Post-transplantation encapsulating peritoneal sclerosis in a young child

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Abstract

Encapsulating peritoneal sclerosis (EPS) is a very rare condition in children. Nevertheless, EPS should be considered when a child with a history of peritoneal dialysis (PD) presents with signs of bowel obstruction. We describe a child with post-transplantation EPS and discuss risk factors, diagnosis and treatment options. CT scan should be performed promptly to confirm the diagnosis. Treatment consists of cessation of the PD, if applicable, and adequate nutrition, either parenteral or enteral. Further medical therapy remains controversial but may involve steroids and/or interruption of calcineurin inhibitors.

Keywords: child; peritoneal dialysis; intestinal obstruction; kidney transplantation

Background

Encapsulating peritoneal sclerosis (EPS) is a serious complication of long-term peritoneal dialysis (PD) characterized by intestinal obstruction and radiological or macroscopic evidence of fibrotic thickening of bowel wall or peritoneum [1–10]. Risk factors for EPS include prolonged PD, recurrent peritonitis, decreased ultrafiltration and prolonged administration of hypertonic glucose or acetate-based dialysis solutions [1–9]. Reported prevalences in adults range from 0.7 to 7.3% [3, 6–10]. Reports on EPS in children are rare [1–5]. EPS may either arise during treatment with PD or after switch to haemodialysis. Post-transplantation EPS occurs in increasing frequency in adults [9] but, to our knowledge, has not been reported in children.

PD-related paediatric case reports are mainly from Japan [1–5]. In Japan, PD treatment often is prolonged due to the scarcity of deceased kidney donors. The Japanese paediatric PD registry revealed an EPS prevalence of 1.6% (11 of the 687 children), all of them while on PD. PD was started at a mean age of 9.7 +/− 3.6 years; EPS was diagnosed after a mean of 9.6 +/− 3.3 years of PD treatment. The mortality rate was 27% (3 of 11 children) versus >50% in adults [1–4, 6].

To alert to the possible occurrence of this disease in the paediatric population, we present a young girl who developed EPS after kidney transplantation.

Case report

A 6-year-old girl with bilateral Wilms' tumour at the age of 10 months, refractory to chemotherapy (vincristine, actinomycin, doxorubicin, topotecan), underwent resection of both kidneys. Nightly intermittent peritoneal dialysis was initiated at the age of 17 months. Peritonitis occurred at the age of 23, 35, 36 months and 5 years, caused by Enterobacter cloacae, Pseudomonas stutzeri, Stenotrophomonas maltophilia and Klebsiella oxytoca, respectively. Ultrafiltration capacity gradually decreased, necessitating the use of high glucose (3.86%) dialysate. At the age of 5.5 years, she underwent living donor kidney transplantation. The graft functioned immediately with a nadir of serum creatinine of 32 μmol/L after 3 days. Immunosuppressive regimen consisted of basiliximab, corticosteroids tapered in 1 week and continuous tacrolimus (TCL) and mycophenolate mofetil (MMF). Two days after removal of the PD catheter, which was 2 weeks after transplantation, she developed abdominal pain, diarrhoea and fever, with ascites detected on ultrasound. Peritonitis was considered and treated. Over the following weeks, however, symptoms deteriorated: severe malaise, vomiting, abdominal pain, fever, constipation and cachexia. The abdomen became distended with ascites, tender and firm with high-pitched sounds. CRP rose to 350 mg/L, kidney function deteriorated (maximal creatinine 116 μmol/L). A graft biopsy revealed normal histology. Meropenem was instigated although repeated ascite punctates remained sterile on bacterial culture, including mycobacterial cultures.

Three months after transplantation, an abdominal X-ray showed bowel obstruction. A CT scan confirmed the assumed diagnosis of EPS by visualizing a thickened peritoneum and colon wall, loculation of ascitic fluid and tethering of the bowel without calcifications (Figure 1). A biopsy of the peritoneum revealed sclerosing connective tissue with chronic active inflammation without granulomas (Figure 2). At that time, Pseudomonas aeruginosa was isolated from ascites obtained at laparoscopy and was treated with tobramycin and meropenem. But only when therapy with prednisolon 2 mg/kg/day was started, clinical improvement was observed, CRP normalized and serum creatinine level dropped to 40 μmol/L. Because of its profibrotic action, TCL was replaced by everolimus. Parenteral feeding was initiated because of persistent...
vomiting and ongoing intestinal obstruction. Enteral feeding by nasogastric tube could be restarted after several weeks and lasted until she was able to eat again. One year after transplantation, she is a normal active child, eats small portions and is gradually gaining weight and height. Immunosuppressive therapy consists of low-dose prednisolon, everolimus and MMF. Laxatives and regular enemas are needed for defecation.

Discussion

This is the first case report describing EPS in a young child shortly after kidney transplantation. The classical history, in analogue to reports of post-transplant EPS in adults, included prolonged PD, recurrent peritonitis and ultrafiltration failure necessitating the use of 3.86% glucose dialysate. The onset of EPS is predicted by peritonitis caused by *Pseudomonas aeruginosa*, *Staphylococcus aureus* and fungi [2, 3] and by PD treatment >5 years and by impaired peritoneal ultrafiltration [1–9]. In adults, kidney transplantation more and more seems to be a risk factor for developing EPS. This runs in parallel with the increased use of the profibrotic calcineurin inhibitors (tacrolimus and cyclosporine), in combination with a decreased use of corticosteroids [6, 9, 10].

Ten weeks passed between the onset of symptoms and the diagnosis. Retrospectively, we should have been alerted by the appearance of ascites as an early EPS symptom [6]. Complementary investigations and the clinical response to the change to immunosuppressive therapy confirmed the diagnosis of EPS, instead of bacterial or tuberculosis peritonitis. Central in the presentation of EPS is intestinal obstruction and active inflammation. [9]. In our patient, obstruction resolved, however, constipation remained, suggesting that intestinal transit is still impaired, probably due to adhesions of the intestines due to fibrosis.

The rise in creatinine is probably explained by the high inflammatory state of EPS and its nephrotoxic impact on the transplantation kidney.

Pathophysiology

The pathophysiology of EPS is still unknown. The profibrotic cytokine Transforming Growth Factor (TGF)-β seems to have a role in the formation of peritoneal fibrosis [6, 9, 10]. The second hit theory of Kawanishi is widely accepted. The first hit is disruption of normal peritoneal and mesothelial physiology, caused by long PD treatment. The second hit could be one of the above-mentioned risk factors such as peritonitis or discontinuation of PD treatment or a genetic predisposition [9]. In our case, the transplantation could be the trigger (second hit) of development of EPS. We could not find any signs of inflammation or obstruction of the intestine during PD. Nevertheless, there is only a short period of time after transplantation suggesting that the process has been simmering (first hit).

Diagnosis

A CT scan confirms the diagnosis by visualizing peritoneal and bowel wall thickening, loculation of fluid collections, tethering of the small bowel, bowel dilatation or peritoneal calcifications [7, 8]. A biopsy is not necessary but can support the diagnosis [1–4].

Treatment

Therapeutic options are limited. The cornerstone of the treatment is adequate food intake, either parenteral or enteral. Immunosuppressive prednisolone is the basis of the first active inflammation stage [1–10]. In the adult literature, tamoxifen has been described as an immune-modulating activity of TGF-β in EPS. Tamoxifen treatment of EPS is associated with reduced mortality in adults but its use may not be without
risks in children, e.g. on strokes, thrombosis and malignancy [10]. Discontinuation of tacrolimus should be considered since tacrolimus promotes TGF-β production [9]. Surgical adhesiolysis in this active inflammatory phase carries the risk of bowel perforation while removing the fibrotic sheet. Although this treatment in adults is promising in the hands of experienced surgeons, the reoperation risk remains high (25.4%) [6]. In adults, Kawanishi et al. [6] reported a lower mortality rate of 6.9% after surgery and adaptation of immunosuppression. Once in the secondary chronic fibrotic end stage, peritonectomy might be only possibility.

Conclusion

EPS is a rare disorder in children associated with high mortality. EPS should be considered in children with abdominal complaints who have been treated with PD for a prolonged time, even if they recently have switched to haemodialysis or a kidney transplantation. An abdominal CT scan should be made without delay. PD should be stopped, adequate food intake must be provided as soon as possible and immuno-suppressive therapy should be adapted.

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References


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