

Case Report

Encapsulating peritoneal sclerosis following renal transplantation despite tamoxifen and immunosuppressive therapy

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Abstract

Encapsulating peritoneal sclerosis (EPS) is a rare disease in patients who have undergone peritoneal dialysis (PD). We report a case of EPS following renal transplantation that highlights important clinical issues. Initially, a presumptive diagnosis of EPS was made following surgical and pathological findings at the time of cholecystectomy. CT imaging at this time did not confirm the diagnosis. The patient continued PD and commenced tamoxifen. Prior to and immediately following transplantation, further CT imaging demonstrated no evidence of EPS. Acute bowel obstruction occurred 5 months post-transplantation and a diagnosis of EPS was made both clinically and on CT imaging, despite immunosuppression and tamoxifen. The role of these therapies in managing EPS post-transplant is discussed, in addition to the need for a high index of clinical suspicion to make the diagnosis.

Keywords: EPS; immunosuppression; tamoxifen; transplantation

Background

Encapsulating peritoneal sclerosis (EPS) is a rare and often fatal disease occurring most frequently in patients who have undergone peritoneal dialysis (PD). It is characterized by progressive intra-abdominal fibrosis resulting in compromised bowel motility and function. Diagnosis is based upon clinical suspicion in combination with CT imaging and surgical findings [1,2]. In addition to surgery and enteric rest, anecdotal case reports have suggested that tamoxifen and immunosuppressive therapy might be useful.

Recently, there have been reports of EPS occurring post-transplantation [3,4]. Here we report a case of EPS in a renal transplant recipient, despite treatment with tamoxifen and immunosuppression. This questions the role of these therapies

in preventing or treating this increasingly recognized condition.

Case

A 60-year-old Indo-Asian male underwent CAPD as a therapy for ESRF of unknown cause, from May 1994 to Feb. 2006, when he was switched to APD. In 1998, he had an uncomplicated episode of culture negative peritonitis treated with two doses of IP vancomycin 1 g/week and netilmycin 50 mg IP daily for 1 week. Two years later, cholecystitis was diagnosed and a cholecystectomy was performed. During surgery, omental adhesions were noted and a peritoneal biopsy revealed marked peritoneal thickening and fibrosis, which suggested a diagnosis of early encapsulating peritoneal sclerosis (EPS). An abdominal CT scan did not, however, demonstrate features of EPS. He was temporarily switched to haemodialysis post-operatively. Following his recovery, CAPD was resumed for lifestyle reasons and tamoxifen 20 mg OD commenced. Serial peritoneal equilibration test (PET) results demonstrated progression from high average to high transporter status suggesting ongoing membrane changes. His PD prescriptions were a PD4 1.36% glucose solution, up until his transporter status changed. Prior to transplantation, he was using a 3.86% glucose solution.

For several months prior to receiving a renal transplant, he was noted to have intermittent abdominal bloating, anorexia and diarrhoea. A diagnosis of irritable bowel syndrome was made following referral to a gastroenterologist. Immediately pre-transplantation, he was asymptomatic, with a weight of 58.5 kg. Three further abdominal CT examinations did not show any features suggestive of EPS.

He received a 1:1:1 mismatched cadaveric kidney transplant placed extra-peritoneally in May 2006. The graft functioned immediately and his serum creatinine fell to a baseline of 60–80 $\mu\text{mol/L}$. Induction immunosuppression was basiliximab and methylprednisolone with tacrolimus monotherapy as maintenance therapy. Target tacrolimus levels of 10–15 $\mu\text{g/L}$ in the early post-transplant period were achieved. In the following week, he developed abdominal pain, nausea, vomiting and diarrhoea. A PD fluid

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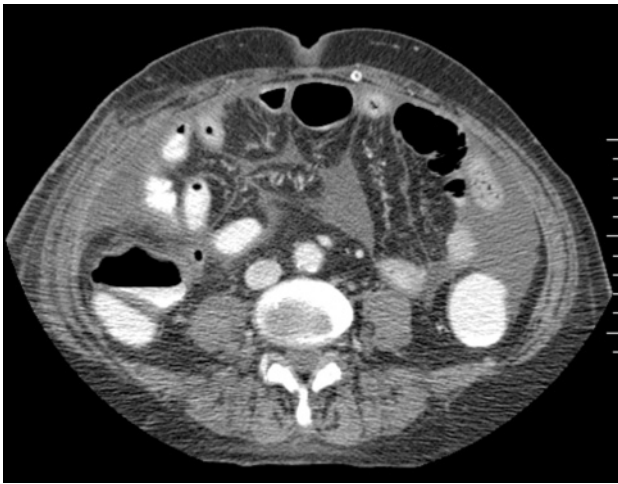


Fig. 1. This section from a CT performed 1 week after transplantation shows no evidence of EPS. There is mild dilatation of small bowel consistent with post-operative ileus.

white cell count was normal. An abdominal CT scan revealed moderate ascites, fluid-filled distended bowel loops and bowel wall oedema (Figure 1). There was no CT evidence of EPS and a diagnosis of post-operative ileus was made. Symptoms persisted and a repeat abdominal CT 1 week later failed to show any changes. Following conservative management and nutritional supplementation, symptoms resolved and he was discharged 3 weeks after transplantation with a serum creatinine of 83 $\mu\text{mol/L}$ and on tamoxifen 10 mg OD. C reactive protein (CRP) prior to discharge was 60 mg/L.

Five months later, the patient complained of increasing abdominal distension and early satiety, and CRP was 64 mg/L. A CT section through the pelvis during IV contrast enhancement at this time demonstrated a loop of dilated small bowel and peritoneal thickening in the left iliac fossa (Figure 2). A diagnosis of EPS with sub-acute bowel obstruction was made, and the patient was listed for an elective peritonectomy and adhesiolysis.

On admission, he weighed 49 kg and complained of anorexia, vomiting and diarrhoea with intermittent colicky abdominal pain. At surgery, the peritoneal membrane appeared brown and grossly thickened, with partial cocooning of the small intestine. The peritoneum was excised and TPN was administered for 2 weeks until line sepsis prompted cessation. At this stage, the patient was tolerating oral nutrition. One month later, prior to his discharge, a barium follow through showed several adhesions with no obvious strictures or obstruction and a normal bowel transit time. Despite his peritonectomy and continuing tamoxifen treatment, symptoms continued with early satiety, regular vomiting and weight loss to 44 kg. A repeat peritonectomy was performed 6 months later. CRP at this time was 16 mg/L. At surgery, the bowel was again immobilized by a fibrous cocoon, with no visible peristalsis. On mobilizing the small bowel from the duodenojejunal to the ileocaecal flexure, peristalsis was seen. Prednisolone was commenced at a dose of 10 mg/day. Currently, his symptoms are markedly improved with infrequent vomiting and achievement of a normal diet and a stable weight.



Fig. 2. Five months following transplantation: a CT section through the pelvis during IV contrast enhancement demonstrating the grafted kidney in the right iliac fossa with a loop of dilated small bowel present. There is an area of peritoneal thickening present in the left iliac fossa.

Discussion

This case report highlights some important clinical issues regarding diagnosis, treatment and management of EPS. Firstly, a diagnosis of EPS was made following the surgical and pathological findings of adhesions and peritoneal fibrosis with inflammation at the time of his cholecystectomy. CT imaging done at this time and subsequently prior to his renal transplant did not demonstrate any evidence of EPS. Thus, it is unclear whether these findings represent early EPS or peritoneal sclerosis in a PD patient, with adhesions secondary to cholecystitis. Furthermore, this case also questions the value of CT as a screening tool. On re-reviewing the CT images from the early post-transplant period in light of his subsequent history, the pictures are those of a post-operative ileus.

Despite medical advice, this gentleman chose to remain on PD for lifestyle reasons and started tamoxifen treatment in the hope of preventing further deterioration of his peritoneal membrane. Tamoxifen has been proposed in several case reports and small case series as a potential therapeutic and prophylactic agent in the management of EPS [5–7]. The rationale for its use has come from its role in other conditions such as retro-peritoneal fibrosis [8]. This treatment continued pre- and post-transplantation but failed to prevent disease progression and the ensuing sub-acute bowel obstruction. It is possible that tamoxifen did afford protection or slow disease progression until an unidentified trigger, at the time of transplantation, led to rapid EPS progression.

The role of immunosuppression in the management of EPS is further questioned by this case. Agents such as cyclosporine, steroids, azathioprine and mycophenolate have been suggested as potential treatments [9]. There are also anecdotal reports suggesting that transplantation may result in remission of EPS [10,11]. We have shown previously that mycophenolate mofetil can certainly cause diagnostic confusion [3] due to its side-effect profile. We are currently attempting to address the role of immunosuppression using the UK EPS Registry [12]. It is also interesting to note that

there was a recurrence of bowel obstruction 6 months after the initial peritonectomy during which time the patient was also receiving tamoxifen and immunosuppression.

Finally, the importance of a high index of clinical suspicion is highlighted by his diagnosis with irritable bowel syndrome prior to transplant. There is a marked overlap in symptoms between these two conditions, which may lead to diagnostic confusion for specialists unfamiliar with the disease. It is possible, despite normal CT examinations, that these symptoms heralded disease progression. Thus, familiarity with EPS and the need for a high index of clinical suspicion are important determinants in making the diagnosis, and this is an important lesson from this case.

In conclusion, this report questions the role of both tamoxifen and serial CT imaging in the management of patients either at risk of or with early stages of EPS.

Conflict of interest statement. None declared.

References

1. Kawanishi H, Moriishi M. Epidemiology of encapsulating peritoneal sclerosis in Japan. *Perit Dial Int* 2005; 25(Suppl 4): S14–S18
2. Summers AM, Clancy MJ, Syed F *et al.* Single-center experience of encapsulating peritoneal sclerosis in patients on peritoneal dialysis for end-stage renal failure 1. *Kidney Int* 2005; 68: 2381–2388
3. de Freitas D, Jordaan A, Brenchley PEC *et al.* Encapsulating peritoneal sclerosis (EPS) following renal transplantation. *Perit Dial Int* 2006; 26(Suppl 2): S116
4. Fieren MW, Betjes MG, Korte MR *et al.* Posttransplant encapsulating peritoneal sclerosis: a worrying new trend? *Perit Dial Int* 2007; 27: 619–624
5. Allaria PM, Giangrande A, Gandini E *et al.* Continuous ambulatory peritoneal dialysis and sclerosing encapsulating peritonitis: tamoxifen as a new therapeutic agent? *J Nephrol* 1999; 12: 395–397
6. del PG, Bajo MA, Gil F *et al.* Clinical experience with tamoxifen in peritoneal fibrosing syndromes. *Adv Perit Dial* 2003; 19: 32–35
7. Moustafellos P, Hadjianastassiou V, Roy D *et al.* Tamoxifen therapy in encapsulating sclerosing peritonitis in patients after kidney transplantation. *Transplant Proc* 2006; 38: 2913–2914
8. Kinzbrunner B, Ritter S, Domingo J *et al.* Remission of rapidly growing desmoid tumors after tamoxifen therapy. *Cancer* 1983; 52: 2201–2204
9. Junor BJ, McMillan MA. Immunosuppression in sclerosing peritonitis. *Adv Perit Dial* 1993; 9: 187–189
10. Bhandari S. Recovery of gastrointestinal function after renal transplantation in patients with sclerosing peritonitis secondary to continuous ambulatory peritoneal dialysis. *Am J Kidney Dis* 1996; 27: 604
11. Hawley CM, Wall DR, Johnson DW *et al.* Recovery of gastrointestinal function after renal transplantation in a patient with sclerosing peritonitis secondary to continuous ambulatory peritoneal dialysis. *Am J Kidney Dis* 1995; 26: 658–661
12. Summers AM, Brenchley PEC. An international encapsulating peritoneal sclerosis registry and DNA Bank. Why we need one now? *Perit Dial Int* 2006; 26: 559–563

Received for publication: 29.1.08

Accepted in revised form: 14.7.08