

CASE REPORT

Successful Treatment of Encapsulating Peritoneal Sclerosis With Immunosuppressive Therapy

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Encapsulating peritoneal sclerosis is a rare, but potentially lethal, complication of peritoneal dialysis. Treatment of patients with encapsulating peritoneal sclerosis is controversial. Conservative treatment carries a poor outcome, and immunosuppressive drugs are now used frequently. Most commonly, these immunosuppressive regimens include steroids with or without azathioprine or cyclosporine. Mycophenolate mofetil is a reversible DNA synthesis inhibitor that frequently replaces azathioprine in renal transplantation because of its improved immunosuppressive potency and better side-effect profile. We report 3 cases of encapsulating peritoneal sclerosis in continuous ambulatory peritoneal dialysis patients for which an association of prednisone and mycophenolate mofetil significantly modified the evolution of the disease. All 3 patients showed significant improvement within a month and are still alive more than 2 years after the diagnosis of encapsulating peritoneal sclerosis. None experienced a relapse or abdominal symptoms, and body weights are stable. This is the first report of 3 cases of successful treatment of patients with encapsulating peritoneal sclerosis with prednisone and mycophenolate mofetil.

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INDEX WORDS: Encapsulating peritoneal sclerosis; immunosuppression; mycophenolate mofetil; peritoneal dialysis; encapsulating sclerosing peritonitis.

Encapsulating peritoneal sclerosis (EPS) is a rare, but potentially lethal complication of peritoneal dialysis. In 1 center in Canada, the annual incidence was 0.37 cases/1,000 patient-years from 1977 to 1997.¹ Treatment of patients with EPS is controversial, and the mortality rate is high (24% to 83%).¹⁻⁴ We report 3 cases of EPS in continuous ambulatory peritoneal dialysis patients for which an association of prednisone and mycophenolate mofetil (MMF) significantly modified the evolution of the disease.

CASE REPORTS

Patient 1

A 43-year-old woman of Asian origin with immunoglobulin A nephropathy experienced 7 peritonitis episodes during 7 years of follow-up. In July 2001, she was admitted for peritonitis caused by *Enterobacter cloacae* refractory to intraperitoneal antibiotic therapy, leading to removal of the catheter and transfer to hemodialysis therapy. Three abdominal computed tomographic (CT) scans showed increasing multiloculated ascites with no abscess formation. Finally, a few days after antibiotic therapy was stopped, she showed clinical improvement and was discharged.

In January 2002, the patient presented with recurrent abdominal pain, loss of appetite, weight loss of 13 kg, vomiting, and constipation. She had a low-grade fever (100.4°F [38°C]) with abdominal distension and tenderness. A CT scan showed abundant multiloculated ascites and thickening of the intestinal wall (Fig 1A). A small-bowel follow-through study showed predominantly distal cocooning of the small bowel (Fig 2). Indium-111-

labeled leukocyte scintigraphy results were negative. The diagnosis of EPS was retained.

The patient received a trial of immunosuppressive treatment: colchicine, 0.6 mg/d for 2 months; prednisone, 50 mg/d for 2 weeks with progressive tapering to 25 mg/d; and MMF, 500 mg twice daily. The patient's condition drastically improved. Recurrent abdominal pain disappeared and serum albumin level increased to 3.5 g/dL (35 g/L). In March 2002, a control CT scan showed resolution of most of the ascites and less thickening and infiltration of the mesenteric root (Fig 1B). Results of a small-bowel follow-through study were normal. When she underwent living donor kidney transplantation in 2003, she was still on prednisone (10 mg/d) and MMF therapy.

Patient 2

A 54-year-old woman on continuous ambulatory peritoneal dialysis for 12 years because of dense-deposit membranoproliferative glomerulonephritis with 2 previous cadav-

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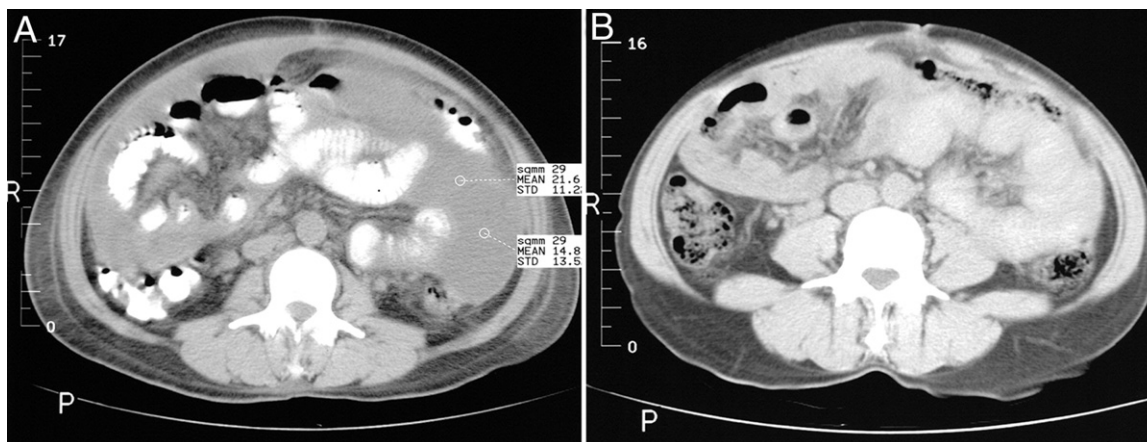


Figure 1. Computed tomographic scans from patient 1 show (A) thickening of the intestinal wall, dilatation of the small bowel, mesenteric infiltration with adenopathy, and abundant loculated ascites and (B) disappearance of ascites and no thickening of the intestinal wall on a control CT scan after 3 months of immunosuppressive therapy.

eric kidney transplants experienced 3 episodes of bacterial peritonitis. She was admitted in April 2004 for bacterial peritonitis. *Staphylococcus epidermidis* was isolated from the peritoneal fluid, and antibiotic treatment was initiated. Her catheter was removed 9 days later because of a tunnel abscess. Despite transfer to hemodialysis therapy and adequate antibiotic treatment, abdominal symptoms and fever persisted. In May 2004, *Candida parapsilosis* was isolated from a percutaneous peritoneal tap. She was treated with a 5-week course of oral fluconazole, without significant improvement. A CT scan did not show specific abnormalities except for moderate ascites, probably partly bloody. A diagnosis of EPS was made at the end of May 2004. Total parenteral nutrition and an immunosuppressant regimen were started (prednisone, 25 mg/d tapered over 2 months to 15 mg, and MMF, 500 mg twice daily). Abdominal symptoms and fever improved rapidly. Both prednisone and MMF therapy were stopped after 6 months of treatment.

Patient 3

A 51-year-old black woman with focal glomerulosclerosis on continuous ambulatory peritoneal dialysis therapy for 4 years was treated for coagulase-negative staphylococcus peritonitis in July 2002. In November 2002, she was admitted for abdominal pain. A peritoneal fluid culture was positive for *Candida glabrata*. The peritoneal catheter was removed, and she was treated with caspofungin for 4 weeks. Fever and abdominal pain recurred 3 weeks after admission. At that point, results of an abdominal CT scan and small-bowel follow-through study were negative. However, the CT scan was repeated in January 2003 and showed thickening of the intestinal wall. Prednisone, 50 mg/d, and MMF, 500 mg twice daily, were started for probable EPS. The abdominal pain and fever resolved rapidly, and she was discharged in mid-January. MMF therapy was stopped, and prednisone therapy was withdrawn rapidly in February 2003 because of disseminated herpes zoster. A new CT scan in March 2003 showed almost complete resolution of abnormalities seen in January.

As of February 2007, all 3 patients are alive without relapse or abdominal symptoms. Body weights are stable. Peritoneal dialysis therapy was not attempted again in the 3 patients after the diagnosis of EPS.

DISCUSSION

EPS is characterized by extensive intraperitoneal fibrosis with retractile mesenteritis and ultimately cocooning of the small bowel. This even-

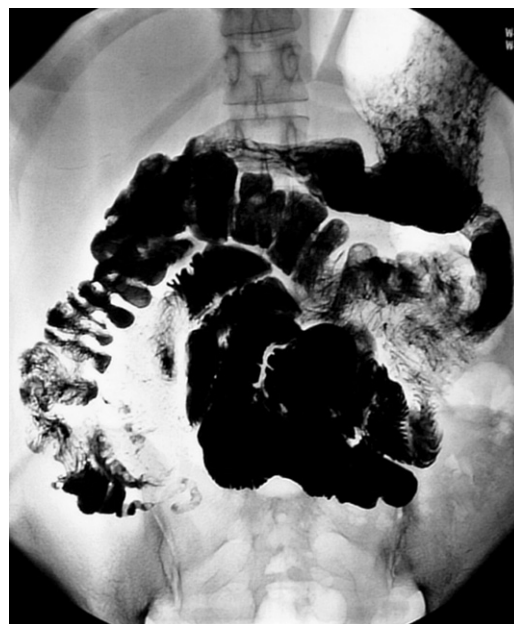


Figure 2. A small-bowel follow-through study from patient 1 shows cocooning of the small bowel (predominantly distal).

tually leads to intestinal malabsorption and partial or complete intestinal tract obstruction. Patients may present with anorexia, weight loss, and abdominal pain and swelling, or nausea, vomiting, and a frank intestinal obstruction syndrome.^{3,5}

Increased levels of inflammatory markers may be found in blood, but are not specific. A CT scan may help confirm the diagnosis, showing intestinal adhesions, infiltration of mesenteric root and cocooning of the small bowel, parietal peritoneal thickening, and multiloculated ascites.⁶

Several risk factors for EPS have been suspected: β -blockers, chlorhexidine, acetate dialysate, and peritonitis. Only 1 of our 3 patients was on β -blocker therapy. The newest possible risk factors include long duration of peritoneal dialysis therapy, high peritoneal membrane transport, and discontinuation of peritoneal dialysis therapy.^{3,7} Peritonitis occurring in the few months before EPS is very common, ranging from 25% to 100%.^{1,4,8,9} *Staphylococcus aureus* is the most frequent germ, but fungi seem to be overrepresented, accounting for 7% to 18% of cases.^{1,4,9} In the 3 patients we report, 2 had fungal peritonitis. Causes of EPS remain poorly understood, but an immunologic mechanism was hypothesized.²

Treatment of patients with EPS is controversial. Conservative treatment, including total parenteral nutrition and peritoneal rest, was associated with a poor outcome when used alone.³ Surgery was associated with a high complication rate and is not recommended.

Steroids alone may be efficacious,⁸⁻¹¹ but many investigators administered a combined regimen of steroids and azathioprine or cyclosporine.^{2,4,12,13} However, evidence from these few observational studies is still anecdotal. Some investigators suggested steroid therapy, mainly in the inflammatory stage of EPS.¹⁴ After publication of some cases with clinical improvement or even cure of EPS after kidney transplantation (and its accompanying immunosuppressive therapy), immunosuppressive drugs were administered to patients with EPS.¹³ Because the efficacy of steroid therapy alone is unpredictable (range, 0% to 100%) and EPS is a possibly fatal disease, we decided to use an immunosuppressive regimen and not steroids alone. In patient 1, we tried a regimen similar to that of Fagugli et al,¹² but replaced azathioprine with MMF because azathioprine was temporarily not avail-

able. In the other 2 patients, MMF was chosen again, encouraged by the success with the first patient. The duration of immunosuppressive treatment was empirical and adapted to the clinical evolution of the patient.

MMF is a reversible DNA synthesis inhibitor that frequently replaces azathioprine in renal transplantation because of its improved immunosuppressive potency. After gastrointestinal absorption, it is rapidly converted by the liver to mycophenolic acid, the active compound. The metabolite selectively blocks the proliferation of B and T lymphocytes through purine synthesis inhibition. Also, MMF inhibits the proliferation of smooth muscle cells, fibroblasts, and endothelial cells. The main side effects of MMF are gastrointestinal (nausea, diarrhea, and abdominal pain) and hematologic (leukopenia). Those side effects usually resolve with dose adjustment. Because MMF is slightly less tolerated in patients with end-stage kidney disease and our patients had abdominal pain caused by EPS, we chose a relatively low dose of MMF (500 mg twice daily).

To our knowledge, this series of 3 patients is the first therapeutic trial with a combination of steroids and MMF for the treatment of EPS. Steroids were also administered; therefore, we cannot dissociate their effects from the effect of MMF. One case of EPS was reported in a renal transplant recipient with a maintenance immunosuppressive therapy of MMF, prednisone, and tacrolimus.¹⁵ Consequently, MMF may not be efficacious in every patient or may need to be associated with prednisone to be effective. An anecdotal report with sirolimus in 1 patient was not successful.¹⁶

In conclusion, the combination of prednisone and MMF was effective for the treatment of EPS in 3 patients. Immunosuppressive drugs may have an important role in the treatment of this morbid complication of peritoneal dialysis. However, a systematic review of the treatment of EPS with immunosuppressive therapy is needed.

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