



# ENCAPSULATING PERITONEAL SCLEROSIS – SUCCESSFUL MEDICAL/SURGICAL TREATMENT AND KIDNEY TRANSPLANTATION: A CASE REPORT

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**SUMMARY** – The patient was born in 1967. In 2004 the patient started renal replacement therapy with peritoneal dialysis.

In 2010, after the first episode of peritonitis caused by *Staphylococcus aureus*, due to poor response to antibiotic therapy, the peritoneal catheter was removed. A month after this episode, pain accompanied by fever and an increase in inflammatory parameters occurred. Initial computed tomography scans did not show any specific abnormalities and the second CT two months later diagnosed sclerosing peritonitis. Corticosteroid and tamoxifen therapy with enteral nutrition was initiated. Five months after the symptoms started, the patient developed intestinal obstruction, so a nasogastric tube was placed and total parenteral nutrition was introduced.

After four months, the patient was surgically treated at the Manchester Royal Infirmary, resection of the terminal ileum and caecum was performed, and an ileocecal anastomosis with enterolysis was performed.

Then, in 2012, a successful kidney transplant was performed. The patient has since remained without clinical signs of obstruction.

Tamoxifen and corticosteroid therapy with adequate nutritional support, surgical treatment, and transplantation with long-term immunosuppressive therapy may be reasons for long-term remission and survival ten years after EPS diagnosis.

**Key words:** *Encapsulating peritoneal sclerosis (EPS); peritoneal dialysis (PD); EPS surgical treatment, kidney transplantation EPS*

## Introduction

Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication of peritoneal dialysis (PD), with significant morbidity and mortality. Reported mortality is around 50%, usually within 12 months after the diagnosis is made.<sup>1,2</sup> Incidence varies across the

globe: for instance, cumulative incidences in Australia and New Zealand at 3, 5, and 8 years over a 13-year period were 0.3, 0.8 and 3.9%<sup>3</sup>, whereas in Japan, the reported incidences at 3, 5, 8, 10, 15, and more than 15 years were 0%, 0.7%, 2.1%, 5.9%, 5.8 and 17.2%<sup>4</sup>. Factors that may contribute to this variation include the study size, single-center vs. registry data, retrospective vs. prospective, prevalent vs. incident patients, criteria to establish the diagnosis, and potential true differences in incidence. EPS is characterized by persistent,

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intermittent, or recurrent adhesive bowel obstruction, resulting in malnutrition as the cause of death. The origin of this disease is probably multifactorial, and it is uncertain whether all registered clinical cases should be classified as a single disease of the same origin. Intraoperative macroscopic phenotypes could vary from thickened peritoneum or resolvable cobweb-like inter-enteric cover to classic type intestinal cocooning<sup>5</sup>. There are also many subclinical cases or cases without manifestation of intestinal obstruction, usually not classified as EPS, that could be considered as an early stage or milder form of the same disease. The diagnosis of EPS requires both the clinical feature of intestinal obstruction or disturbed gastrointestinal function and the evidence of bowel encapsulation determined either radiologically or pathologically.

### Case report

A 37-year-old female patient developed end-stage kidney disease in 2004 due to hypertensive kidney disease and started treatment with continuous ambulatory peritoneal dialysis.

In 2008, she was admitted to the hospital in a state of hemorrhagic shock with blood detected in the peritoneal cavity during the peritoneal exchange. Open laparotomy revealed a ruptured ovarian cyst, and partial ovariectomy was performed. However, since the patient refused to change the renal replacement modality and insisted on continuing with peritoneal dialysis after surgery, we started automated peritoneal dialysis with small drain volumes.

Starting from 2008, d/p creatinine was increasing from 0,67 to 0,83 in 2009 and 0,87 in 2010. The patient was on glucose solution and icodextrin, and received atenolol as antihypertensive therapy.

In May 2010, after a wedding party, she was admitted to the hospital with diarrhea, abdominal discomfort, fever, and a cloudy dialysate. On admission, acute peritonitis and infection at the exit site were diagnosed by clinical examination and confirmed by white cell count in the PD fluid. Intraperitoneal therapy with vancomycin and ceftazidime was introduced. Once *Staphylococcus aureus* had been isolated from swabs taken from the exit site and the dialysate culture, only vancomycin was continued.

After seven days of antibiotic treatment, normalization of dialysate leukocytes and inflammatory blood

parameters has not been achieved, so the peritoneal catheter was removed.

After removal of the peritoneal catheter, hemodialysis was initiated. The patient became asymptomatic with laboratory improvement.

In June 2010, she presented with fever and abdominal discomfort after eating.

Physical examination revealed a regularly built female with high blood pressure up to 200/120 mmHg. A holosystolic heart murmur of grade 2 intensity could be heard over the anterior chest wall, radiating to the left axilla. Abdominal examination revealed a distended but soft abdominal wall with diffuse tenderness to palpation, mostly in the epigastric area. There was a scar in the median line due to previous laparotomy and peristalsis was audible. Other aspects of the clinical examination were normal.

The laboratory analysis indicated elevated inflammatory parameters. Ultrasound examination revealed a collection of fluid in the abdominal cavity. Leukocyte count in the ascitic fluid was normal, and ascitic culture was sterile.

An abdominal X-ray was performed (Figure 1.)

The fractionated intestinal passage was performed, and bowel obstruction was not found, only accelerated passage (Figure 2.). Computed tomography (CT) was performed, and except for liquid found in the abdomen, there was no other pathology. The patient's laboratory parameters indicated worsening of prior known normocytic anemia and elevated inflammatory markers. *Clostridium difficile* was isolated from coprocultures. Hemocultures were sterile. In July 2010, plain film radiographs of the abdomen showed dilation of the bowel with air-fluid levels. In August, another CT was performed: areas of loculated ascites, convolutions of the small intestines were distended, fixed, and calcifications were seen in the serosa (Figure 3.).

The patient was treated with methylprednisolone, tamoxifen, nutritional therapy, antihypertensive medication, and erythropoietin. Her condition got significantly better, she restored regular bowel movement, and her inflammatory markers started to subside. In November 2010, there was a worsening of the disease, and she gradually started showing signs of ileus and was losing weight. Repeated CT scans showed dilated entire small bowel with total obstruction, ascites, peritoneal, and mural calcifications (Figure 4). The jejunum and ileum convolutions were largely distended,



Figure 1. Abdominal X-ray June 2010.

the small intestine was 6.6 cm wide, and everything pointed to the small bowel ileus. The terminal ileum was of the proper size, and the entire colon was nearly empty with a normal width.

Corticosteroid therapy was continued, and a central venous catheter was placed for parenteral nutrition. From that day on, for most of the time, the patient had a nasogastric tube placed. She was fed with total parenteral nutrition that included vitamins and essential trace elements through a permanent therapeutic jugular catheter. After training, she performed total parenteral nutrition at home and in the center during hemodialysis.

In February 2011, she was referred to the surgical unit at Central Manchester University Hospital, at the Renal Transplant Department, Manchester Royal Infirmary in the UK. Laparotomy, enterolysis, peritonectomy, and partial right hemicolectomy was performed. After the procedure, the patient no longer had signs of intestinal obstruction, and tamoxifen treatment (6 months) and methylprednisolone were continued.

Control CT performed six months after surgery showed a small collection of fluid in front of the liver and peritoneal calcification near the spleen (Figure 5.). The bowel looked normal and enlarged lymph nodes



Figure 2. Fractionated intestinal passage June 2010.

were not found. Twenty months after the diagnosis of encapsulating peritoneal sclerosis, she was asymptomatic and referred to a transplant nephrologist for kidney transplant listing. After complete diagnostic procedures, she was put on the Eurotransplant kidney waiting list. On May 12th, 2012, kidney transplantation was performed. She received basiliximab as induction therapy and triple immunosuppressive maintenance therapy with corticosteroids, mycophenolate mofetil and tacrolimus were given later on. The operation and early postoperative course were successful without any intestinal or other complications. Primary graft function was achieved. Later she experienced two severe infectious episodes, nine and sixteen months after transplantation. The first one was E.coli sepsis, which originated from a tubo-ovarian abscess and the second infection was from a subcutaneous upper leg abscess. Both were treated successfully with parenteral antibiotics and, for the leg abscess, surgical drainage was performed.

Regular abdominal CT was performed in April 2015, and it did not reveal any new signs of EPS (Figure 6.).

In early 2016, an indicative kidney biopsy was performed due to a recorded increase in creatinine. Histo-

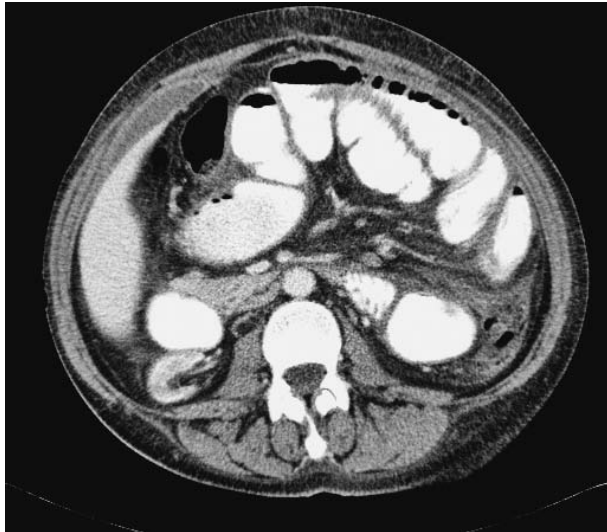


Figure 3. Computed tomography August 2010.



Figure 5. Computed tomography August 2011.



Figure 4 Computed tomography November 2010.

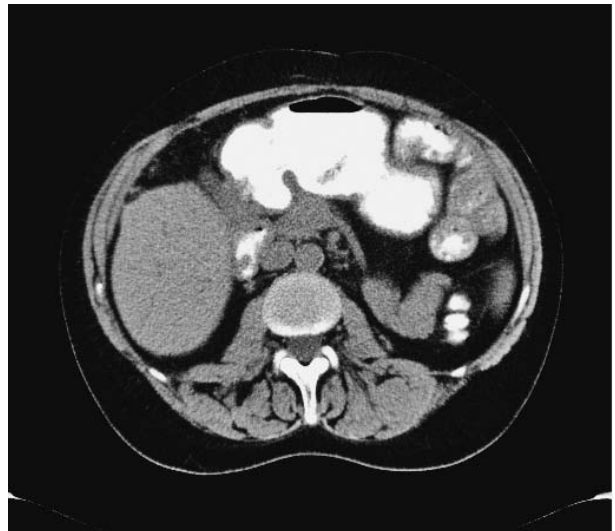


Figure 6. Computed tomography April 2015.

logically, the borderline acute cell-mediated rejection was confirmed and was not treated at the time due to an active urinary tract infection. In the further course, the patient had satisfactory graft functions with creatinine values of 150-170  $\mu\text{mol/L}$ , without proteinuria. Still, in 2019 she was monitored again for a gradual creatine surge, and in August 2019, a kidney biopsy was performed again. Histology confirmed chronic active cell-mediated rejection, IA with severe capillaritis, but without glomerulitis. Donor-specific antibodies were not detected. Corticosteroid treatment with infection prophylaxis was performed. A follow-up bi-

opsy performed 2 months after treatment indicated persistent chronic active cell-mediated rejection, IA with blood creatinine values up to 250  $\mu\text{mol/L}$ . Given the finding of steroid-resistant rejection in a hospital setting, a second line of treatment, anti-thymocyte globulin, was administered. After the treatment, there was a gradual recovery of graft function with a decrease in blood creatinine levels to stable values around 180-200  $\mu\text{mol/L}$ .

Now the patient receives corticosteroids, mycophenolate mofetil, and tacrolimus and feels well. There is no clinical sign of encapsulating peritoneal sclerosis.

Her clinical condition is stable, with a good nutritional status and without any clinical symptoms of EPS.

## Discussion

The cause of EPS is thought to be multifactorial. Possible causes include PD vintage, exposure to dialysis solutions with high glucose concentrations, the use of acetate as a dialysate buffer, and bioincompatible dialysate as risk factors and frequent and severe peritonitis<sup>6</sup>. The condition is rare, but the mortality rates are still high. For instance, in a national cohort study done from the Scottish Renal Registry, the mortality rate was 42% at 1 year *post diagnosem* with a median survival of 149 days<sup>7</sup>. In a national study in Japan, mortality rates were 28.6%, 61.5% and 100% for patients treated with PD for 10, 15, and more than 15 years<sup>4</sup>.

The symptoms of EPS can be intermittent or chronic, mild or severe. They include bowel obstruction symptoms (persistent/intermittent, partial/complete, abdominal pain, distension, nausea, vomiting), abdominal mass, malnutrition with failure to thrive, hemoperitoneum, and sterile non-resolving or recurrent PD “peritonitis”. Association of ultrafiltration loss and an increase in peritoneal membrane small solute transport has been found in many EPS patients, but the causal relationship between these parameters and the development of EPS has not yet been established.<sup>8</sup> Recently, two groups from Netherlands and Belgium revealed that late ultrafiltration failure, dominantly decreased free water transport marked by the loss of osmotic conductance could predict the development of EPS<sup>9,10,11,12</sup>. To determine the diagnosis, CT scanning showed best sensitivity and specificity, it is widely available and has the greatest reproducibility.<sup>13</sup> Peritoneal calcification, bowel thickening, bowel tethering, and bowel dilatation as signs of EPS are the features that most radiologists agree upon. However, to determine the diagnosis of EPS, both clinical and radiological features should be present.

Once the diagnosis of EPS is made, PD should be terminated in most cases and the patient transferred to HD. Mild EPS cases could potentially worsen after stopping PD, and patient-related factors need to be taken into consideration. As severe malnutrition is a crucial factor in the morbidity and mortality associated with EPS, nutrition support (parenteral nutrition in severe cases) is an important part of treatment. Many

of the patients will recover with conservative treatment, including nutrition support alone.<sup>14</sup> Kawanishi *et al.* proposed four ESP stages to target therapeutic options: pre-symptomatic, inflammatory, encapsulating, and ileus.<sup>15</sup> While corticosteroids, immunosuppressants, and tamoxifen have been used to treat EPS, there is no clear evidence-based drug therapy for EPS due to the lack of randomized controlled trials regarding drug therapy. A large UK series showed no improvement in outcomes for patients treated with steroids, immunosuppressants, tamoxifen, or combinations of these compared with patients not receiving these drugs.<sup>2</sup>

Since the high mortality rate is usually caused by a bowel obstruction, for recurrent or refractory bowel obstruction, surgical therapy should be considered. In the past, surgery was associated with high mortality rates and was contraindicated since most patients died of peritonitis as a postoperative complication. These deaths occurred because, in many cases, simple resection of adherent intestinal loops with enteroanastomosis was performed. Referral to surgical units with expertise in EPS surgery has resulted in high rates of symptomatic improvement and survival.<sup>15,16,17,18</sup>

## Conclusion

Tamoxifen and corticosteroid therapy with adequate nutritional support despite ileus, surgical treatment in a center with experience in EPS treatment, and transplantation with long-term immunosuppressive therapy may be the reasons for long-term remission and survival ten years from diagnosis EPS in this patient.<sup>19</sup>

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#### Sažetak

### INKAPSULIRAJUĆA PERITONEALNA SKLEROZA- USPJEŠNO MEDICINSKO / KIRURŠKO LIJEČENJE I TRANSPLANTACIJA BUBREGA: PRIKAZ SLUČAJA

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Bolesnici rođenoj 1967. godine, 2004. godine započeto je nadomještanje bubrežne funkcije peritonejskom dijalizom.

2010. godine bolesnica je imala prvu epizodu peritonitisa uzrokovanu *Staphylococcus aureus*om. Zbog nepostizanja adekvatnog odgovora na ciljanu antibiotsku terapiju, izvađen je peritonejski kateter i bolesnica je transferirana na hemodijalizu. Nakon kliničkog i laboratorijskog poboljšanja, mjesec dana kasnije javila se bol nakon jela uz povišenu temperaturu i porast upalnih parametara. Inicijalno učinjen CT abdomena nije bio specifičan, tek na ponovljenom CT-u dva mjeseca kasnije nađeni su znaci sklerozirajućeg peritonitisa. Započeta je terapija kortikosteroidom i tamoksifenom uz enteralnu prehranu. Pet mjeseci od pojave sklerozirajućeg peritonitisa bolesnica je razvila sliku intestinalne opstrukcije, pa je plasirana nazogastrična sonda i uvedena je totalna parenteralna prehrana.

Nakon četiri mjeseca bolesnica je operativno liječna u Manchester Royal Infirmary, učinjena je resekcija terminalnog ileuma i cekuma i formirana je ileocekalna anastomoza, te enteroliza preostalih crijeva.

Potom je 2012. godine učinjena uspješna transplantacija bubrega.

Bolesnica od operativnog liječenja je bez kliničkih znakova opstrukcije.

Terapija tamoksifenom i kortikosteroidima uz odgovarajuću prehranbenu podršku unatoč ileusu, kirurško liječenje u centru koji ima iskustva u liječenju EPS-om (enkapsulirajuća peritonealna skleroza) i transplantacija s dugotrajnom imunosupresivnom terapijom mogu biti razlozi dugotrajne remisije i preživljenja deset godina od dijagnoze EPS-a.

Ključne riječi: *Enkapsulirana peritonealna skleroza (EPS); peritonealna dijaliza (PD); Kirurško liječenje, transplantacija bubrega*