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【 CASE REPORT 】

Encapsulating Peritoneal Sclerosis in a Patient Receiving Peritoneal Dialysis and Glucocorticoid Therapy

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Abstract:
Encapsulating peritoneal sclerosis (EPS) is a fatal complication of peritoneal dialysis. A 68-year-old man undergoing peritoneal dialysis for 10 years started receiving daily 50 mg of glucocorticoids for idiopathic pulmonary sclerosis. At the transition to hemodialysis, a peritoneal biopsy was performed, which demonstrated mild histological changes, including no fibrin formation and mild T lymphocyte infiltration at the time of 6.5 mg glucocorticoids. However, five months later, he developed EPS when receiving 2.5 mg glucocorticoids. Afterward, over 5 mg daily glucocorticoids were required to avoid the recurrence of EPS. These findings suggest that glucocorticoids may conceal peritoneal inflammation, a main contributor to EPS.

Key words: encapsulating peritoneal sclerosis, peritoneal dialysis, prednisone, duodenal stenosis, end-stage renal disease

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Introduction

Encapsulating peritoneal sclerosis (EPS) is the most severe complication of peritoneal dialysis (PD). Previous attempts to reduce the incidence of EPS have included utilizing neutral peritoneal fluid and avoiding glucose-rich fluid (1). However, the duration of PD is still associated with the occurrence of EPS (2).

The mortality rate among patients with EPS is approximately 25-74%, depending on the severity of the disease (1, 3). EPS is characterized by intraperitoneal inflammation and fibrosis, which results in bowel loop encasement and obstruction (4). It is diagnosed based on clinical symptoms, including intestinal obstruction and an altered gastrointestinal function, as well as radiologic or pathologic evidence of bowel encapsulation. It typically occurs a few years after the termination of PD therapy. A pathological evaluation of the peritoneum, obtained during PD catheter removal, aids in predicting EPS development (5). The representative morphological changes in the peritoneum among patients with EPS are denudation of mesothelial cells, sclerotic changes in submesothelial connective tissues, vasculopathy, angiogenesis, and new membrane formation (6).

Elderly patients are susceptible to multiple chronic comorbidities, including autoimmune diseases and chronic lung injury. Thus, the use of glucocorticoids has been increasing in frequency as Japan becomes an aging society. Glucocorticoids are reportedly effective in suppressing inflammation in targeted organs but also affect nontargeted tissues. Thus, partial peritoneal damage may be alleviated with glucocorticoids, and the degree of peritoneal damage may be underestimated in PD patients undergoing glucocorticoid treatment.

We herein report the clinical course of a PD patient undergoing glucocorticoid treatment for idiopathic pulmonary sclerosis. Five months after having a peritoneal biopsy, which showed mild morphological changes, the patient developed EPS. Thus, we demonstrated the possibility that glucocorticoids may conceal peritoneal inflammation, one of the major contributors to EPS, which can make it difficult to predict the occurrence of EPS by a peritoneal biopsy in patients taking glucocorticoids.

Case Report

A 68-year-old man undergoing PD presented with progressive abdominal pain, severe constipation, nausea, and

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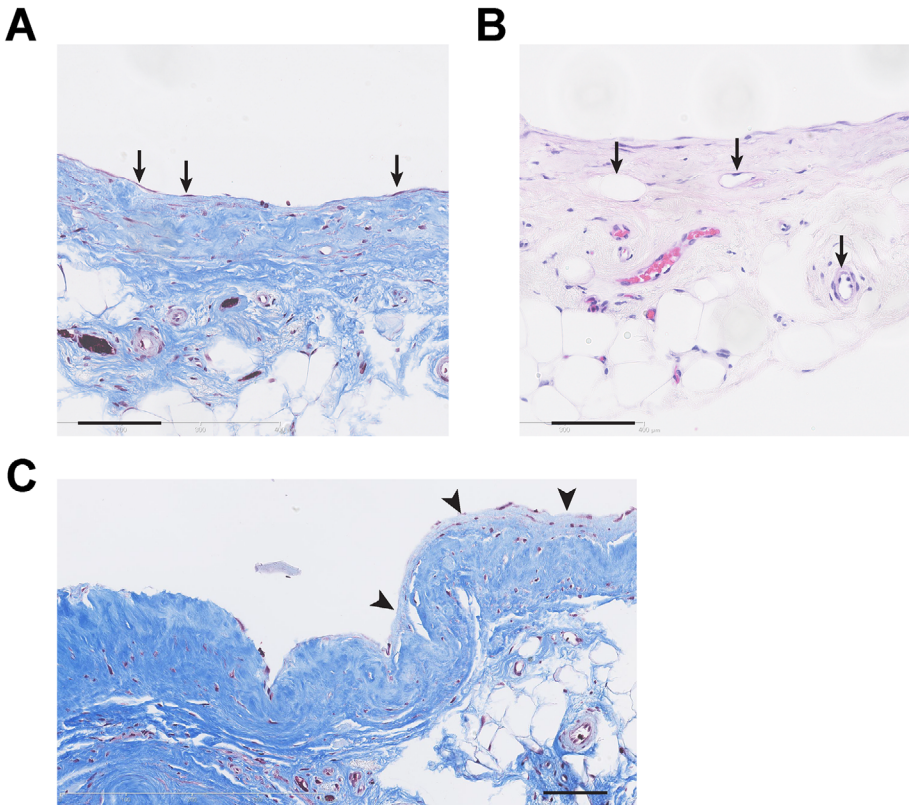

Figure 1. Histological findings of the peritoneal biopsy in the present case. (A) No findings of swelling or proliferation of mesothelial cells on the peritoneum were noted in the present case (arrows). Scale bar: 100 μm. (B) Hyalinosis of PCV is seen; however, no narrowing or occlusion of the PCV is observed (arrows). Scale bar: 100 μm. (C) A thinned neoplastic membrane (50 μm) was seen in some areas on the peritoneum (arrowheads). Scale bar: 100 μm. PCV: postcapillary venule

vomiting. An abdominal ultrasound detected massive ascites with no noted neutrophilia or lymphocytosis in the ascitic fluid. Although the count of white blood cells in the blood remained at 4,400-5,400/mL, the proportion of eosinophilia increased to 5.2-6.3% when he began to show EPS-related symptoms. Laboratory tests showed a serum C-reactive protein value of 1.68 mg/dL and a normal serum procalcitonin level. The serum albumin-ascites albumin gap, a diagnostic tool for ascites, was 1.4, which indicated transudative ascites. While a total of 10 cells (1 polynuclear leucocyte and 9 mononuclear cells) were identified in his peritoneal fluid, no eosinophils were observed. In addition, levels of adenosine deaminase, a marker of tuberculosis-related peritonitis, were found to be within the normal range. Bacteria and abnormal cells were not found in the ascitic fluid.

At 58 years old, PD therapy had been initiated for end-stage renal disease due to diabetic nephropathy. The period of using 1.5% dextrose neutral-pH peritoneal dialysis fluid was 42 months and that of 2.5% dextrose neutral-pH peritoneal dialysis fluid was 73 months. In addition, a 10-h dwell of icodextrin solution was performed for 90 months. Kt/V was 1.46-1.68 overall. PD-related bacterial peritonitis and tunnel infection were not observed during the whole PD period. His residual renal function then gradually declined, resulting in poorly controlled fluid retention. Two years later, hemodialysis (HD) was performed weekly in addition to PD. During this time, the patient had no gastrointestinal symptoms, and the peritoneal equilibration test showed a low average. At 68 years old, the patient was diagnosed with idiopathic organic pneumonia. Thus, he was treated with intravenous methylprednisolone pulse therapy and subsequent oral prednisone at an initial dose of 50 mg daily, tapered gradually to 2 mg daily for a year. In December of the same year, the patient started receiving HD and underwent peritoneal lavage for a year. In addition to a too-long period of PD, no excessive ascites fluid was observed during peritoneal lavage, thus enabling the patient to completely transition to HD.

When his PD catheter was removed, he received 6.5 mg daily of glucocorticoids, and peritoneum was collected to evaluate morphological changes and thereby assess the risk of EPS. The biopsy showed mild hyalinizing fibrosis of the submesothelial compact zone, slightly increased vascularity of peritoneal adipose tissues, and partially encapsulated membrane formation. However, the proliferation and swelling of mesothelial cells were not observed (Fig. 1A). In addition, narrowing and occlusion of the intravascular lumen were not found (Fig. 1B). The thinned neoplastic membrane measured approximately 50 μm in diameter (Fig. 1C), and fibrin production was not found. No increase in the number

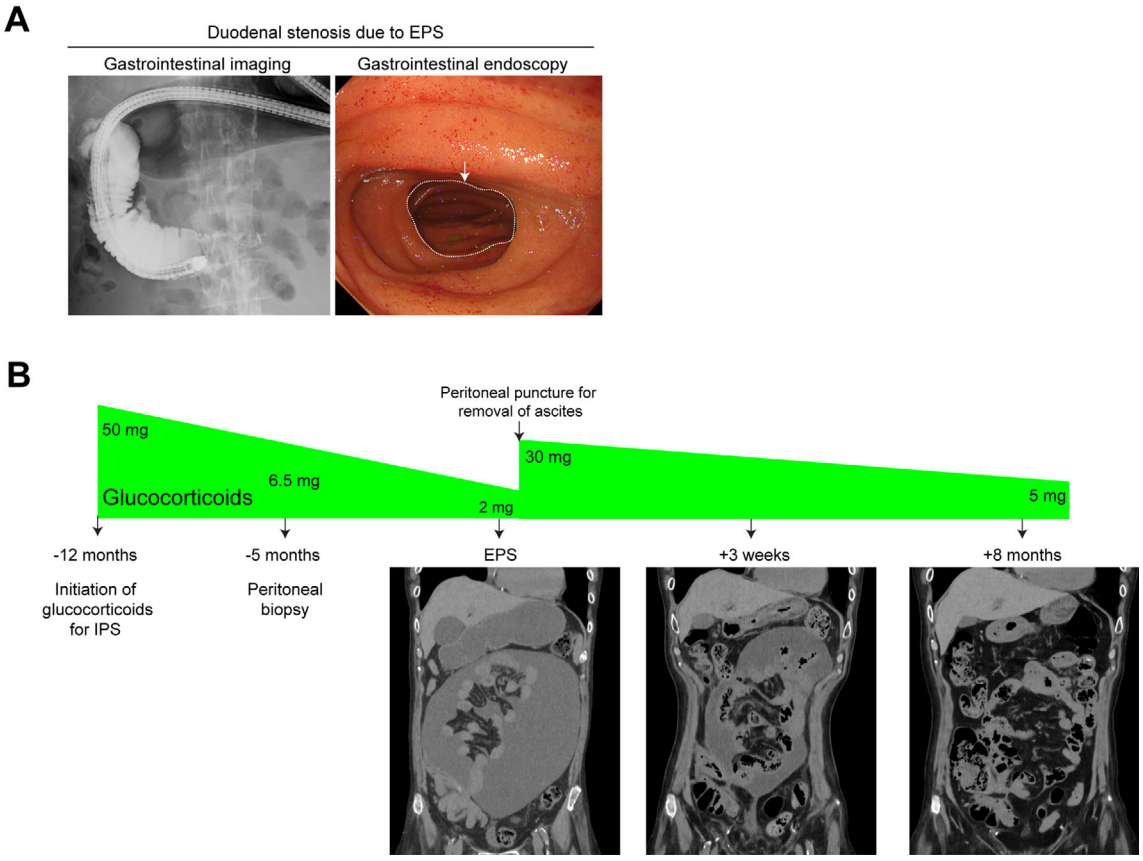

Figure 2. Clinical images of the present case. (A) Representative images of upper gastrointestinal endoscopy for duodenal stenosis in the present case. (B) The clinical course of the present case with the dosages of glucocorticoids before and after the occurrence of EPS and representative images of abdominal computed tomography. IPS: idiopathic pulmonary sclerosis, EPS: encapsulating peritoneal sclerosis

or proportion of eosinophils was observed during the tapering of glucocorticoids.

Although glucocorticoids were tapered to 2 mg daily during the next 5 months, the patient noted ascites symptoms, including abdominal pain, nausea, and vomiting. Computed tomography (CT) showed duodenal stenosis, subsequent gastric dilation, and ascites encapsulated within the bowels (Fig. 2A). Duodenal stenosis was appreciated, and no intestinal tumors were detected through the upper gastrointestinal scope, which enabled us to diagnose the patient with EPS-induced duodenal stenosis.

An ultrasound-guided peritoneal puncture was performed to drain the ascitic fluid, and the dosage of glucocorticoids was increased to 30 mg daily. The ascites was immediately alleviated, and the patient reported improvement in his abdominal symptoms. The serum C-reactive protein concentration also decreased. CT showed improvement of duodenal stenosis (Fig. 2B).

Based on the clinical course, we suspect that the increased pressure within the encapsulated bowel loop compressed the upper gastrointestinal aorta, which narrowed the space between the abdominal aorta and upper gastrointestinal aorta, possibly causing duodenal stenosis. After tapering glucocorticoids, the patient still required over 5 mg daily glucocorticoids to prevent the recurrence of EPS.

Discussion

We herein report the clinical course of a patient presenting with encapsulated ascites, which led to duodenal stenosis, five months after a peritoneal biopsy at PD catheter removal. The current pathophysiological model for EPS risk is based on chronic inflammation and fibrosis within the peritoneum. Thus, glucocorticoids (7), tamoxifen (7, 8), and other immunosuppressants (9, 10) have been used to treat EPS. Although there have been conflicting results concerning the efficacy of immunosuppressants for EPS (11), glucocorticoid treatment substantially improved EPS symptoms in the present patient. In addition, considering that tapering the dosage of glucocorticoids to <5 mg per day resulted in the recurrence of ascites, the inhibition of peritoneal inflammation via glucocorticoids is possibly essential to suppress the onset of EPS.

From this point of view, immunosuppressive therapy may conceal PD-related histological findings, including inflammation, submesothelial cell layer thickening, vasculopathy, arterial occlusion, tissue calcification, and ossification (12). Thus, a peritoneal biopsy in patients undergoing glucocorti-

coid treatment likely underestimates the risk of the future occurrence of EPS. Previous studies revealed that peritoneal fluid inflammatory biomarkers, such as interleukin (IL)-6 (13), tumor necrosis factor-α (TNF-α) (14), monocyte chemoattractant protein-1 (15), and plasminogen activator inhibitor-1 (16), are decreased in patients taking immunosuppressants (17). The peritoneal solute transport rate (PSTR) reflects the degree of peritoneal inflammation (18, 19). Given that EPS is an inflammatory condition (20, 21), the change in PSTR may have the potential to predict the occurrence of EPS. In the present case, the peritoneal equilibration test, performed during the last 4 years before the initiation of glucocorticoid therapy for idiopathic pulmonary sclerosis showed an average 4-h D/P_{ratio} of 0.74±0.03. Following glucocorticoid treatment, it dropped to 0.59 (Fig. 3). This finding suggests that glucocorticoids affected the PSTR, possibly by suppressing angiogenesis and restoring vascular permeability (22). The assessment of sodium sieving by evaluating the reduction rate of sodium from dialysate at 60 minutes has been shown to be another candidate diagnostic tool for EPS development (23). Further investigations are required to confirm the predictive power of sodium sieving for EPS in patients treated with glucocorticoids.

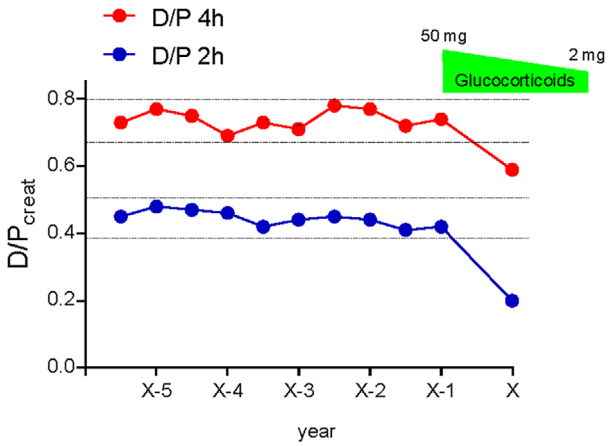

Figure 3. The relationship between the peritoneal solute transport status and glucocorticoids in the present case. PET: peritoneal equilibration test

Glucocorticoids have anti-inflammatory effects, as they suppress T-cell functions, downregulate arachidonic acid cascade-related enzymes, including cyclooxygenase-2 (24) and phospholipase A2 (25), and reduce the production of inflammatory cytokines, such as IL-6, IL-8, TNF-α and interferon-γ. In the present case, the number of $CD3^+$ T cells in the peritoneum was reduced compared to that of a non-EPS patient with a five-year history of PD treatment without glucocorticoid treatment (Fig. 4). Because an increased number of $CD3^+$ T cells was shown to be associated with a high prevalence of EPS in patients with PD (26), it is natural to consider that glucocorticoids and other immunosuppressant agents prevent EPS by inhibiting immune cell infiltration. The peritoneal biopsy results of patients undergoing glucocorticoid treatment should be interpreted carefully, as glucocorticoids interfere with peritoneum conditions, such as inflammation and vasculopathy. It should be noted that evaluation of T lymphocyte infiltration using a parietal peritoneum might be different from that of a visceral peritoneum, which is directly related to EPS. This point is considered one of the limitations in the present study. Further investigations are recommended to determine the minimum effective dosage of long-term glucocorticoids without causing adverse effects and to identify novel histological markers for

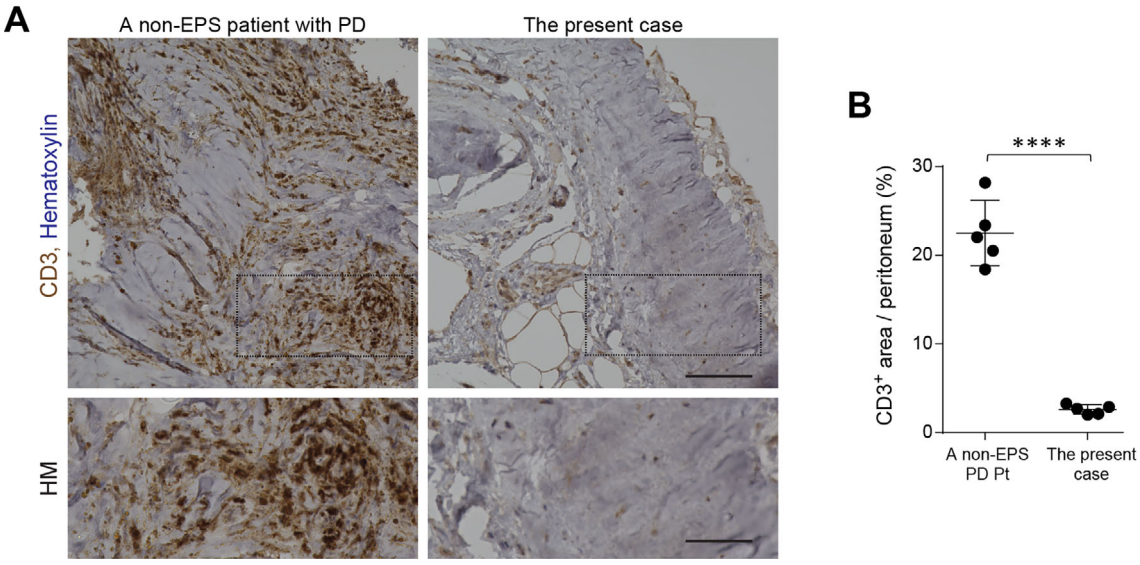

Figure 4. Immune cell infiltration in the peritoneum in the present case and a nonencapsulating peritoneal sclerosis patient with peritoneal dialysis. (A) Representative images of $CD3^+$ T cells in the peritoneum in the present case and a nonencapsulating peritoneal sclerosis patient with peritoneal dialysis. Scale bar: 100 μm. (B) The corresponding quantification of $CD3^+$ area/peritoneum (%) in a nonencapsulating peritoneal sclerosis patient with peritoneal dialysis and the present case.

predicting the development of EPS.

Conclusion

We described the clinical course of an EPS patient receiving glucocorticoid therapy who presented with mild histological peritoneal changes. Since glucocorticoid treatment significantly affected the histologic findings and PSTR results, the risk of EPS in patients receiving glucocorticoids may be underestimated with the current prediction tools. Further investigations are recommended to develop novel options for predicting the development of EPS in this patient population.

Informed consent for publication was obtained from the patient.

The authors state that they have no Conflict of Interest (COI).

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