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CASE REPORT

Liver transplantation in a patient with encapsulating peritoneal sclerosis

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ABSTRACT

Encapsulating peritoneal sclerosis (EPS) is a poorly understood condition in which excess fibrosis results in an encasement of the small bowel, which can clinically result in obstruction. The condition is thought to be related to the persistent expression of transforming growth factor beta on mesothelial cells causing proliferation of subserosal fibroblasts, massive production of extracellular matrix and loss of mesothelial cells. We report a patient with liver cirrhosis in whom the diagnosis of EPS was made. During laparotomy for liver transplantation the complete peritoneum was found to be thickened, consisting of white sheets; liver transplantation was deferred. Histological examination showed peritoneal sclerosing fibrosis. Immunosuppressive medication was started and a difficult but successful liver transplantation followed. If EPS is diagnosed during laparotomy for organ transplantation, adjusted immunosuppression is preferred as calcineurin inhibitors such as cyclosporin and tacrolimus may accelerate EPS while prednisone and some other drugs may stop progression.

KEYWORDS

Immunosuppressive therapy, proliferation, TGF-β

INTRODUCTION

Encapsulating peritoneal sclerosis (EPS) is a rare cause of small bowel obstruction in which there is encapsulation of the small bowel by a fibrous membrane which can clinically result in obstruction. It occurs in a variety of clinical conditions.[1] We report a case of liver transplantation in a patient with EPS.

CASE REPORT

A 65-year-old male patient was diagnosed with liver cirrhosis associated with a heterozygote α1 antitrypsin deficiency (α1 AT Pi MZ). Liver biopsy showed macronodular cirrhosis with intracytoplasmatic periodic acid schiff (PAS)-positive globules (*figures 1* and *2*). After a variceal bleeding in 2000 he started taking propranolol 80 mg slow-release tablets. The diagnosis of spontaneous bacterial peritonitis (SBP) was never made. Because of progressive liver failure and fatigue, he was put on the waiting list for liver transplantation. In July 2006, a liver graft became available. During laparotomy the complete peritoneum and especially the peritoneum surrounding the liver and hepatoduodenal ligament were found to be thickened, consisting of white sheets as shown in *figure 3*. The results of frozen section biopsies were inconclusive. Since malignancy could not be excluded liver transplantation was deferred. The liver graft was transplanted successfully into another recipient. EPS was diagnosed on histological examination showing peritoneal sclerosing fibrosis (*figure 4*). Preoperative and postoperative computed tomography (CT) and ultrasound of the abdomen showed a small cirrhotic liver with portal hypertension and ascites, but no other abnormalities. In November 2006 we started prednisone, azathioprine and tamoxifen. Only seven days after starting this medical therapy a donor liver became available. During transplantation, no differences with respect to the thickened peritoneum were seen, compared with the first laparotomy. Due to extensive fibrosis an *en-bloc* resection of the liver and partial diaphragm took place with above average blood loss. After a prolonged postoperative period the patient could be discharged in a good condition. No cyclosporin or tacrolimus were given. His current medication consists of mycofenolate mofetil and prednisone.

Figure 1. *Liver biopsy showing macronodular cirrhosis with intracytoplasmatic periodic acid schiff-positive globules (100 x)*

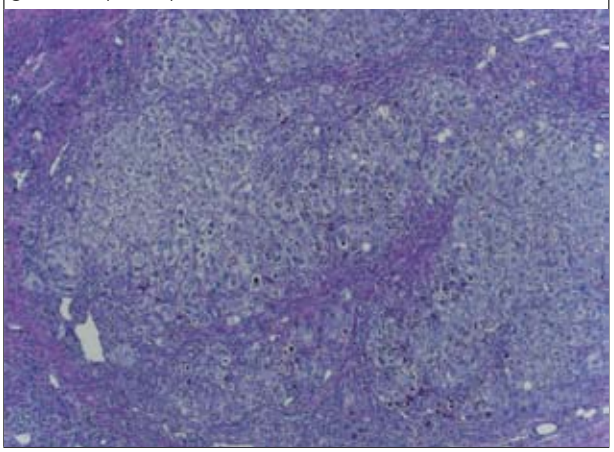


Figure 2. *Liver biopsy showing numerous intracytoplasmatic periodic acid schiff-positive globules consistent with (partial) α1 antitrypsin deficiency (400 x)*

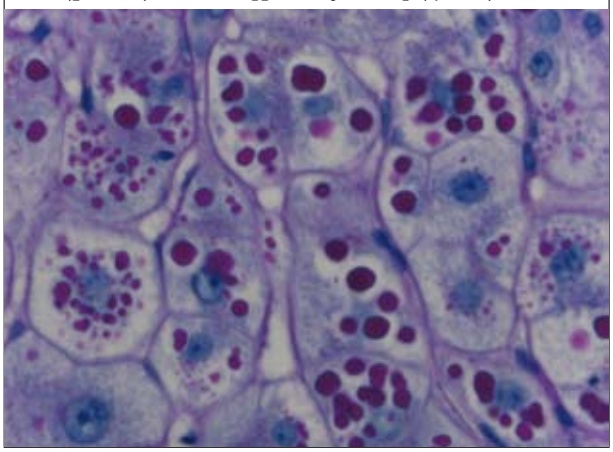


Figure 3. *Thickened peritoneum found during laparotomy*

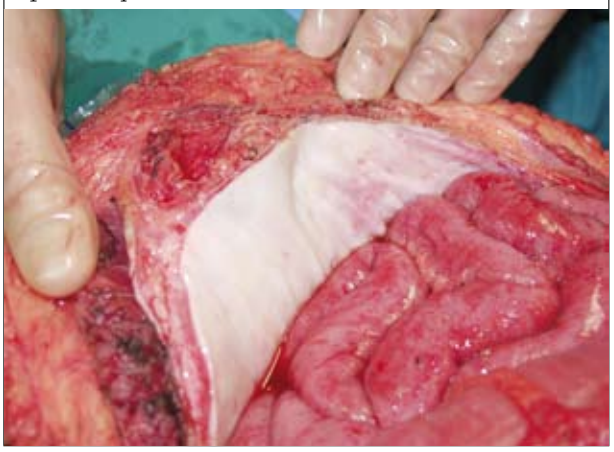
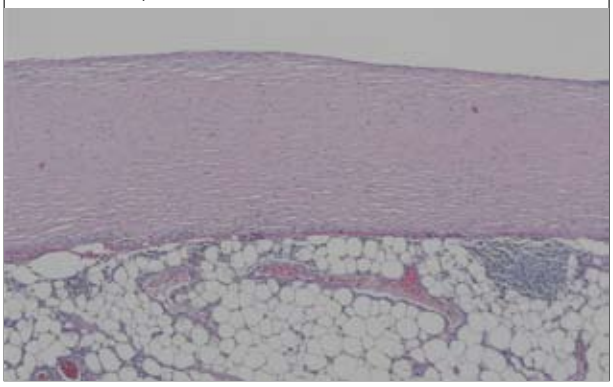


Figure 4. *Thickened peritoneum with proliferation of fibroblasts, deposition of collageneous extracellular matrix and loss of mesothelial cells (Haematoxylin Eosin, 100 x)*



DISCUSSION

EPS is a poorly understood condition in which excess fibrosis results in an encasement of the small bowel, which can clinically result in obstruction. The condition is thought to be related to the persistent expression of transforming growth factor beta (TGF-β) on mesothelial cells.[2,3] Patients with EPS presenting with symptoms have signs of bowel obstruction including abdominal pain, anorexia, nausea and weight loss.[1] However, the condition does not generally cause symptoms, as in the present case. In our patient, this might be explained by the fact that the visceral peritoneum covering the gut was relatively spared from fibrosis. In the work-up for liver transplantation, EPS was not detected on radiological examinations including ultrasound and CT. In patients with EPS, abdominal ultrasound and CT may show increased peristalsis and small bowel dilatation as well as thickened adherent bowel loops.[4] The histological changes consist of diffuse loss of mesothelial cells, proliferation of subserosal fibroblasts and massive production of extracellular matrix (ECM).

EPS is described in the context of chronic ambulatory peritoneal dialysis (CAPD), recurrent peritonitis, the use of β-adrenergic blockers and ventriculoperitoneal shunting.[2,3]
Prevalence estimates of EPS in CAPD patients range from 0.54 to 7.3%.[1] It is related to time on dialysis and may be related to the nonphysiological composition of dialysis solutions as well as the direct action of glucose and glucose degradation products.[5]
In patients with liver cirrhosis, EPS is extremely rare. There might be a relation to the occurrence of SBP. Recently two patients with liver cirrhosis and EPS after recurrent peritonitis were reported. In one of them, liver transplantation was halted because of EPS.[6]

In the late 1970s a relation between EPS and the use of practolol, a β-adrenergic blocker, was reported. Practolol was withdrawn after recognition of its toxic effects on skin, eyes, ears, peritoneum, and lungs.[7] The exact pathogenesis remained unknown. A role for β-adrenergic blockers other than practolol in EPS is less likely considering that only a few cases have been reported.[8]

Ascites flow through a peritoneal venous shunt (PVS) and fibrin deposition in the peritoneum may lead to chronic inflammation and cause EPS in patients with liver cirrhosis. A recent case report described a patient who underwent PVS drainage for treating refractory ascites. During surgery for liver transplantation, EPS was diagnosed. Two weeks after liver transplantation emergency surgery was necessary for small bowel obstruction caused by EPS.[9]

The pathogenesis of EPS in the patient we describe here remains unknown. A relation with his underlying disease (α1 AT Pi MZ) cannot be ruled out. On the other hand this is the first case of EPS reported in the many patients with α1 antitrypsin deficiency who underwent liver transplantation. In the past, the diagnosis of SBP had not been made in our patient. One could speculate on a genetic predisposition, e.g. polymorphism of fibroblast activity, possibly triggered or aggravated by the long duration treatment with propranolol.

To our knowledge only one case report has described a patient with EPS not before but following liver transplantation. This patient had been on tacrolimus since the liver transplantation and presented with EPS nine months later.[10] Calcineurin inhibitors such as cyclosporin and tacrolimus may activate TGF-β, induce fibrinogenesis and accelerate EPS. Therefore they should probably be avoided.[11]

Several studies in CAPD patients with EPS describe the successful treatment with immunosuppressive therapy (i.e. prednisone and azathioprine).[12] Also, treatment with tamoxifen might be helpful.[13] Tamoxifen has been successfully used in the treatment of retroperitoneal fibrosis. It may alter the balance of growth factors in such a way that fibroblast proliferation is inhibited. The exact mechanism is, however, not yet understood.[14] Whether our patient benefited from the combined immunosuppressive therapy and tamoxifen started after the first laparotomy was not obvious during the second laparotomy for liver transplantation; however, treatment had started only one week before.

Based on 32 cases of surgically treated patients with EPS, recommendations were made when EPS is found during laparotomy. These included that if the membrane is easily cleavable, it should be removed as completely as possible; however when enterolysis is difficult, extreme caution must be exercised not to perforate the intestine. If EPS is discovered as an incidental finding, surgical treatment is not indicated.[15]

CONCLUSION

EPS is a not well understood condition involving TGF-β, which does not generally cause symptoms. This may result in difficult decision-making at times of surgery as described in the present case. In asymptomatic patients, immunosuppressive therapy with prednisolone and azathioprine seems the treatment of choice. After liver transplantation an adjusted immunosuppressive regimen seems preferable.

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