A New Experience With Encapsulating Peritoneal Sclerosis
Role of Early Intervention

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After 20 years of peritoneal dialysis in Iran, we have encountered with several cases of encapsulating peritoneal sclerosis (EPS) in past few years. Many of these cases remained undiagnosed until advanced stages due to lack of suspicion. In centers with more experience about EPS, mortality has decreased by early diagnostic interventions. Peritoneal dialysis nurses may not be aware of EPS and radiologists are usually not familiar with EPS, either. To increase knowledge about this condition, we decided to present this review article with the case study of one of the 1st patients with EPS at our center. Currently, we have had no data registry of EPS in Iran, yet. Our plan is to develop a national EPS registry in our country which will help to closely monitor these patients.

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INTRODUCTION

Peritoneal dialysis (PD) is a well-established modality of renal replacement therapy in the past 40 years. However, long-term exposure to poor biocompatible glucose-based solutions cause some changes in peritoneal membrane which leads to different degrees of neo-angiogenesis and fibrosis. In a very rare percentage of patients, encapsulating peritoneal sclerosis with malnutrition, ileus, complete intestinal cocooning, and obstruction are developed.[1] Encapsulating peritoneal sclerosis (EPS) is the most serious complication of PD, which was described in 1980 by Gandhi and coworkers in 5 patients.[2] This entity is also coated by other terminologies in the literature such as: *peritoneal fibrosis*, *peritoneal sclerosis*, *sclerotic obstructive peritonitis*, *peritonitis chronic fibrosa encapsulata*, and *calcific and sclerosing peritonitis*. Due to lack of sever inflammation, some authors prefer to use *peritoneal encapsulation*, *abdominal cocoon*, and EPS. The incidence of EPS varies between 0.7% and 7.3% in different populations (2 centers in Iran have reported 2.1% to 2.5%; unpublished data). Mortality and morbidity increases by the length of the time being on dialysis from 3% after 3 years to 100% after 15 years.[3] Peritoneal dialysis, however, is one of the etiologies of EPS among a long list of different conditions shown in Table 1.[4,5]

CASE STUDY

We present a 43-year-old paraplegic man on peritoneal dialysis for the past 58 months. His kidney disease was due to spinal cord injury and reflux nephropathy. He had mild hypertension and secondary hyperparathyroidism without evidence of diabetes mellitus or coronary artery disease. Tables 2 and 3 represent laboratory data of the patient during these months. He had experienced 2 episodes of bacterial peritonitis in the 4th and 8th months of PD.

By the 48th month, blood pressure mildly elevated, and therefore, amlodipine, 5 mg/d, was started. Four months later, his blood pressure continued rising up to 230/125 mm Hg and in spite of several medications, it remained high. By the 54th month, he was admitted because of dyspnea. On imaging studies, he had right pleural effusion, pulmonary collapse, and cardiomegaly (Figure 1). Pleural fluid was transudate with low glucose. Owing to the respiratory distress and

Table 1. Etiologies of Encapsulating Peritoneal Sclerosis[4,5]

Conditions not associated with peritoneal dialysis
Primary
Idiopathic or unknown etiology
Secondary
Medication (β-blockers and calcineurin inhibitors), autoimmune diseases (eg, lupus), peritoneal sarcoidosis, peritoneovenous shunt, diseases of reproductive organs, luteinized thecoma of the ovary, endometriosis, peritoneal and intra-abdominal malignancies, gastrointestinal diseases, cirrhosis with ascites, intraperitoneal chemotherapy and other chemicals, hazardous substances (eg. talc, asbestos, and silicosis), familial Mediterranean fever, abdominal surgery, intra-abdominal infections (eg, tuberculous), peritoneal lavage using certain disinfectants, and hemodialysis
Conditions associated with peritoneal dialysis
Duration of peritoneal dialysis, high peritonitis rate (severity, *Staphylococcus aureus*), acetate buffers, chlorhexidine, plasticizers, hypertonic glucose solution, Inadequate dialysis

Table 2. Laboratory Data Before and During Continuous Ambulatory Peritoneal Dialysis

Parameter	Continuous Ambulatory Peritoneal Dialysis					
	Initiation	6th Month	22nd Month	36th Month	48th Month	52nd Month
Hemoglobin, g/dL	7.5	11.3	9	6.5	7.7	9.2
Erythrocyte sedimentation rate, mm/h	80	83	54	67	40	49
Iron, mg/dL		60	58	8	15	23
Ferritin, mg/dL		372	323	265	270	310
Total iron binding capacity, %		172	275	272	180	165
Alkaline phosphatase, U/mL	564	347	347	392	265	216
Intact parathyroid hormone, pg/mL		147	51	649	> 1060	> 1000
Albumin, mg/dL	2.6	2.7	2.1	2.9	2.6	2.6
C-reactive protein, mg/L		17	48	7	19	35

massive pleural effusion, thoracentesis was done which resulted in improvement in respiratory symptoms. Owing to the frequent episodes of recurrent symptomatic pleural effusion, which required thoracentesis during about 3 months, the pulmonalogist recommended pleurodesis. Animal tetracycline, 8 mg, was instilled into the pleural cavity through the chest tube. Symptoms improved and there was not any problem on the control chest imaging. During these months, blood pressure was not controlled in spite of administration of high doses of several antihypertensives. Finally, 10 days after pleurodesis, he was discharged home with partially controlled blood pressure, while he was complaining of mild nausea and was advised to take antiemetic medicine whenever it was necessary. Six days later, he presented with nausea, vomiting, abdominal pain, loss of appetite, and feeling of fever. On admission, he was ill and pale but conscious. He reported no history of recent

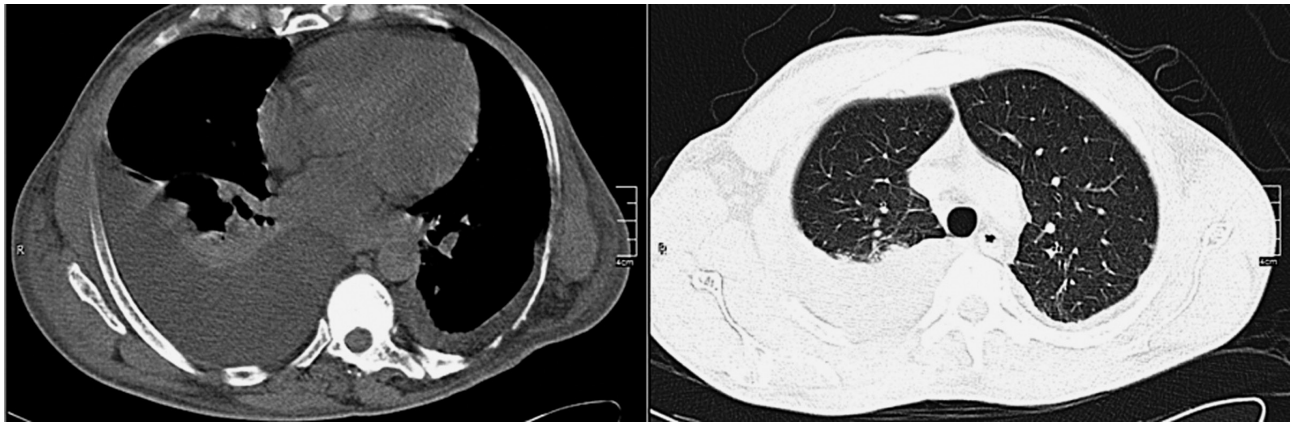

Figure 1. Chest computed tomography scan showed pleural effusion, pulmonary collapse, and cardiomegaly

Table 3. Peritoneal Dialysis-related Parameters During Continuous Ambulatory Peritoneal Dialysis

Parameter	Continuous Ambulatory Peritoneal Dialysis									
	2nd Month	5th Month	9th Month	13th Month	21st Month	36th Month	40th Month	48th Month	51st Month	54th Month
Peritoneal dialysis fluid administered, L	2 x 3 (1.5%) x 1 (2.5%)	2 x 4 (1.5%)	2 x 3 (1.5%) x 1 (2.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)	2 x 4 (1.5%)
Urine volume, mL	600	1000	1000	1300	1500	1200	1200	1700	700	1300
Ultrafiltration, mL/min	2000	900	1500	1200	1100	1500	600	150	0	800
Weight , kg	65	65	65	66	68	72	65	67	65	65
Blood pressure, mm Hg	90/50	100/60	100/60	90/70	120/80	110/70	110/70	120/80	110/70	170/100
Edema	Mild	...	...	...	...	...	Mild	Mild	Mild	...
Renal creatinine clearance, mL/min	18.96	23.26	27.19	26.96	59.17	38.15	11.73	11.82	5.69	16
Peritoneal creatinine clearance, mL/min	52.83	47.98	49.32	54.02	50.30	50.20	36.28	39.92	42.97	45.39
Total creatinine clearance, mL/min	71.79	71.24	76.52	82.98	109.47	88.36	48.01	51.74	47.97	61.39
Renal KT/V	0.18	0.21	0.25	0.29	0.23	0.23	0.12	0.17	0.08	0.09
Peritoneal KT/V	1.86	1.50	1.55	1.78	1.23	1.57	1.17	1.19	1.25	1.46
Total KT/V	2.05	1.72	1.80	2.07	1.45	1.80	1.30	1.36	1.33	1.55
Glomerular filtration rate, mL/min	2.01	2.47	2.88	3.09	6.40	4.23	1.30	1.27	0.6	1.70
Transport type	0.75 (HA)	0.75 (HA)	0.87 (H)	0.84 (H)	0.76 (HA)	0.81 (H)	0.65 (HA)	0.75 (HA)	0.52 (LA)	0.52 (LA)

bloody and cloudy effluent.

On physical examination, blood pressure was 160/90 mm Hg in spite of no antihypertensive medication taken, due to severe nausea and vomiting. The body temperature was 37.5°C; respiratory rate, 20 per minute; and heart rate, 90 per minute. Respiratory and heart sounds were normal; the abdomen was without signs of peritoneal irritation; the exit site was intact; and mild edema was present in the lower extremities. When the abdomen was dry, some uncertain masses were palpated.

Peritoneal fluid analysis showed high protein concentrations without signs of infection or malignancy (Table 4); abdominal ultrasonography and upper gastrointestinal endoscopy were unremarkable. Based on surgical consultation acute abdomen was not considered. The symptoms were monitored. Abdominal computed tomography (CT) scan, reviewed by 3 radiologists, revealed no masses (Figure 2).

Finally, given the persistent gastrointestinal symptoms, we consulted with an expert surgeon for laparoscopic evaluation, which showed mild evidence of early EPS. After 1 month of conservative therapy, changing the dialysis modality, hyperalimentation, and discontinuation of oral feeding the patient showed no improvement; therefore, a classic surgical intervention of EPS consisting release of adhesions and enterolysis was performed (Figure 3). The patient's condition was deteriorated during next 3 months in spite of using methyl prednisolone pulses and tamoxifen, and he died with the picture of hypotension and sepsis. On the last admission, abdominal CT scan showed evidence of advanced EPS (Figure 4).

Figure 2. Abdominal computed tomography scan with intravenous contrast

Table 4. Peritoneal Fluid Analysis During Continuous Ambulatory Peritoneal Dialysis

Parameter	Continuous Ambulatory Peritoneal Dialysis					
	1st Month	6th Month	8th Month	36th Month	55th Month	Recent Admission
Leukocyte	0	0	110	0...1	0	5
Erythrocyte	0	0	0	0	0	5
Protein	...	...	...	...	115	6100
Lactate dehydrogenase	...	...	...	...	251	838
Glucose	...	...	...	...	525	136
Cytology for malignancy	...	...	...	...	...	Negative
Culture	...	...	...	...	Negative	Negative

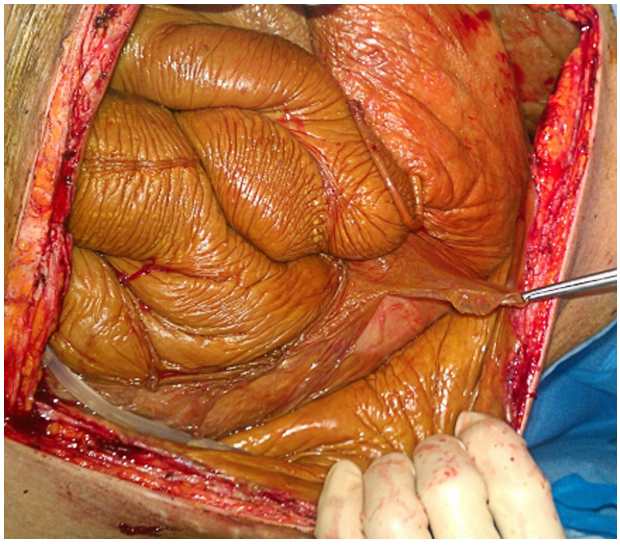

Figure 3. Peritoneal dialysis catheter and thick peritoneal membrane over the intestine.

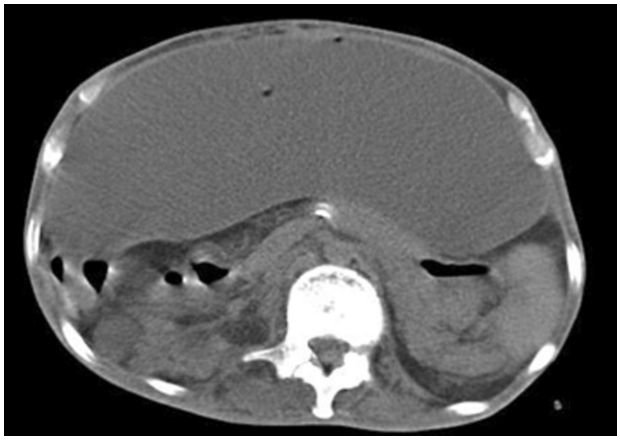

Figure 4. Abdominal computed tomography scan without contrast on the last admission before death.

PATHOGENESIS

Long exposure of the peritoneum to toxic agents (fluids with high osmolarity, lactate, glucose, glucose degradation products, advanced glycation end products, and low pH), peritonitis, and uremic environment induce damages, which lead to production of some inflammatory factors. These factors cause structural and functional damage.[6,7] Among the mediators, transforming growth factor-β (TGF-β), vascular endothelial growth factor (VEGF), interleukin-6 (IL-6), and plasminogen activator inhibitor-1 (PAI-1) are the most important factors. Especially, TGF-β1 and VEGF has central roles in angiogenesis, lymphangiogenesis, and fibrosis. They are secreted by mesothelial cells under the influence of factors derived from white blood cells. Long-term exposure to poor biocompatible solutions and peritonitis are 2 major factors which stimulate expression of these receptors.[8,9] Interleukin-6 is a marker of local inflammatory changes in peritoneal membrane; it is secreted by various inflammatory cells and fibroblast, mesothelial, and endothelial cells, and leads to induction of acute phase reactant.[10] Plasminogen activator inhibitor-1 (PAI-1) is a tissue inhibitor of plasminogen activator. Seventy-four percent of effluent PAI-1 is produced locally by vascular endothelial and smooth muscle cells. It seems PAI-1 has 2 different effects on the peritoneum; the first one is protective effect by inhibiting fibrinolytic pathways; and the second is its probable role in activation of matrix metalloproteinases (MMPs), which results in extracellular matrix degradation. Along with this degradation, the matrix will be replaced with fibrosis. Ninety percent of effluent MMP is locally produced in the peritoneal membrane and, in combination with collagenase, has a complementary role in degrading collagen fibrils. Disequilibrium between collagen formation and degradation leads to fibrous formation.[11] Cancer antigen 125 (CA125) is produced by mesothelial cells and not affected by growth factors and cytokines. As noted above, mesothelial to mesenchymal transition and decrease in total mesothelial mass during the

time on PD leads to reduction of its production.[10] More biocompatible PD fluids with lower toxicity usually are less harmful in this regard.

Structural changes are mesothelial to mesenchymal transition, vasculopathy, neo-angiogenesis, submesothelial fibrosis, and peritoneal thickening from 20 μm to more than 1500 μm in simple sclerosis, and eventually EPS.[7] The peritoneal membrane is composed of 1 layer of mesothelial squamous cell, submesothelial compact zone which consists cells, fibroblasts and macrophages, and vascular beds.[9] The first alteration is gradual breaking apart in peritoneal barrier by interruption of the unity of mesothelial intercellular junctions and loss of their polarity, so some of these cells are separated and shed into the peritoneal cavity, while the others invade submesothelial compact zone and change to myofibroblasts.[8] This transition is necessary for repairing of peritoneal membrane but in long-term, uncontrolled transformation leads to fibrosis.[9] These new transformed cells are more invasive. They could potentiate fibrogenic process by secreting cytokines and growth factors which lead to inflammation, angiogenesis, and fibrosis. Transforming growth factor-β is the key factor for mesothelial to mesenchymal transition.[8]

The other feature of the long-term change is hyalinizing vasculopathy. Luminal narrowing, distortion and occlusion by connective tissue could be seen according to the severity of the lesions. Sometimes, there are small areas of fine calcification in these vessels. The more is PD duration, the more is the severity of vasculopathy. One study stated that tissue ischemia following vasculopathy and vascular occlusion seemed to be an important event in inducing peritoneal fibrosis. Neo-angiogenesis and neolymphangiogenesis are 2 other findings in long-term, but these vessels are not mature functionally.[7]

These alterations which are called "simple sclerosis," usually happen in patients who are experiencing PD-related problems in the 1st 5 years and not in all patients. Encapsulating peritoneal sclerosis develops only in a rare percentage of simple sclerosis and has the following histologic changes more severe than single sclerosis: fibrin deposition, fibroblast swelling (enlargement), capillary angiogenesis, mononuclear cell infiltration, and presence of several immunohistochemical markers for peritoneal fibroblast activation and proliferation.[12]

Not all the patients with ultrafiltration failure develop EPS; therefore, Honda and Oda[12] suggested the second hit theory. The first hit is disruption in function and structure of peritoneal membrane following chronic exposure to PD solutions, and then, the second hit triggers progression to EPS. The most important second hits are peritonitis and paradoxically discontinuation of PD,[3,9,13] although some studies reported equivocal role for peritonitis as the second hit.[1] One study reported more episodes of bacterial peritonitis by some organisms comparing with the control group, which indicates type of organism has a more important role than the number of episodes, especially organisms with more virulence such as *Staphylococcus aureus*, *Peudomonas*, and fungi could trigger EPS with more probability.[9] Wong and colleagues supposed that persistent sterile peritoneal inflammation after catheter removal due to refractory bacterial peritonitis is common and these patients are at high risk for progression to complete feature of ESP.[14] More than half of the patients have stopped PD and transferred to hemodialysis or kidney transplantation before presentation of EPS.[15,16] In a study in the Netherlands, comparing 63 cases of EPS with 126 controls, the annual incidence rate of EPS in the first year posttransplantation increased from 1.8% to 7.5%, but it was decreased 7% yearly thereafter. In their study, transfer to hemodialysis with any reason other than being suspicious of EPS was not associated with it.[1] The average posttransplantation time to presentation of EPS was 5.4 months in the Pan Thames study.[9]

Genetic predisposition may induce the development of EPS in patients who have already had peritoneal changes as a result of PD. Polymorphisms of premotor region of the IL-6 gene, TGF-β, and VEGF have been proposed. In 2010, occurrence of EPS in some patients with Alport syndrome as the kidney failure cause proposed this syndrome as a probable predisposition factors for developing EPS.[9]

Ultrafiltration failure and fast transporter status is the final points of functional damages of peritoneum. Ultrafiltration failure means less than 400 mL of ultrafiltration after 4 hours dwell time with 4.3% glucose solution. It develops in 30% to 50% of the cases receiving peritoneal dialysis and is the cause of PD dropout in 24% of cases.[14,17] In

the first 2 years, increased lymphatic absorption is the major cause of ultrafiltration failure, but decreased glucose osmotic conductance has a more importance role after 2 years.[4,9,10,18] Ultrafiltration failure could be the early change in EPS patients, and leads to a higher cumulative dose of glucose exposure, especially in association with loss of residual kidney function.[9] Some authors believe that 3 years after ultrafiltration failure appearance, about 50% of patients develop EPS.[11]

Free water transport is assessed with sodium dip at the 60th minute during exchange with 4.3% solution. During the first hour, water diffuses through the aquaporine-1 channels solely, which results in a decrease in sodium concentration in the peritoneal cavity (sodium dip). When it does not happen, it means aquaporin has lost its function. It seems interstitial fibrosis has causative role in this regard. Free water transport at the 60th minute and net ultrafiltration at the 240th minute gradually decrease along the time in patients with frank ultrafiltration failure as well as cases with EPS and could not be as a marker for differentiation of these two entities. Effective lymphatic absorption, which could differentiate ultrafiltration failure from EPS, increases gradually in the former, while in EPS, it freezes without any increment.[19] Another sign of membrane failure is the high transport status. The pattern of small solute transport is the same in the two groups and significantly higher than normal cases. Small solute transport increases during the time on PD probably due to neo-angiogenesis and extensive effective surface area, and it is in maximum level about 2 years before EPS presentation. During the last 2 years, it could be decreased in a minority of patients, probably due to progressive fibrotic changes.[15] Finding the slow transport status on a peritoneal equilibration test or having significant ultrafiltration do not preclude the EPS diagnosis.[20,21] Our patient had enough ultrafiltration with average transport status, but he had had aquaporin deficiency since 1 year before presentation of EPS.

CLINICAL FEATURE AND DIAGNOSIS

Presentation of EPS has an extensive spectrum from a mild systemic disease and nonspecific inflammatory state to the complete presentation of life threatening encapsulating peritoneal sclerosis. A slow and nonspecific course is usually a consequence of long-term peritoneal dialysis, but severe fulminant disease is usually triggered by the second hit (eg, our case) Nakamoto has suggested a staging system for EPS as follows: (1) pre-EPS, which has nonspecific symptoms; (2) inflammatory state; (3) encapsulating stage; and (4) obstructive stage.[13] Malabsorption and obstructive symptoms are due to rigid entrapment by encapsulating process and disruption of mesenteric plexus by progressive fibrotic changes.[4]

Sign and symptoms in the pre-EPS stage are ultrafiltration failure, fast transporter state, anemia, high C-reactive protein level, hypoalbunimia, and ascites with pathological findings of epithelial-mesenchymal transition, vasculopathy, peritoneal thickening, and fibrosis, which are nonspecific. In this stage, the patient is asymptomatic because the capsule is thin.

In the inflammatory stage, fibrin degradation end product, and calcification on imaging are seen along with the thickening of the peritoneal membrane loss of appetite, weight loss, fever, changes in bowel habit, bloody effluent, high C-reactive protein level, and leukocytosis with pathological evidence of inflammation. The encapsulation stage is associated with thick membrane that leads to intestinal obstructive signs, abdominal complaints (such as pain, obstipation, nausea, fullness, and vomiting), ascites, abdominal mass, severe calcification, and bloody effluent along with adhesion formation and progressive encapsulation in peritoneum (as in our patient). The obstructive stage is defined by anorexia, complete ileus and bowel obstruction, abdominal mass and cocoon formation without evidence of inflammation. Clinical features may be intermittent or persistent.

The largest retrospective case series, Pan-Thames, studied on the clinical picture of 111 cases, reported abdominal pain in 67%, vomiting in 59%, ascites in 39%, and weight loss 20%. Mortality was 53%, which usually happened 7 months after diagnosis.[20]

Plain radiography, contrast studies, and ultrasonography may show some conclusive information,[23] but CT is the most informative imaging study that could score variable diameters of bowel segments, adherent dilated loops, air-fluid level, increased density of mesenteric fat, and calcification, loculated ascites, thickened intestinal wall, and peritoneal membrane.[4] Although these features are suggestive, they are not diagnostic

and might be seen in a patient on long-term PD without EPS. Thus, we cannot use CT scan for screening purposes.[16] In a study by Goodlad and colleagues, which compared CT images done some months before diagnosis of EPS with control group, EPS patients had higher CT scoring.[24]

Macroscopic findings are morphologic changes seen by surgeon during surgery that confirms the diagnosis. These include extensive encapsulation, cocooned bowel, hemoperitoneum, loculated ascites, thickened peritoneum, brownish peritoneum, and adhesive bands.[9,18] Even diagnostic laparoscopic evaluation in probable cases is highly recommended by the experts to look for the same features more specifically before making decision for major surgery.[25]

Some of peritoneal effluent biomarkers have been investigated in patients who eventually have developed EPS. Among them CA125, IL-6, and PAI-1 are promising in prediction of EPS. Cancer antigen 125 appearance rate of less than 334 U/min in combination with IL-6 appearance rate of more than 350 pg/min could predict EPS with a sensitivity of 70% and a specificity of 89%.[10] It seems the specificity will rise to 100% if ultrafiltration failure is present, as well.[9] Lopez Barreto and coworkers found increased effluent level of PAI-1 in patients on long-term PD. The highest quartile of PAI-1 showed significant correlation with longer duration of PD, more MMP2 and IL-6 production, but lower fluid transport. The authors introduced PAI-1 as a potential marker of fibrosis and its promising benefit in predicting progressive sclerosis.[11] They also investigated 11 cases of EPS comparing 33 control cases in another study. They reported discriminative increased appearance rate of more than 0.77 (95% confidence interval, 0.63 to 0.91) for PAL-1 one year before EPS presentation. Thus, it is wise to monitor these patients more closely when PAI-1 appearance rate exceeds 0.77.[26]

TREATMENT

There are 3 options for treating these patients: supportive care, medications, and surgical operation. Supportive care includes stopping PD, peritoneal lavage, nutritional support.[18,27-29] The mainstay of therapy is discontinuation of PD and commencement of another modality to prevent more damage to the peritoneum, because length of time on PD is strongly correlated with severity of damage. Considering that more than 50% of EPS cases are seen after stopping PD paradoxically, the suggested mechanism is remaining of inflammatory cytokines in abdominal cavity, which leads to maintenance of damage to peritoneal membrane. By this reason, some authors have proposed leaving catheter and doing peritoneal lavage to remove fibrin clots, cytokines, and growth factors. Although it seems reasonable and could delay developing EPS theoretically, it has no significant clinical effect and could lead to peritonitis.[28,29]

Accounting the gastrointestinal tract as the main organ involved by EPS, dietary consultation to plan nutritional support has a major importance, but it is not effective alone.[30] The method of support depends on patient's nutritional status. Ignoring patient nutrition leads to weight loss due to malabsorption, malnutrition, and inflammatory state.[28] Freitas and colleagues investigated on 23 cases of EPS and reported more than 10% weight loss before diagnosis correlated with poor outcome after surgery.[31] Albumin could be used to monitor patient's nutritional status.[28]

The two best documented medications are tamoxifen and corticosteroids. Large clinical trials with enough cases have not been done, so using these agent are controversial. Some other medications such as mycophenolate mofetil, rapamycin, and azathioprine were used alone or in combination with glucocorticoids. Data for using these agents are anecdotal.[28] Tamoxifen is a selective estrogen receptor modulator. According to therapeutic effects in fibrotic disorders such as fibrosing mediastinitis, sclerosing cervicitis, and desmoid tumor, it was considered for EPS. It acts through estrogen receptor-independent pathways because peritoneal tissue does not express estrogen receptor.[28] A suggested mechanism is induction of MMP9, which degrades collagen type IV.[32] A Dutch multicenter EPS study on severe cases of EPS reported lower mortality and better survival in the group treated with tamoxifen comparing with the untreated arm (mortality rate, 45.8% versus 74.4%, $P = .03$).[30] Considering antifibrotic effects of tamoxifen, Eltoum and coworkers proposed that it may have beneficial prophylactic influences in mild forms of EPS.[34] A daily dose of 20 mg to 40 mg has been suggested for at least 1 year. Adverse effects include stroke, thromboembolic events, hot flashes, and endometrial carcinoma.[28]

With a therapeutic dose of 10 mg/d to 20 mg/d, side effects are rare.[9]

Corticosteroids have been used successfully in the treatment of EPS. If it starts immediately after EPS process initiates, it will inhibit inflammation, ascites, production, and maturation of collagen in the peritoneum and consequent events.[22,28-30] Many studies revealed good results with steroids, except in patients with advanced encapsulation, in which it is not effective.[28] Prednisolone, 0.5 mg/kg to 1 mg/kg, is prescribed in the 1st month followed by 0.25 mg/kg to 0.5 mg/kg in the 2nd and 3rd months and then will taper to 10 mg during the next 3 months. Tapering steroid dosage may lead to recurrence.[29] Some physicians prefer starting treatment with pulses of 500 mg to 1000 mg of methylprednisolone for 2 or 3 consecutive days. In patients with clinical response whose C-reactive protein level remains high, increasing the period of high-dose treatment would be the better strategy. Sudden rising in C-reactive protein level while using corticosteroids should warn the physician that spontaneous intestinal perforation might happened.[28]

Although it has not been established yet whether prophylactic steroid is useful, there are some suggested indications for it, as follows[29]: biopsy-proven cellular inflammatory infiltration before initiation of EPS process, persistent elevation in C-reactive protein level in the absence of other causes, a rapid increase in ascites fluid volume, and an increase in fibrinolytic, coagulative, and inflammatory markers in effluent such as, IL-6, PAI-1, and fibrin degradation products.

Supportive care must not cause to miss the golden time for surgery. Enterolysis is the best established treatment and mortality will be less by experienced hands. By enterolysis the fibrous tissue peels away from intestinal wall and adhesion bands destroys. It is a time-consuming procedure which lasts about 6.9 hours.[10] High-dose immunosuppressive decreases the probability of recurrence.[9] One major factor which influences recurrence rate is microvascular hyperplasia. The more microvascular hyperplasia leads to higher recurrence rate.[30] Although surgery is the best way which removes invasive fibrous tissue, it is not curative completely and recurrence rate is 25% during the first 2 years.[30,32] In the study of Kawanishi and colleagues on 130 cases of EPS, 22% were treated with enterolysis and postoperative mortality was 6.9%.[28]

The main indications for surgery are recurrent persistent or subacute intestinal obstruction, patient's poor nutritional status that does not respond to supportive care, signs and symptoms of peritonitis, and intrapertioneal hemorrhage.[27] As noted previously, it is wise to use more biocompatible solutions, prevent peritonitis, and monitor patients on long-term dialysis closely, especially in cases with more than 8 years of being on dialysis and high transporter type status.[29] These parameters should be looked out cautiously: sign and symptoms, solute transport, ultrafiltration status, and effluent biomarkers.

It is important to note that along with increasing the time on PD, EPS is more likely to happen as a serious complication. In any PD patient with systemic inflammatory signs or abdominal discomfort, we have to think about EPS as a probable diagnosis. Presence of intestinal motility disorder and obstructive signs in conjunction with imaging and morphological evidence and biomarkers are necessary and proper diagnosis and management of these patients needs cooperation of experienced surgeon, nephrologist, and expert radiologists in this field.

CONCLUSIONS ON CASE STUDY

Our patients did not have any sign and symptoms related to EPS basically. He was a low average transporter and had no ultrafiltration failure. Fulminant EPS presented after pleurodesis with doxycycline fibrotic agent. We had no access to check inflammatory biomarkers of effluent, but there was a very high level of effluent protein with low leukocyte count which resembles inflammation and not infection. Our patient's transport status was in average range without ultrafiltration failure and we did not expect EPS presentation in him. About 1 week after doing pleurodesis, he progressed to complete feature of fulminant EPS. We suggest doxycycline as the possible second hit, as it has been reported for chemotherapeutic agents, talc, acetate, chlorhexidin, asbestos, and silica previously. However, more information was needed to explain the causal relationship status in this patient.

CONFLICT OF INTEREST

None declared.

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