Complications of peritoneal dialysis (PD) create a significant burden for patients and providers. Some complications, such as infections and leaks, are preventable or easily treatable; however, potential fatal complications, such as encapsulating peritoneal sclerosis (EPS), cost patients their lives. Here, we present the case of a PD patient who might have had early, subtle, but ominous symptoms and signs of EPS, diagnosed in its early stages and promptly managed.

A 57-year-old man who had been receiving PD for 6 years began having recurrent episodes of abdominal pain, blood-tinged effluent, and peritonitis. Even after successful treatment of his peritonitis episode, his dialysate effluent would be intermittently hazy or pinkish. When he presented with similar complaints for the third time, he was diagnosed with EPS after laparoscopy for further evaluation during his hospitalization.

Encapsulating peritoneal sclerosis is a rare complication of PD. The advanced stages of EPS with “EPS syndrome” portend a grave prognosis because of small-bowel obstruction, malnutrition, infection, and death. Early recognition and timely intervention can be a strategy to potentially prevent the progression of EPS.

Key words
Encapsulating peritoneal sclerosis

Introduction
Encapsulating peritoneal sclerosis (EPS) is a rare and fatal complication of peritoneal dialysis (PD). Since EPS was first reported in 1980, its incidence has been rising as a consequence of increased awareness and patients staying longer on PD. The incidence has increased from 0.9% in 1996 to 3.3% in 2005, and worldwide, the current incidence in PD patients ranges between 0.7% and 3.3% (1). Randomized studies in EPS are lacking because of its rare occurrence, chronic and indolent symptoms, and clinical presentation.

The full-blown or late stage of EPS is associated with very poor outcomes: mortality is increased to as much as 25% – 55%, predominantly within 1 year after diagnosis, and median survival is about 180 days from diagnosis (1). Under appropriate circumstances, given unique clinical findings and radiologic and pathologic evidence, EPS can potentially be diagnosed in its early stages, and interventional treatment strategies can help to prevent serious complications and disease progression. Here, we present the case of a patient that we believe had an early case of EPS in which we intervened at an early stage.

Case description
A 57-year-old African American man presented to our emergency room with complaints of 10 – 12 hours of abdominal pain. He had developed left-sided abdominal pain during PD, and the pain had persisted and mildly worsened. The pain was associated with episodes of nausea and emesis, but no fever or diarrhea. The patient did report problems with constipation. He denied cloudy fluid, and he had no problems with catheter drainage, no pain or swelling, and no discharge at the catheter exit site.

The patient had a history of hypertension, and he developed end-stage renal disease in 2000. After failure of a living unrelated kidney transplant in 2011, he was started on PD. In recent months, he had suffered 2 episodes of secondary peritonitis.

On the patient’s first presentation with abdominal pain, culture of cloudy and blood-tinged fluid
showed infection with *Corynebacterium jeikeium*. Corynebacteria are gram-positive, catalase-positive, aerobic, mostly non-motile rods. An opportunistic pathogen, *C. jeikeium* commonly colonizes the skin, especially in immunocompromised hosts. Because of its broad-spectrum resistance to antimicrobial agents, the susceptibility of *C. jeikeium* strains to a wide range of antibiotics has been studied. Resistant strains are particularly common in neutropenic patients with intravascular catheters, prolonged neutropenia, or receipt of multiple antibiotic regimens. Our patient was treated for 2 weeks with intraperitoneal antibiotics.

The second time the patient presented with a similar set of problems, including bloody PD effluent, cultures were negative. He then experienced persistent pain and blood-tinged fluid on and off for several months before the current presentation.

On examination, the patient’s vital signs were stable, and he was afebrile. Mild tenderness was evident on the left side of the abdomen. The exit site was normal. Analysis of the PD effluent showed a white blood cell count of 1785/μL (935 being neutrophils) and a red blood cell count of 8000/μL, consistent with peritonitis.

Plain radiography of the abdomen resulted in no acute findings. The tip of the catheter was in left upper quadrant. The patient was admitted to hospital and treated with broad-spectrum intraperitoneal antibiotics while final effluent culture results were awaited. By day 3, the patient’s constipation had improved, but his abdominal pain persisted and progressed in severity. He also had persistent bloody dialysate. Repeat fluid analysis showed a red blood cell count of 36,000/μL and a white blood cell count of 2673/μL, with 84% neutrophils.

We suspected catheter-related trauma to intra-abdominal organs or blood vessels and so consulted vascular surgery for a laparoscopic evaluation. Laparoscopy showed copious serosanguinous fluid, unhealthy-looking peritoneum that was diffusely oozing blood, and extensive adhesions between the abdominal wall and bowel.

Because of the laparoscopic findings and a concern for early EPS, PD was discontinued. Computed tomography (CT) imaging of abdomen and pelvis showed a thickened and enhancing peritoneum and many pockets of fluid collection in the anterior abdominal cavity between the mesenteric fat and the bowel loops (Figure 1).

The patient’s dialysis modality was switched to hemodialysis, and he was continued on intravenous vancomycin, because his effluent culture was again positive for *C. jeikeium*. The PD catheter was removed, and a biopsy of peritoneum was obtained. Grossly, the peritoneal biopsy was reported as consisting of tan-pink, soft, rubbery tissue; the histology was reported as dense fibrosis with acute and chronic inflammatory findings, capillary angiogenesis, and hemosiderin deposition (Figures 2 and 3). We felt that these clinical findings could be either a severe infection with *C. jeikeium* or an early manifestation of EPS.

The patient is continuing on in-center hemodialysis 3 times weekly, with complete resolution of symptoms.

**Discussion**

In PD patients, EPS is a well-known, but less-described or -studied complication. The condition is also reported in non-PD patients and in patients after cessation of PD. The mortality rate from EPS is very high, but given its rarity, patients should not be precluded from initiating PD—a generally safe modality of renal replacement therapy.

The chief risk factor for EPS is duration of PD. Per a report from a Japanese prospective study, the incidence of EPS is 0.7% after 5 years, 2.1% after 8 years, 5.9% after 10 years, and 17.2% after 15 years of PD therapy (2). Discontinuation of PD (cessation
Bleeding Peritoneum During PD Related to Early EPS

“two-hit” theory. The uremic state, the presence of a PD catheter, and bioincompatible dialysate (low pH and a high glucose concentration that forms advanced glycation endproducts) initiate inflammation in the peritoneum (6). Inflammation happens in both layers of the peritoneum, but the visceral peritoneum is the most affected. This “first hit” disrupts membrane histology, leading to loss of the peritoneal mesenchymal layer and setting the stage for progressive sclerosis, called “simple sclerosis.” Subsequently, when a “second hit” occurs (by acute cessation of PD, peritonitis, organ transplantation, or a genetic predisposition), the simple sclerosis progresses to dense fibrosis, whereby the peritoneum encapsulates the bowels. Thus, the terms “abdominal cocoon” or “fibrous cocoon” were coined.

In 2005, Nakamoto (7) proposed four clinical stages for EPS depending on the inflammatory state and encapsulation:

- Stage 1, pre-EPS stage: asymptomatic with mild ascites and no inflammation
- Stage 2, inflammatory stage: mild inflammation with fibrin exudation, partial encapsulation of bowel causing nausea and diarrhea
- Stage 3, encapsulation: mild-to-severe inflammation causing the peritoneum to form a fibrous cocoon and causing symptoms of bowel obstruction
- Stage 4, chronic stage of ileus: patients with absolute bowel obstruction, little or no inflammation present

Clinically, patients can be divided into those with early- and late-stage EPS. In the early stage, nausea, vomiting, anorexia, early satiety, and altered bowel habits are usually seen. Ultrafiltration failure occurs, and the patient’s membrane status changes to high transport. Bloodstained ascites, fever, and elevated C-reactive protein can also be present. In the late stage, abdominal pain and signs and symptoms of overt bowel obstruction can be present because of the formation of a fibrous cocoon. Progression of bowel obstruction leads to malnutrition, weight loss, bowel ischemia, strangulations, infection, and death (8).

The ability to diagnose EPS in its early stages is very debatable even now, because peritoneal sclerosis is common in PD patients and not all simple sclerosis progresses to EPS. The diagnosis is obvious in the late stage, when the abdominal cocoon forms, causing
bowel obstruction. But in the early stages, a diagnosis is perplexing because of a lack of definitive diagnostic criteria. In the proper context, a patient’s vague clinical complaints might raise the index of suspicion for EPS, and noninvasive testing with CT imaging can help to establish the diagnosis.

Imaging by CT is the test of choice, recommended by many authorities, with findings of peritoneal thickening, peritoneal enhancement, calcifications, bowel wall thickening, bowel tethering, and signs of bowel obstruction and fluid loculations or septations being the characteristic intra-abdominal findings (9). A peritoneal biopsy can aid in establishing a diagnosis of EPS, but biopsy is not generally recommended for important reasons. In the presence of EPS, any surgical intervention worsens the postsurgical complications (adhesions, poor healing). In addition, the histologic features of early EPS can overlap with peritoneal findings of peritonitis or ultrafiltration failure (10). Surgery, either by laparotomy or laparoscopy, with peritoneal biopsy, can be used to establish diagnosis in cases with a very high index of suspicion for EPS (11). Macroscopically, the typical findings are thick brown peritoneum and cocoon-like encapsulation of the bowel loops by the visceral peritoneum. In severe cases of inflammation, there could be adhesions between the parietal and visceral layers of the peritoneum (10).

Garosi et al. (12) compared peritoneal histology in PD patients with simple sclerosis and in those with sclerosing peritonitis, establishing significant characteristic findings for EPS. Those findings include thickened sclerosis in the range 250 – 4000 μm, active inflammation, granulation tissue, arterial alterations (thickening, occlusion, calcification, ossification), and tissue calcification. The thickness of the sclerosis in EPS is greater in the visceral than in the parietal peritoneum. Another study that compared sclerosis with EPS found that capillary angiogenesis and mononuclear cell infiltration were common in EPS (13).

Newer methods to diagnose EPS in its early stages have been used in research, but are not yet validated and approved for clinical use. Biomarkers such as cancer antigen 125 (low concentration indicating loss of mesenchymal cells) and interleukin 6 (high concentration indicating inflammation) in PD effluent were found to be useful. Imaging by dynamic cinematographic magnetic resonance can also be useful for diagnosing early EPS (14).

Management of EPS works toward reducing inflammation and applying antifibrotic agents, techniques that are based on case reports and series. There is general agreement to stop PD once EPS is diagnosed so as to remove the triggering factor. In advanced cases of EPS with bowel obstruction, patients need nutritional support with total parenteral nutrition.

Steroids are the drug of choice to improve inflammation; they are very useful in early-stage EPS (15). When used as a single agent, steroids have been associated with clinical improvement in 38.5% of cases (2). Tamoxifen, with its antifibrotic properties, has been used with some success in various case reports and series (16). A recent retrospective study in the Netherlands (17) also demonstrated significantly lower mortality in EPS patients treated with tamoxifen (45.8%) than in those treated without it (74.4%). The Pan- Thames EPS study, reported in 2009, was a retrospective analysis of outcomes in EPS patients; it showed no added benefit of treatment with steroids, tamoxifen, or a combination of immunosuppressive agents (18). Based on the case reports, tamoxifen and steroids are suggested as the treatment of choice for EPS (16). Surgery (peritonectomy and enterolysis) is indicated for severe cases of EPS causing bowel obstruction or presenting with acute abdomen. Postoperative mortality in such cases is high, ranging between 19% and 34.5%, and recurrence rates are also high, up to 25% (19). The recent development of a surgical procedure called noble plication (suturing of the intestines together) and enterolysis has reduced the recurrence rate to 12.3% (15).

Various measures have been proposed to prevent EPS, but putting them into practice is difficult because of a lack of high-level evidence. Switching the dialysis modality to hemodialysis after the patient has been on PD for more than 5 years was proposed, but not all PD patients—even those with sclerosis—progress to EPS. The use of tamoxifen or angiotensin-converting enzyme inhibitors to prevent fibrosis has also been advised, but no studies have been undertaken to demonstrate an actual benefit (19).

Our patient had symptoms and signs suggestive of early-stage (inflammatory stage) EPS with abdominal pain, bloody PD fluid, peritoneal thickening on CT imaging, and biopsy findings suspicious for EPS. He was taken off PD and started on oral tamoxifen and prednisone and on hemodialysis. After almost 10 months of therapy, the patient has reported feeling
better. He will be under close follow-up and surveillance to monitor clinical progression.

**Summary**

Encapsulating peritoneal sclerosis is a rare and dreaded complication of PD. There is a huge knowledge gap concerning this disease process because of a lack of proper evidence concerning its pathophysiology, clinical varieties and diagnosis, and management. Based on the existing studies, case reports, and case series, it seems prudent to stop PD upon early suspicion of EPS to prevent, if possible, progression to full-blown EPS.

**Disclosures**

We understand that *Advances in Peritoneal Dialysis* requires disclosure of any conflicts of interest, and we declare that we have no conflicts to disclose.

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