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Case Report of a Patient Undergoing Peritoneal Dialysis with Encapsulating Peritoneal Sclerosis Superimposed With Calciphylaxis

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Abstract

Introduction: Encapsulating peritoneal sclerosis (EPS) is a rare but devastating complication of peritoneal dialysis (PD). Tamoxifen has been generally well-tolerated, even without randomized controlled trials.
Case Presentation: Herein, we report a case of a patient undergoing 12 years of PD who developed EPS and calciphylaxis simultaneously. We also provide a comprehensive discussion about the association between EPS and calciphylaxis. Moreover, although tamoxifen is used in EPS due to its inhibition of fibroblast-transforming growth factor beta (TGFβ) production, it may worsen the calciphylaxis due to a hypercoagulable state.
Conclusions: We suggest avoiding the use of tamoxifen for EPS in patients with superimposed calciphylaxis.

Keywords: Encapsulating Peritoneal Sclerosis, Tamoxifen, Calciphylaxis

1. Introduction

Encapsulating peritoneal sclerosis (EPS) is a rare but devastating complication of peritoneal dialysis (PD). In this condition, the peritoneum is covered with fibrotic encapsulations, which leads to bowel obstruction (1). The risk factors for EPS include a history of more than 8 years of peritoneal dialysis (PD), repeated peritonitis, and higher concentrations of glucose in the dialysate. Unfortunately, there are no reliable markers for this disease, nor any clear pathogenesis or curative treatments (2). According to Ridvan Yavuz (3), tamoxifen has been generally well-tolerated even without randomized controlled trials. Calciphylaxis is a severe vascular complication in patients with end-stage renal disease (ESRD). One-year survival is reported to be 45% - 80% (4). To the best of our knowledge, the association between EPS and calciphylaxis has not been discussed, nor has the use of tamoxifen in this context. Herein, we report a case of a patient undergoing 12 years of PD, who developed EPS and calciphylaxis simultaneously. We also present an extensive literature review.

2. Case Presentation

Our patient was a 65-year-old man who received PD for 12 years due to a 20-year history of type 2 diabetes mellitus (DM). He was under long-term follow-up at Taichung Veterans General Hospital in Taichung, Taiwan. He had also received type A aortic dissection repair 15 years previously. He presented with poor appetite and a weight loss of 3 kg in 6 months, starting in January 2015. His serum albumin had dropped to 3.2 g/dL. His PD regimen was 1.5%*2L*2 + 2.5%*2L*2 + Icodextrin*2L*1 and the amount of daily ultrafiltration was 1000 ml. Weekly creatinine clearance was 65 L, and Kt/V was 1.6. The result of the peritoneal equilibrium test was at a high-average level. Blood urea nitrogen was 91 U/L and serum creatinine was 13.1 mg/dL. Even while taking three tablets of calcium acetate (667 mg) with each meal, his calcium level was 8.8 mg/dL, phosphate was 7.7 mg/dL, and intact parathyroid hormone was up to 675 pg/mL. He experienced peritonitis three times during the PD period (all cultures grew *Staphylococcus aureus*). Due to no apparent cause for his poor nutrition and poor appetite, we performed abdominal computed tomography (CT) to rule out EPS. Unsurprisingly, CT disclosed diffuse thin calcifications of the serosal surface of the small intestinal loops (arrow, Figure 1C). We reviewed the patient's kidney, ureter, and bladder (KUB) x-ray from three months before the CT, and noted EPS in the wall of small intestine (arrow, Figure 1A). Therefore, EPS was diagnosed by the radiologists due to cachexia, very low serum albumin, low clearance of the peritoneum, and diffuse calcifications of the intestinal serosal surface. Moreover, there was abdominal dissection

with diffuse calciphylaxis (arrowhead in Figure 1A, arrow in Figure 1B), as well as skin ulcers over the lower extremities. For the diffuse calciphylaxis, we changed to sevelamer, two tablets per meal. For the EPS, the PD was changed to hemodialysis with low-calcium dialysate and exchange of 2 L of dialysate every two weeks. We also prescribed prednisolone 30 mg per day and colchicine 1 mg per day. However, questions were raised about the use of tamoxifen for EPS, as this seems to be contraindicated in a patient in a state of calciphylaxis. However, this dilemma has seldom been discussed in the current literature.

Table 1. All variables in the Case

Variable	Result	Unit
Basic characteristic		
Body height	172	cm
Dry weight	69	kg
Blood pressure	149/69	mmHg
Laboratory data		
Albumin	3.2	g/dl
Total protein	5.3	g/dl
White blood cells	5,630	/mm^3
Hemoglobin	11.2	g/dl
Platelets	190,150	/μl
Blood urea nitrogen	91	U/L
Creatinine	13.1	mg/dl
Calcium	8.8	mg/dL
Phosphate	7.7	mg/dL
Intact parathyroid hormone	675	pg/mL
C-reactive protein	2.8	mg/dl
Adequacy of dialysis		
Weekly creatinine clearance	65	L/week
Kt/V	1.6	
Ultrafiltration	1,000	ml

3. Discussion

This patient had many risk factors for EPS, including high-concentration glucose in the dialysate, a long period of PD (8 months), and repeated peritonitis. He also had risk factors for calciphylaxis (4), such as a severely dysregulated calcium-phosphorus metabolism, a 32-year history of DM (5), type A dissection, a dialysis period of more than 6 - 7 years (6), hypoalbuminemia (7), and long-term prescription of high-dose calcium-based phosphate binders (8). After a study by Pinho et al. (9), this is the second study mentioning a relationship between EPS and calciphylaxis. EPS-related hypoalbuminemia will exacerbate calciphylaxis. Fetuin-A and matrix Gla protein (MGP) can both inhibit calcification, but they are stabilized by serum albumin (10). In other words, EPS-related hypoalbuminemia will cause lower levels of fetuin-A and MGP, causing further vascular calcification. In addition to identify the similar pathogeneses of EPS and calciphylaxis, we also questioned and opposed the use of tamoxifen for EPS in patients with calciphylaxis because tamoxifen produces estrogenic-like effects, which could cause venous thromboembolism (11). Thromboembolism and vascular calcification are both vessel disorders.

Experience with the use of tamoxifen in EPS due to its inhibition of the production of fibroblast-transforming growth factor beta (TGFβ) has grown, and such use is widely considered suitable. The side effects are generally well-tolerated, such as nausea or hot flushes in women. However, we believe it is another story when it comes to the use of tamoxifen in EPS patients with superimposed calciphylaxis. Calciphylaxis is mostly due to an imbalance between calcium and phosphate. According to Harris et al. (12), a hypercoagulable state indeed plays an important role in the pathogenesis of calciphylaxis; for example, 38% of calciphylaxis patients had decreased protein C levels and 43% had decreased levels of protein S (12). Tamoxifen can lead to a hypercoagulable state in the following ways. First, it increases the influx of calcium into platelets, leading to platelet activation, and it acts synergistically with other platelet agonists (13). Second, it increases factor VIII, factor IX, and von Willebrand's factor, while it decreases antithrombin, total protein S, protein C, and plasminogen activator inhibitor-1 (14). Therefore, tamoxifen probably causes calciphylaxis. Its pro-coagulation character superimposed on pre-existing calciphylaxis will worsen tissue ischemia and necrosis.

3.1. Conclusions

EPS will exacerbate calciphylaxis, and the use of tamoxifen in patients with EPS and calciphylaxis should be reconsidered. In the absence of evidence from randomized controlled trials for the use of tamoxifen in EPS, along with its known adverse effects on calciphylaxis, we suggest that tamoxifen should not be used in patients with both EPS and calciphylaxis.

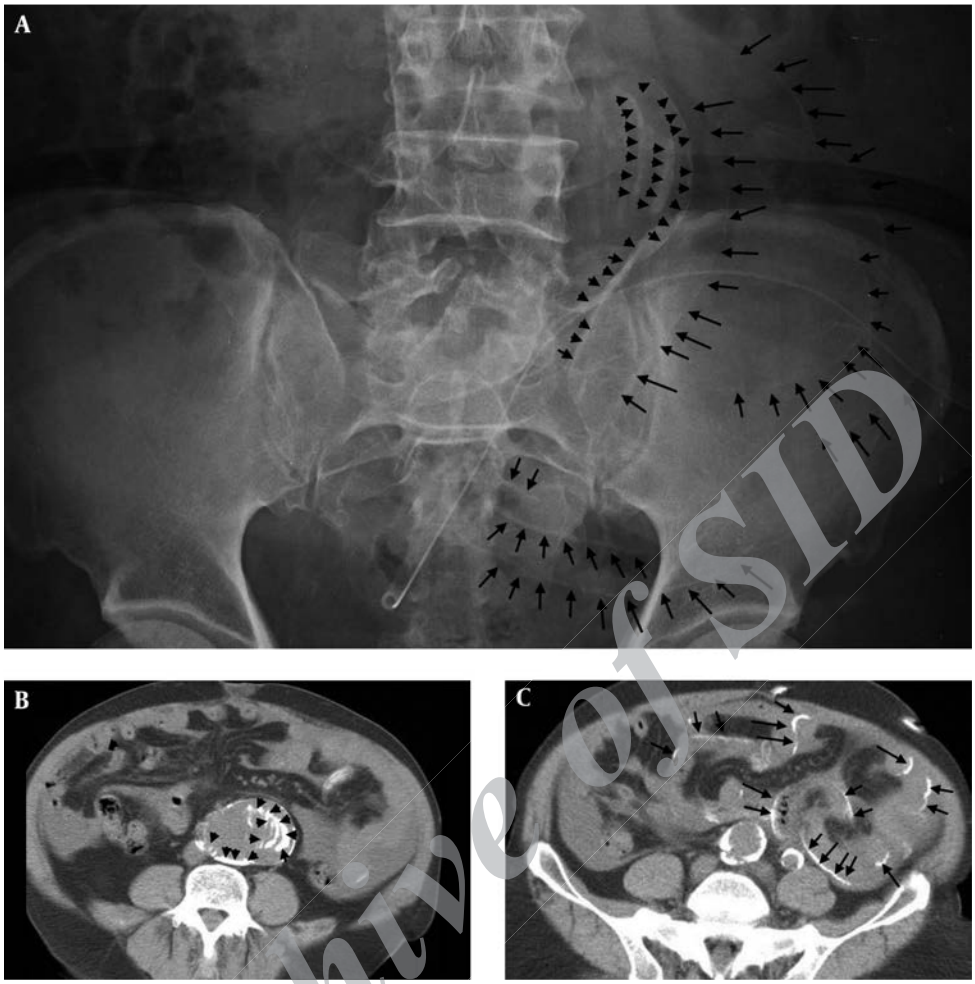

Figure 1. A, KUB x-ray showing uremic arterial calcifications of the abdominal aorta with dilatation (arrowhead) and encapsulating peritoneal sclerosis in the wall of the small intestine (arrow); B, CT image showing calciphylaxis in the abdominal aorta (arrowhead); C, CT image showing diffuse thickening of the peritoneal wall of the small intestine

Footnotes

Conflict of Interest: We do not have any relationships with pharmaceutical companies or other entities, such as employment contracts, consultancy, advisory boards, speaker bureaus, membership on boards of directors, or stock ownership that could be perceived to represent a financial conflict of interest.

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