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CASE REPORT

Encapsulating Peritoneal Sclerosis: Actually Rare or An Underdiagnosed Complication?

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ABSTRACT

Encapsulating Peritoneal Sclerosis (EPS) is a rare complication occurring in patients on peritoneal dialysis, often underestimated and probably under diagnosed. We report the case of a woman on long-standing peritoneal dialysis, who developed clinical EPS within three years from renal transplantation, while she was assuming immunosuppressive agents. She developed a progressive inflammatory systemic disease with severe malnutrition and recurrent bowel sub-occlusive episodes. Despite the patient had almost all the well-known risk factors for this complication, three years were needed to make the right diagnosis. Afterwards, the patient underwent surgical treatment and took tamoxifen for six months with complete clinical remission.

Background

EPS, first described in 1980 [1], is a rare but severe complication of peritoneal dialysis (PD) and associated with significant morbidity and mortality. Its incidence varies between 0.7 and 3.3% in patients on PD [2] and is directly related with PD duration. The mortality rate is high, however, between 25 and 55% [2-6,]. As showed by experimental animal models and clinical studies, long term exposure to PD leads to peritoneal changes, such as mesothelial denudation, fibrosis, vasculopathy and angiogenesis. In this regard high concentration glucose solutions, acidic pH, glucose degradation products and advanced glycation end products have been variously suggested to have a possible pathogenic role. Then, according to some AA [7-9], the occurrence of episodes of acute bacterial peritonitis could act as a "second hit" to trigger the disease.

The natural history of EPS seems to progress through various stages of inflammation, encapsulation and finally chronic ileus [10]. Therefore clinical presentations may be various (persistent-intermittent symptoms of bowel obstruction, abdominal mass, abdominal pain, nausea, vomiting, malnutrition, hemoperitoneum, ultrafiltration problems) and symptoms of EPS can also first occur after shifting from PD to hemodialysis (HD) or after kidney transplantation [11,12], being described in patients receiving calcineurin-inhibitor based immunosuppressive therapies [13,14].

Currently, early markers of EPS are not known and our ability to detect the disease in its early stages is limited. Usually, making the right diagnosis by only imaging techniques [15,16] may be very hard in just less than final stages, often requiring surgery and peritoneal biopsy [17,18].

Among the therapeutic agents used for EPS are steroids, immunosoppressive (anti-inflammatory) agents and tamoxifen (anti-fibrotic). Enterolysis and peritonectomy should be considered for treatment in the more advanced stages of the disease.

We report a paradigmatic case of EPS developed after kidney transplantation in a patient previously on PD and successfully treated with surgical intervention and tamoxifen.

Case Presentation

A 65-year-old woman was on peritoneal dialisys from 2000 to 2009. She had three episodes of Staphilococcus aureus and Enterococcus faecium peritonitis, responding to intra-peritoneal antibiotic therapy.

In August 2009 she underwent renal transplantation from deceased donor, with no clinical immunological or infectious complications. She started immunosuppressive induction therapy with steroids and basiliximab, followed by mantainance treatment with steroids, cyclosporin and micophenolate mofetil.

In June 2010 the patient was hospitalized for acute abdominal pain. An abdominal CT scan showed minimal loculated perihepatic and left pericolic peritoneal fluid and minimal small bowel distention. The patient was dismissed after pain spontaneously remission of the pain. During the following three years she developed a progressive systemic inflammatory state, with malnutrition, altered bowel habit and subocclusive episodes. In May 2013 she came to our observation for abdominal pain, progressive ascites and edema of the legs. She was in poor clinical conditions and malnourished.

Biochemical analysis showed worsening of renal function, iron deficiency anemia and positive fecal occult blood tests. Gastrointestinal endoscopy was not significant. A paracentesis yelded four liters of serous-hematic fluid containing normal levels of alpha-fetoprotein, CEA and, CA 125. An abdominal angio CT scan showed a loculated peritoneal fluid mass, 32 cm extended from subdiaphragm to hypogastric area, 4 cm thicked. The mass was delimited by tickened peritoneal membrane. A MR imaging confirmed the extension of the mass and detected peritoneal calcifications and nodularity (Figure 1A). A laparoscopy found 2.5 liters of serous-hematic fluid, fibrous tissue and peritoneal thickening with adhesion to bowel tracts (Figure 2A). A peritoneal biopsy confirmed the diagnosis of EPS with pathologic findings of chronic inflammation and fibrosis (Figure 3A).

A CT scan performed three months later, before surgical intervention, confirmed the multiloculated mass with increased thickness (10,3 cm) and constrictive effect on the whole bowel (“ fibrous cocoon”) (Figure 4A).

Enterolysis and terminal ileum resection with output ileostomy was performed in August 2013, followed by oral therapy with tamoxifen for six months.

The treatment (surgery followed by tamoxifen) was associated to complete clinical remission and recovery of a good health status. An abdominal CT scan performed in October 2014 (fourteen months after surgery) showed disappearence of the fibrous cocoon (Figure 1B, 2B).

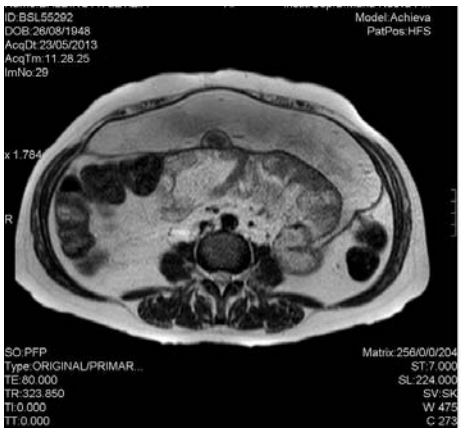
Discussion

EPS is a severe but luckily rare complication of long-term peritoneal dialysis, strongly associated with duration of PD. Pathogenesis of EPS remains partly understood. Several cases are reported in literature.

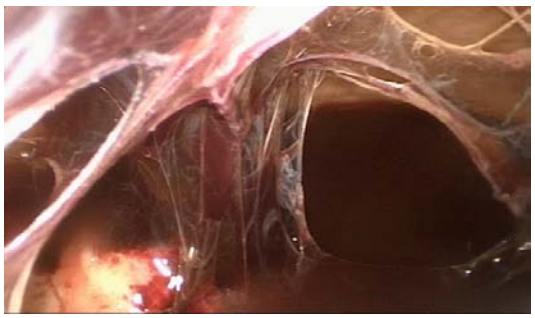
Recently, features of peritoneal cell infiltrate of EPS were studied. A characteristic mononuclear cell infiltrate consisting of CD4+ and CD163+ cells dominates the peritoneum of EPS patients. These findings suggest a role for both CD4+ T cells and M2 macrophages in the pathogenesis of EPS [19].

Increased serum sCD25 concentrations and peritoneal lymphocytosis in EPS patients indicate the involvement of activated T cells in the pathophysiology of excessive fibrosis [20].

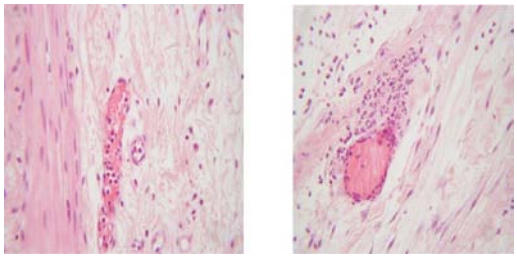
No evidence based therapy for EPS exists. Treatments include cessation of PD, shifting to hemodialysis,



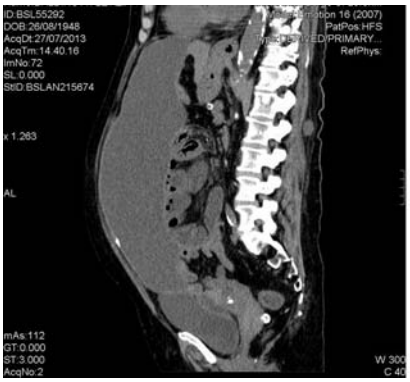
Imagine 1. MR imaging: extension of the mass,peritoneal calcifications and nodularity.



Imagine 2. Laparoscopy: fibrous tissue and peritoneal thickening.

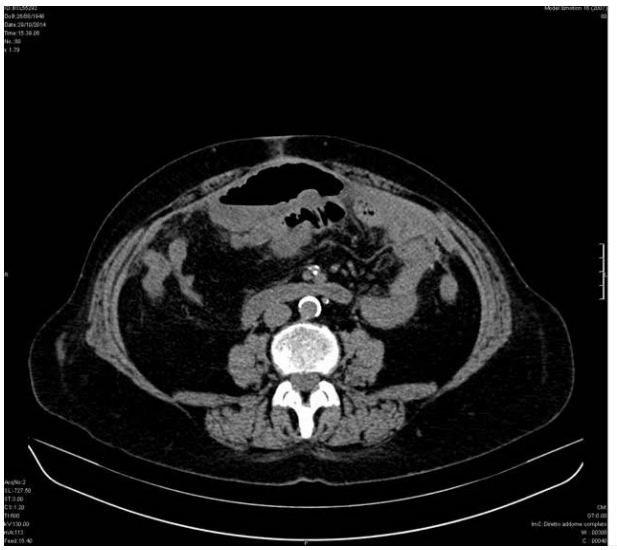


Imagine 3. Peritoneal biopsy: chronic inflammation and fibrosis.

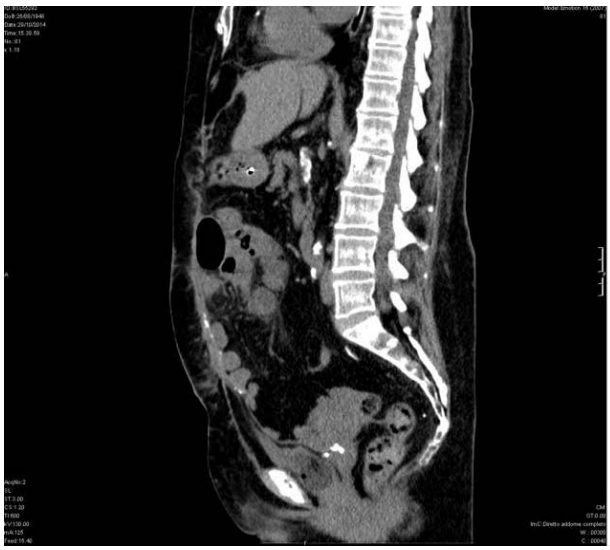


Imagine 4. CT scan: multiloculated mass constricting the whole bowel ("fibrous cocoon").

Panel A:
Figure 1A: MR imaging: extension of the mass,peritoneal calcifications and nodularity.
Figure 2A: Laparoscopy: fibrous tissue and peritoneal thickening.
Figure 3A: Peritoneal biopsy: chronic inflammation and fibrosis.
Figure 4A: CT scan: multiloculated mass constricting the whole bowel ("fibrous cocoon").



Imagine 1. CT scan afer therapy: disappearence of the fibrous cocoon



Imagine 2. CT scan afer therapy: disappearence of the fibrous cocoon

Panel B:
Figure 1B: CT scan afer therapy: disappearence of the fibrous cocoon
Figure 2B: CT scan afer therapy: disappearence of the fibrous cocoon

nutritional support, tamoxifen and immunosuppressive therapy. Surgery is performed in patients with advanced stages of EPS, with clinical pictures of bowel obstruction or acute abdomen.

The evaluation of peritoneal cell infiltrate in patients on PD affected by acute peritonitis could be probably useful to distinguish between infective peritonitis and early cases of EPS. Early diagnosis and early treatment with steroids and immunosuppressive agents could be the key to avoid major surgical interventions.

Learning Points/Take Home Messages

1: This is a paradigmatic case of EPS. Our patients had almost all the well-known risk factors for EPS. She was on peritoneal dialysis for long time, had bacterial peritonitis, underwent renal transplantation and assumed calcineurine inhibitors (cyclosporin). Clinical presentation was didactic with abdominal pain, altered bowel habits, malnutrition, bowel obstruction, ascites and edema.

Despite a significative clinical history and a typical clinical presentation, three years were needed for making the right diagnosis.

2: EPS is a rare complication in long –term PD patients. The insidious features of EPS and the lack of early markers of the disease limit the possibility of early diagnosis. Indeed, EPS may be more a underdiagnosed than a rare complication of PD.

3: Early diagnosis and early treatment could probably allow to avoid surgical intervention and ileostomy, which have a considerable impact on patient's life.

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