Encapsulating Peritoneal Sclerosis in a Kidney Graft Recipient Unmasked by Everolimus Switch

Encapsulating peritoneal sclerosis (EPS) is a serious complication of peritoneal dialysis (PD), associated with high morbidity and mortality (30 – 57%) (1). The incidence of EPS is variable (0.3 – 17.2%) and increases with the duration of PD

therapy (1). Peritonitis and bioincompatible dialysis solutions are associated with EPS (1). However, the role of immunosuppressive drugs in post-transplant EPS pathogenesis remains unclear (2).

CASE DESCRIPTION

A 21-year-old woman underwent continuous ambulatory PD in September 1991 (end-stage membranoproliferative glomerulonephritis type 2). Five years later, she received a renal graft, but she resumed PD due to recurrence of the primary disease (June 1997). In 2000, we started continuous cyclic PD 15 L (Dianeal DP4). In 2005, we switched to Physioneal (2.27% glucose) and added Extraneal (Baxter Healthcare Corporation, Deerfield, IL, USA). During 14 years of PD therapy, we documented 8 bacterial peritonitis episodes. In 2007, a second renal transplantation was successful on mycophenolate mofetil (MMF), methylprednisolone (MPD), thymoglobulin, and tacrolimus (TRL). Two years later, faced with TRL nephrotoxicity, we started everolimus (EVL), and 3 months after this switch, she began to complain about abdominal pain, vomiting, and weight loss. In March 2010, laboratory tests showed increased levels of serum C-reactive protein (17 mg/dL; $N < 1.0$), serum creatinine (1.3 mg/dL; $1.3 \times N$), and anemia (hemoglobin level 9.5 g/dL, $N 13 - 15$). Microbiological analyses (blood, urine, ascites) were negative. Abdominal computed tomography demonstrated ascites, several peritoneal calcifications, and thickening (Figure 1a). Diffusion-weighted magnetic resonance imaging (DW-MRI) showed diffuse hypointense areas in the parietal peritoneum (Figure 1b-c). A peritoneal biopsy confirmed severe submesothelial fibrosis (Figure 1d-e). We decided to replace EVL and azathioprine by TRL and MMF, increase MPD (6 mg daily), and initiate tamoxifen (TXF, 10 mg daily) and enteral nutrition. During the following 4 years, renal graft function remained stable and the patient's general status significantly improved.

DISCUSSION

Post-transplant EPS has been related mostly to cyclosporine use (1,2). We observed a patient with a renal transplant previously on PD who was receiving EVL. In addition to the use of bioincompatible PD solutions, withdrawal of PD, peritonitis, and beta-blockers, our patient presented the most recognized epidemiological risk factors for EPS: young age and long PD duration (1,2). The involvement of EVL in clinical manifestations of EPS in our case is plausible for the following reasons: 1) no clinical evidence of EPS after the first renal transplantation (immunosuppression without EVL); 2) worsening of symptoms rapidly after EVL initiation during the second transplantation; and 3) stabilization of EPS after EVL discontinuation, which is hard to prove as we started MPD-TXF bi-therapy. The use of mammalian target of rapamycin inhibitors (mTORi) in patients at risk for EPS remains controversial (2,3). Antiproliferative effects on vascular smooth muscle cells and anti-inflammatory

Figure 1 — (A) Abdominal CT: peritoneal calcifications (arrows). (B) MRI T2 sequence: ascites and mild contrast enhanced parietal peritoneum. (C) Diffusion weighted - MRI: signal attenuation in the parietal peritoneum (arrows). Peritoneal biopsy (D) control, (E) severe submesothelial fibrosis (EPS patient). Masson Trichrome staining; $\times 200$. CT = computed tomography; MRI = magnetic resonance imaging; EPS = Encapsulating peritoneal sclerosis.

properties of mTORi have been beneficial in rat models of EPS (4). The ascites have been reported in renal transplant recipients after mTORi and were related to the increased vascular permeability (5,6). Our observation demonstrates that 1) currently advised therapy and EVL discontinuation may have been associated with prevention of EPS progression to the occlusive stage; and 2) in addition to "cine" MRI (7), DW-MRI could present a non-nephrotoxic radiological screening for patients at risk of EPS, thereby ensuring early detection and adequate management.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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