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CASE REPORT

A case of encapsulating peritoneal sclerosis presented shortly after renal transplantation

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Abstract Encapsulating peritoneal sclerosis (EPS) is a rare but serious complication of peritoneal dialysis (PD), characterized by extensive intraperitoneal fibrosis and encasement of bowel loops. It typically associates with long-term PD and progressive loss of ultrafiltration. The management of EPS has evolved substantially from the original report of this entity and now includes immunosuppressive agents, antifibrotic agents, nutritional support, and surgical intervention. Although the exact cause of this condition remains obscure and despite the possible positive effect of immunosuppression on EPS, it has been described in the post-transplant setting upon the discontinuation of PD. We report such a case of a former PD patient who presented with EPS a month after renal transplantation. This article will highlight the current views regarding the management of post-transplant EPS and introduce the problem of long-term PD patients on the deceased-donor transplant waiting list.

Keywords Encapsulating peritoneal sclerosis · Immunosuppression · Peritoneal dialysis · Transplantation

Introduction

More than 30 years ago, Gandhi et al. [1] identified encapsulating peritoneal sclerosis (EPS) as a possible complication of peritoneal dialysis (PD). Nowadays, it is known as a deleterious complication mostly affecting patients who remain in PD for more than three to five years. It is defined as a clinical syndrome with persistent, intermittent, or recurrent presence of intestinal obstruction with or without co-existence of inflammation and existence of peritoneal thickening, sclerosis, calcification, and encapsulation confirmed by macroscopic inspection or radiological findings [2]. Reported mortality rates are approximately 50 % usually within the first year of the diagnosis [3].

The etiology of EPS is believed to be multifactorial and many hypotheses have been proposed for its pathogenesis. The most widely accepted theory describing the pathogenesis of EPS is Kawanishi's "two-hit" hypothesis [4]. The "first hit" leads to peritoneal deterioration in terms of both structure and function. However, a "second hit" is necessary for the full picture of EPS to occur. A key pathological mechanism may be the epithelial to mesenchymal transition of mesothelial cells, with TGF-beta considered to be one of the central regulators [5, 6].

Renal transplantation has been reported as effective therapy for EPS, possibly due to immunosuppressive therapy given to transplant recipients [7]. However, a form of EPS that develops shortly after kidney transplantation has been recognized as a distinct clinical entity [8], although only a few cases have been published so far. Here, we report such a case of complicated, fibrotic stage EPS presented a month after renal transplantation.

Case report

A 51-year-old Caucasian male renal transplant recipient presented with abdominal malaise and anorexia. One

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month previously, he had received a first deceased-donor renal transplant. He was treated with continuous ambulatory PD consecutively for the last ten years, during which he experienced two cases of peritonitis. He did not experience any weight loss, anorexia, or change in bowel habits before transplantation. The patient's history included arterial hypertension and chronic hepatitis B infection (HBV DNA negative). The patient refused on several occasions change of renal replacement method to hemodialysis due to personal reasons.

As induction treatment, he received basiliximab, while the maintenance immunosuppressive regiment consisted of methylprednisolone (20 mg/day gradually decreasing), tacrolimus (0.075mg/kg/day), and mycophenolic sodium (720 mg twice daily). His short-term post-transplant course was uneventful, with no need for dialysis after transplantation. Renal graft function was satisfactory at presentation of symptomatology, with a serum creatinine (sCr) of 1.5 mg/dl (132.6 mmol/L) and estimated glomerular filtration rate (eGFR) [CKD epidemiology collaboration formula] 50 ml/min/1.73 m^2 [immunosuppression consisted of methylprednisolone 16 mg/day, mycophenolic sodium 720 mg twice daily, tacrolimus 2 mg twice daily (FK506 levels at 8.5 ng/ml)].

By the time patient became symptomatic, physical examination showed slight diffusible epigastric discomfort, with no sign of inflammation at the site of transplant incision. His laboratory results revealed mixed metabolic acidosis with no deterioration of renal function. Abdominal ultrasound and an upper gastrointestinal tract endoscopy were within the normal range. A week after the onset of epigastric discomfort, acute abdominal pain with vomiting presented. An abdominal plain radiography revealed air–fluid levels indicating small bowel obstruction, while abdominal computed tomography (CT) scan (Fig. 1) showed overt obstruction, and a laparotomy was performed. It revealed a thickened peritoneum encasing the entire large bowel, as well as the last loops of the ileum that were compressed into a "cocoon" with complete interloop adhesions. Through a small enterotomy, a massive phytobezoar was discovered (Fig. 2). Thus, resection of the distal ileum was inevitable and an ileo-transverse colon anastomosis was performed. Peritoneal biopsy showed peritoneal thickening and fibrous tissue deposition (Fig. 3). The patient was then placed on fasting and total parenteral nutrition gradually showing clinical signs of improvement, and he was discharged on the 29th postoperative day. The next day, the patient's condition acutely deteriorated. He was re-admitted with acute abdomen that led to another laparotomy, where anastomotic leak and secondary fecal peritonitis were discovered. A terminal ileostomy and a loop transverse colostomy were performed. Culture of peritoneal fluid showed *Candida albicans*, *Klebsiella*

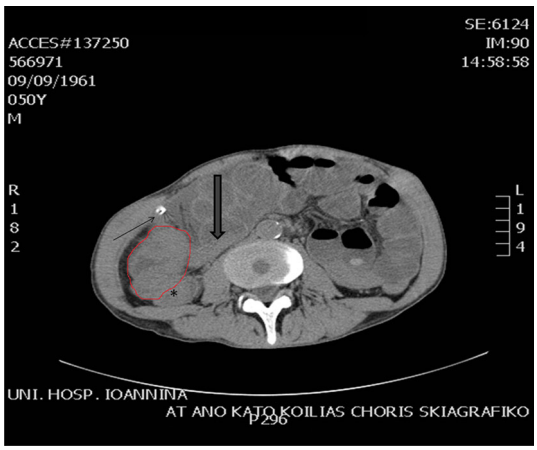

Fig. 1 Abdominal computed tomography (CT) imaging depicting the stenosis at the terminal ileum (*thick black arrow*) and the dilated proximal intestinal loops. The transplanted kidney can be seen in the right iliac fossa (encircled by a continuous *red line*), lying just above the cecum (*asterisk*). The *thin black arrow* shows the peritoneal dialysis catheter

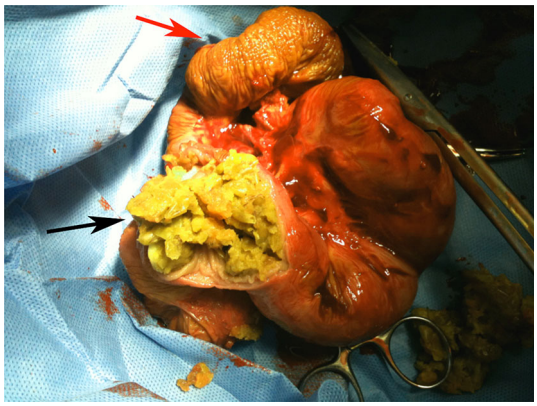

Fig. 2 The obstructed loop of distal ileum containing a phytobezoar (*black arrow*). The entire small bowel is covered with dense fibrotic tissue (*red arrow*)

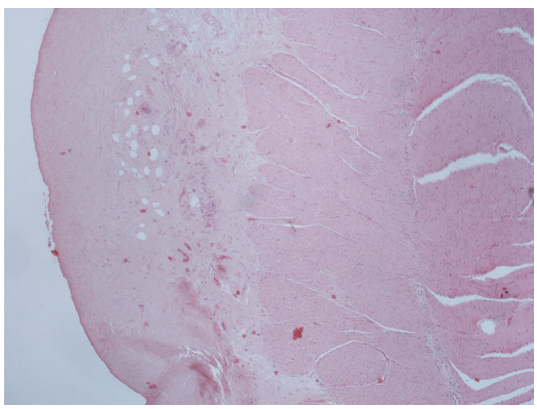

Fig. 3 Peritoneal biopsy image: the serosal surface of the intestinal has been transformed into a thick layer of fibrin tissue

pneumoniae, and *Enterobacter cloacae* infection and he was treated according to the antibiogram results. Twenty days later, a third re-laparotomy was necessitated due to the establishment of tertiary peritonitis. Continuous peritoneal lavage with normal saline solution was installed and the patient showed a steady improvement with regards to clinical condition and inflammation markers. Six months after the onset of EPS, the patient was discharged from hospital with no signs of peritonitis or any other systematic infection. Renal function remained satisfactory [sCr 1.0 mg/dl (88.4 mmol/L), eGFR 86 ml/min/1.73 m^2], despite the diminution of immunosuppression.

Discussion

Despite the use of non-invasive methods (prolonged total parenteral nutrition) in the management of EPS, approximately 50 % of patients eventually require surgery [3]. Surgical management in such patients is technically demanding. Enterolysis as well as stripping of the fibrous cocoon whenever possible are indicated [3]. These procedures are proved to be safe and effective when performed in an experienced center, with low mortality rates [3], even though mortality as high as 40 % has been reported in some series after enterolysis [9]. It is important that surgical intervention should be performed before the patient develops severe malnutrition, which increases post-operative morbidity and mortality [10]. Patients with EPS who develop surgical complications have an overall mortality rate close to 60 % [10]. This mortality could be much higher in renal transplanted patients due to the co-existing immunological compromise.

The above poor results of surgical management have concentrated efforts on the prevention and medical treatment of EPS. Time on PD therapy, prevention/optimal treatment of peritonitis, and discontinuation of modality are considered to be essential for EPS. Even though removal of the peritoneal catheter and cessation of PD at the onset of EPS are recommended [5], existing evidence showed possible worsening of the disorder after PD cessation [8]. Peritoneal lavage with various solutions has been used, although there is no sufficient evidence of this [11]. It has been shown to be effective in the mechanical prevention of peritoneal adhesions and the removal of inflammatory substances or fibrin from the peritoneal cavity and Yamamoto et al. [12] concluded that lavage is effective in reducing the incidence of EPS after PD withdrawal. Tamoxifen, a non-steroidal, anti-estrogenic drug with antifibrotic properties, has been used for almost a decade in EPS treatment [13]. Case series describing the use of tamoxifen alone or in combination with corticosteroids have demonstrated some efficacy in the management of post-transplant EPS patients [14]. Recent data suggest that the use of tamoxifen is associated with lower mortality rates [15].

Some reports support the recovery of gastrointestinal function in patients with EPS after successful renal transplantation, suggesting that this condition may improve because of the anti-inflammatory effects of immunosuppression or the reversal of the uremic state [16]. Immunosuppressive regimes for EPS therapy have been discussed for more than 15 years. Experimental animal studies along with case reports suggest that high doses of corticosteroids may have therapeutic value in the management of EPS, especially during its initial inflammatory stage [17]. A series of three cases reported the successful treatment of EPS by using a combination of steroids and mycophenolate mofetil (MMF) [18]. The mammalian target of rapamycin (mTOR) inhibitors are suggested to have therapeutic value in the management of EPS according to studies from animal models, while data from case reports do not seem to confirm these experimental findings [14, 19, 20]. It is obvious that all the above therapeutic approaches lack high-level supportive evidence and, thus, can be only recommended with reservation.

Although still rare, recently, an increasing number of reports on EPS cases manifesting after renal transplantation [20, 21] suggest that transplantation might compromise the "second hit" in the development of EPS. From the existing literature, two different courses of EPS can be distinguished. Firstly, the common chronic and more insidious course and, secondly, the course of EPS in the immediate post-transplantation period—between one and several months—characterized by an acute onset suggesting that transplantation-related factors could be implicated in the initiation or deterioration of EPS. In addition to the termination of PD, factors specific to kidney transplantation could be incriminated, such as particular immunosuppressive agents. There are findings showing that CNIs, cyclosporine, and, to a greater degree, tacrolimus have profibrotic properties [22]. Furthermore, the rapid reduction of corticosteroids, due to the use of other immunosuppressive agents, after transplantation may contribute to the establishment of post-transplant EPS [16] and it is suggested that this practice should not be rigorously pursued in PD patients [8].

Taking into consideration that mentioned above, it becomes obvious the arising problem regarding PD patients waiting for a kidney transplant, especially in countries where the PD modality is considerably utilized and, moreover, the mean time on the deceased transplant list is, unfortunately, prolonged. In this situation, PD patients awaiting transplantation should be appropriately screened for EPS with an abdominal CT scan. Transfer from PD to hemodialysis should be under serious consideration in

patients eligible for kidney transplantation as soon as indications of ultrafiltration failure or CT findings indicating incipient EPS are present or, even more strictly, after a period of 3–5 years on PD. A serious dilemma presents when symptomatic EPS manifests while the patient is awaiting transplantation; should this be a contraindication to transplantation? There is no straight answer, but someone could argue that it would be better if the patient be excluded temporarily from the list, transferred from PD to hemodialysis, put under treatment with tamoxifen and/or immunosuppression, and placed under close follow-up until there are signs of amelioration. In that case, the patient could be enrolled anew to the transplant list.

Despite the advances in the understanding of EPS over the past several decades, the field remains obscure. Many limitations in our knowledge on the detection, pathophysiology, and treatment of EPS still exist. To this cause, an EPS registry bank has been established [23]. Such a network will hopefully permit a better understanding of the effects of the treatment and may develop new preventive and therapeutic strategies. Until then, offering a renal transplant to a long-term PD patient constitutes a high-risk procedure and all cases of post-transplant surgically complicated EPS will remain highly challenging with unacceptably high mortality rates.

Conflict of interest All the authors have declared no competing interest.

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