

Several investigators have tried to examine the use of various tests for identifying individuals at high risk for EPS before the development of the full-blown syndrome. The range of abnormalities on computed tomography in asymptomatic individuals who subsequently went on to develop EPS was no different from the range in those individuals who did not develop the disease (15). Then, it follows that the clinical use of serial computed tomography imaging of the abdomen is limited. At least two studies have examined the value of serial peritoneal equilibration testing (16,17). In a nested case control study that included nine patients with EPS, a decrease in osmotic conductance (lower ultrafiltration volume for the same dialysate dextrose concentration without significant change in peritoneal solute transport rate) was evident several years before the clinical development of EPS (16). In contrast, in a single-center Dutch study, the magnitude of change in ultrafiltration volume could not distinguish individuals with ultrafiltration failure with or without EPS (17). Given the inconsistent nature of data, serial peritoneal equilibration testing cannot be recommended for the preclinical diagnosis of individuals at high risk for EPS. Two different studies have identified the appearance rate of selected peritoneal biomarkers (IL-6 and CA-125) or surface area of mesothelial cells in dialysate effluent as predictors for the subsequent development of EPS (17,18). However, these findings need to be replicated and validated before using them in clinical settings. In summary, there is presently no reliable method to identify individuals at high risk for the subsequent development of EPS, and a high index of suspicion should be maintained for the diagnosis of the condition in long-term PD patients.

There is no high-quality evidence for medical or surgical interventions in patients suspected of or diagnosed with EPS. Some investigators have proposed that EPS may have four stages—presymptomatic, inflammatory, encapsulating, and ileus. It has been suggested that a brief course of steroids may be of help during the inflammatory phase and that tamoxifen may help in the encapsulating phase. In a patient with low serum albumin, assessment of systemic inflammation with serum C-reactive protein levels and possible treatment with steroids may be considered.

Disclosures
R.M. is supported by National Institutes of Health Grant DK95668. He has received honoraria and/or grant support from Amgen, Baxter Healthcare, and DaVita.

References


Published online ahead of print. Publication date available at www.cjasn.org.