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ABOUT COVER

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MINIREVIEWS

Encapsulating peritoneal sclerosis

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Abstract

Encapsulating peritoneal sclerosis (EPS) is a debilitating condition characterized by a fibrocollagenous membrane encasing the small intestine, resulting in recurrent small bowel obstructions. EPS is most commonly associated with long-term peritoneal dialysis, though medications, peritoneal infection, and systemic inflammatory disorders have been implicated. Many cases remain idiopathic. Diagnosis is often delayed given the rarity of the disorder combined with non-specific symptoms and laboratory findings. Although cross-sectional imaging with computed tomography of the abdomen can be suggestive of the disorder, many patients undergo exploratory laparotomy for diagnosis. Mortality approaches 50% one year after diagnosis. Treatment for EPS involves treating the underlying condition or eliminating possible inciting agents (*i.e.* peritoneal dialysis, medications, infections) and nutritional support, frequently with total parenteral nutrition. EPS-specific treatment depends on the disease stage. In the inflammatory stage, corticosteroids are the treatment of choice, while in the fibrotic stage, tamoxifen may be beneficial. In practice, distinguishing between stages may be difficult and both may be used. Surgical intervention, consisting of peritonectomy and enterolysis, is time-consuming and high-risk and is reserved for situations in which conservative medical therapy fails in institutions with surgical expertise in this area. Herein we review the available literature of the etiology, pathogenesis, diagnosis, and treatment of this rare, but potentially devastating disease.

Key words: Abdominal cocoon; Sclerosing encapsulating peritonitis; Peritoneal sclerosis; Peritonectomy; Enterolysis; Peritoneal dialysis; Tamoxifen; Corticosteroids

Core tip: Encapsulating peritoneal sclerosis (EPS) is a rare, but potentially devastating disorder. Most literature is derived from the nephrology literature surrounding peritoneal dialysis, however, the gastroenterologist is likely to encounter EPS from a variety of etiologies. We present a comprehensive review of EPS from all etiologies and a summary of treatments from a gastroenterologist's perspective including the role of nutrition, surgery, immunosuppression, anti-fibrotic agents, and the novel use of μ-opioid antagonists and guanylate cyclase C agonists in the management of patients with EPS.

Danford CJ, Lin SC, Smith MP, Wolf JL. Encapsulating peritoneal sclerosis. *World J Gastroenterol* 2018; 24(28): 3101-3111 Available from: URL: http://www.wjgnet.com/1007-9327/full/v24/i28/3101.htm DOI: http://dx.doi.org/10.3748/wjg.v24.i28.3101

INTRODUCTION

Definition

Encapsulating peritoneal sclerosis (EPS) is a rare clinical syndrome characterized by an acquired, inflammatory fibrocollagenous membrane encasing the small intestine, resulting in symptoms of bowel obstruction. It is defined by the International Society for Peritoneal Dialysis as "a syndrome continuously, intermittently, or repeatedly presenting with symptoms of intestinal obstruction caused by adhesions of a diffusely thickened peritoneum"[1]. Owtschinnikow first described encasement of the intestines by a fibrocollagenous membrane in 1907 and coined the term *peritonitis chronica fibrosa incapsulata*[2]. EPS has also been known as *abdominal cocoon* and *sclerosing encapsulating peritonitis*. It should not be confused with peritoneal encapsulation, a congenital condition characterized by an accessory peritoneal membrane encapsulating the intestines, without adhesions to the encased intestine often incidentally recognized during unrelated surgery[3].

Etiology

EPS can be divided into primary (idiopathic) or secondary in which a trigger for the inflammatory process can be identified. Primary EPS was classically thought to afflict adolescent women in tropical and subtropical areas leading to theories of retrograde menstruation or gynecologic infection as the cause. Though the largest studies of primary EPS confirm its equatorial predilection, men are more commonly affected than women in a 2:1 ratio[4,5] and the etiology remains unclear.

In secondary EPS, a local or systemic factor can be identified as triggering peritoneal inflammation. Implicated triggers include medications[6-9], infection[10-16], mechanical or chemical intraperitoneal irritants[17-27], cirrhosis[28], organ transplantation[29-31], endometriosis[32], gynecologic neoplasms[33,34], dermoid cyst rupture[35], and systemic rheumatologic and inflammatory disorders[36-38] (Table 1).

Pathophysiology

EPS is thought to occur when a peritoneal inflammatory process (inciting factor) occurs in patients with a predisposing condition (Figure 1). In peritoneal dialysis (PD) literature, this is referred to as the "two-hit" hypothesis[39] in which the "first hit" or predisposing condition is the non-inflammatory peritoneal sclerosis resulting from repeated dialysis sessions. In support of this, cumulative incidence of EPS increases dramatically with time on PD[40,41]. A proinflammatory "second hit"[42] precipitates a cascade of proinflammatory [transforming growth factor β1 (TGFβ1), interleukin-6 (IL-6), CCN2] and proangiogenic [vascular endothelial growth factor (VEGF)] cytokines[43,44]. TGFβ1 promotes transdifferentiation of peritoneal mesothelial to mesenchymal cells resulting in mesothelial cell depletion[45,46], increased production of extracellular matrix components [collagen type 1, alpha 1 (COL1A1)] and fibrogenesis resulting in a fibrocollagenous cocoon[47] (Figure 1).

In PD, genetic variation in the receptor for advanced glycation end products may predispose an individual to peritoneal deterioration[48]. While no genetic studies exist outside the PD literature, genetic predisposition may explain why only a small proportion of patients with recurrent peritonitis develop EPS or why an individual may develop EPS even with a single, discrete exposure[24]. Among gynecologic neoplasms, reports of EPS are confined to luteinizing neoplasms[33,34] without other overt inflammatory trigger, leading to the hypothesis that they directly stimulate peritoneal inflammation and fibrosis, though the potential stimulatory cytokine has yet to be identified[49].

Epidemiology and natural history

Given its rarity and heterogeneity of etiologies, the incidence and prevalence of EPS as a whole is unknown. In a review of idiopathic EPS, cases were more commonly reported from tropical and subtropical countries [China (54%), India (18%), Turkey (9%), and Nigeria (3%)][6]. The mean age was 34.7 (range 7-87 years) with a 2:1 male predominance.

In peritoneal dialysis, the annual incidence of EPS varies from 0.14% to 2.5%[41,50] with decreasing incidence in more recent studies likely due to improved dialysis techniques[17,50]. The most significant risk factor for EPS development is duration of PD[17] with a low cumulative incidence at 3 years increasing after 5 years[17,40,41]. At 8 years, 10%-20% of PD patients will develop EPS[17,51-54]. The prevalence of EPS in PD has been observed between 0.4% and 8.9%[17]. Mortality in PD patients approaches 50% one year after diagnosis[17,50,55] though it is difficult to ascertain how much of this is related to EPS or the comorbidities that accompany end-stage renal disease.

Table 1 Classification and etiologies of encapsulating peritoneal sclerosis

Primary (idiopathic)	
2:1 (male:female)	
Most commonly reported in tropical/subtropical regions	
Secondary	
Medications	Mechanical or chemical irritation
Practolol[6]	Peritoneal dialysis[17]
Methotrexate[7,8]	Intraperitoneal chemotherapy[18]
Antiepileptic drugs[9]	Ventriculoperitoneal shunt[20]
Infection	Peritoneovenous shunt[21]
Tuberculosis[10]	Intraperitoneal iodine[22]
Non-tuberculous mycobacteria[11]	Abdominal trauma[23]
Bacterial peritonitis[12]	Intraabdominal surgery[24]
Cytomegalovirus[13]	Foreign body[25]
Fungus[14,15]	Talcum powder[19]
Parasite[16]	Asbestos[26]
Cirrhosis[28]	Silica[27]
Organ transplantation	Endometriosis[32]
Liver[29]	Dermoid cyst rupture[35]
Small intestine[30]	Rheumatologic/systemic inflammatory
Renal[31]	conditions
Gynecologic neoplasms	Sarcoidosis[36]
Luteinized thecoma[33]	Systemic lupus erythematosis[37]
Luteinizing granulosa cell tumor[34]	Familial Mediterranean fever[38]

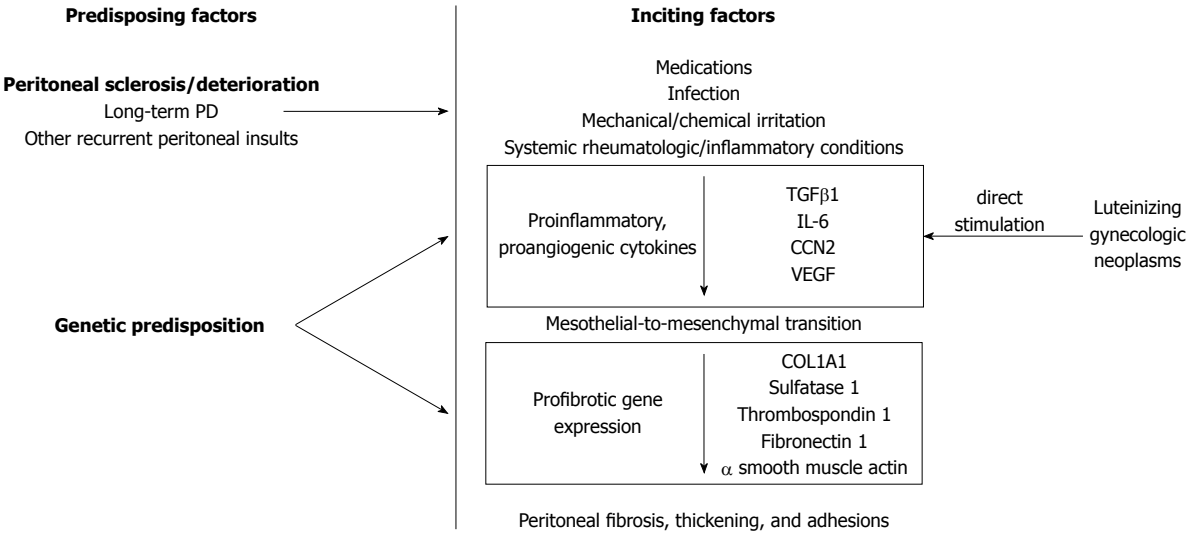

Figure 1 Pathophysiology of encapsulating peritoneal sclerosis. Certain predisposing factors may be present for encapsulating peritoneal sclerosis to form, such as genetic predisposition or being on long-term peritoneal dialysis. Inciting factors that may push the physiology towards a pro-inflammatory and pro-fibrotic state include medications, repeated chemical or mechanical peritoneal irritation, recurrent infections, and systemic rheumatologic or inflammatory conditions.

DIAGNOSIS

Clinical presentation

The diagnosis of EPS is clinical, based on a constellation of clinical findings, and confirmed radiographically or by laparotomy[5,17,56,57]. No gold standard exists for diagnosis. However, a diagnostic algorithm is proposed in Figure 2. A majority of PD-associated EPS patients present after withdrawal of PD, with onset of symptoms occurring up to 5 years later[17]. In the largest case series of idiopathic EPS, the average duration of symptoms was 3.9 years prior to presentation with the vast majority presenting malnourished (75%, mean BMI 17.5 kg/m^2)[4]. The most common presenting symptoms were abdominal pain (86%), abdominal distension (82%), and nausea and vomiting (54%). Twenty-nine percent of patients underwent "emergency surgery" on presentation implying that, despite the chronic, insidious nature of the disease, a significant percentage present with more acute obstruction, ischemia, or perforation[4].

Imaging

Imaging is often helpful in differentiating EPS from other causes of intestinal obstruction. Abdominal plain films showing peritoneal calcification as well as dilated loops of bowel with air-fluid levels may suggest advanced EPS[56,58]. Small bowel follow-through may show delayed transit, distension proximal to small bowel adhesions,

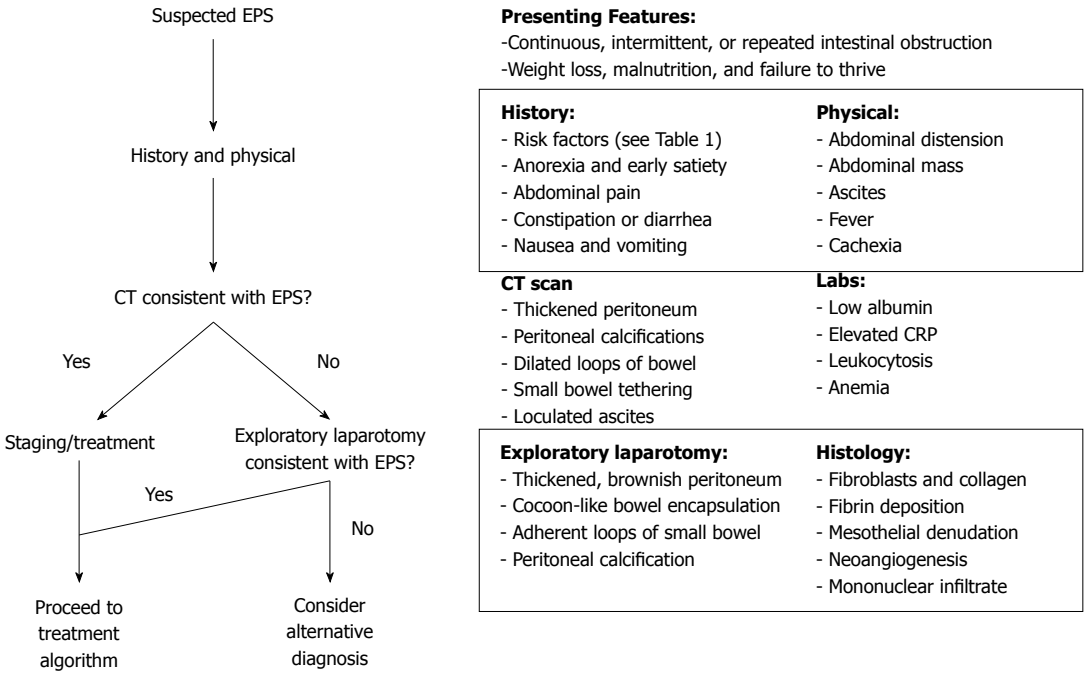

Figure 2 Proposed algorithm for the diagnosis of encapsulating peritoneal sclerosis. The diagnosis of EPS is a clinical one that can be confirmed with imaging or at laparotomy. Various presenting features and symptoms, clues obtained in the history (risk factors) and physical exam can point towards the diagnosis of EPS. CT/MRI findings include thickened peritoneum, calcifications, and may even demonstrate cocooning of the bowel with proximal dilation, as seen in our case. EPS: Encapsulating peritoneal sclerosis

and have a "cauliflower" appearance from compression of tightly adherent loops of bowel by EPS[5]. On ultrasonography, dilated loops of bowel may be matted together and tethered posteriorly or encased by a dense fibrous membrane[5]. Intraperitoneal echogenic strands may cause the bowel wall to appear trilaminar[56,58].

CT scan is currently the best studied and most commonly used imaging technique in the diagnosis of EPS. Small-bowel loops are often tethered together in an enveloping, thickened peritoneum, typically accompanied with proximal bowel dilation[58]. Other radiographic features include loculated ascites, increased density of mesenteric fat, and localized or diffuse peritoneal calcification[56,59]. While the presence of complex loculations could be from intra-abdominal hemorrhage, it should raise suspicion for perforation or sepsis, especially if they contain gas[60]. Increased bowel wall enhancement or thickening indicates ongoing inflammation or transition to transmural fibrosis[58,60]. Magnetic resonance imaging has been used less frequently for diagnosis but likely has similar yields. Advantages include avoidance of ionizing radiation and better delineation of bowel encasement and peritoneal thickening[61].

Laboratory

Laboratory findings in EPS are non-specific and related to underlying infection, malnutrition, and inflammation[30,39,62]. Levels of inflammatory cytokines have been shown to be higher in dialysate in EPS patients compared to PD controls up to years in advance of clinical development of EPS[63-65]. However, no biomarker has been found to be useful in predicting EPS development[64].

Histopathology

Histologic findings in EPS are non-specific and may overlap with findings in simple peritoneal sclerosis or infectious peritonitis[17]. Microscopically, the mesothelial cell layer is denuded with fibroblast proliferation and fibrocollagenous deposition frequently with fibrin deposition[42]. An inflammatory mononuclear cell infiltrate may be present in active inflammation[42]. Podoplanin, a transmembrane glycoprotein found on peritoneal mesothelial cells that binds inflammatory cytokines, helps differentiate EPS from peritoneal sclerosis and peritonitis[45,66]. Generally, a thickened fibrocollagenous membrane in the setting of the previously described clinical syndrome is sufficient for diagnosis.

EPS staging

A staging system has been proposed in the PD-associated EPS literature, based on a combination of clinical, laboratory, and radiographic findings[53,56,57]. Nakamoto *et al*[56] categorized patients with EPS into Stage 1 (pre-EPS), Stage 2 (inflammatory), Stage 3 (encapsulating), and Stage 4 (chronic) based on abdominal symptoms, inflammation, encapsulation, and intestinal findings (Table 2). Different therapeutic approaches have been proposed depending on the stage of disease[53,56,57].

TREATMENT

Treatment of underlying condition

When possible, the underlying condition leading to EPS should be treated. In the case of PD, this involves cessation of peritoneal dialysis and transition to hemodialysis[57]. In non-PD EPS, potential offending medications

Table 2 Stages of peritoneal dialysis-associated encapsulating peritoneal sclerosis with associated clinical, serologic, and radiographic profiles

	Nakamoto 2005		Nakayama 2014	
	Terminology	Clinical findings	Terminology	Clinical findings
Stage 1	Pre-EPS stage	Loss of ultrafiltration capacity Development of a high transport Hypoproteinemia Bloody dialysate, ascites Calcifications in the peritoneum	Pre-stage	Abdominal symptoms: Mild Inflammation: Mild Encapsulation: None
Stage 2	Inflammation stage	Increased CRP, leukocytosis Fever, chills, weight loss, anorexia Diarrhea, ascites	Inflammatory	Abdominal symptoms: Nausea, diarrhea Inflammation: Mild to severe Encapsulation: Partial
Stage 3	Encapsulating stage	Decreased clinical signs of systemic inflammation Early signs of ileus (abdominal pain, nausea, vomiting)	Encapsulating	Abdominal symptoms: Periodic ileus Inflammation: Mild Encapsulation: Present
Stage 4	Ileus stage	Anorexia Complete ileus Abdominal mass	Chronic	Abdominal symptoms: Persistent ileus Inflammation: None to mild Encapsulation: Present

should be withdrawn and underlying infection or inflammatory conditions should be treated. Despite withdrawal of the offending agent or treatment of the underlying condition, resolution of EPS is unlikely given its chronic, fibrotic nature and treatment of ongoing inflammation or the underlying fibrosis is frequently necessary[6,8,14,67].

Nutritional support

On diagnosis of EPS, nutritional status should be assessed. While bowel rest and TPN alone are not effective in treating EPS[68], ensuring adequate nutrition is essential. Given obstruction, enteral feeding is often not tolerated and TPN is required[69]. A case series in China, showed preoperative TPN reduced serious postoperative complications and hospital stay[4].

Immunosuppression

The effect of immunosuppression on EPS was first noted in kidney transplant patients who developed improvement in EPS symptoms after institution of immunosuppression[70]. Numerous medications have been tried targeting the inflammatory component of EPS, including corticosteroids, colchicine, azathioprine, cyclosporine, mycophenolate mofetil (MMF), and mammalian target of rapamycin (mTOR) inhibitors[71-76]. Of these, corticosteroids are the best studied and, while the mTOR inhibitors and MMF carry the theoretical advantage of improving fibrosis as well, evidence is anecdotal and largely confined to post-kidney transplant patients with additional indications for immunosuppression[73,75].

Evidence for corticosteroid use is confined to observational studies with inconsistent formulation, dosing, duration, and end points (Table 3). In the earliest study by Kuriyama *et al*[77], all patients who did not receive corticosteroids died within 8 mo, while those who received prednisolone survived at 1-3 years of follow-up with only one requiring surgical intervention. In a larger retrospective case series without a control comparison group, mortality was 25% for stage 4 EPS over the study period[71] which is lower than what is generally reported in natural history studies[17,50,55].

Despite this, one prospective cohort study found only 38.5% recovered on steroids, while the remainder died or required surgical intervention[68]. Similarly, the largest retrospective study involving steroids found no improvement in median survival, though treatment groups were too heterogeneous for meaningful analysis[55].

While EPS is thought to develop out of an inflammatory insult, active inflammation may not be ongoing at the time of presentation. It is difficult to ascertain which patients are actively inflamed using non-specific markers such as CRP and clinical observation. We recommend targeting immunosuppressive therapy to those thought to have an active inflammatory component after excluding infection. The appropriate dosing and duration of corticosteroids are not established. However the Dutch EPS Registry, in 2011 guidelines, suggests Ⅳ methylprednisolone (500-1000 mg/d) for 2-3 d in those who present with acute obstructive symptoms without infection[78]. In those who present with more subacute symptoms without infection, it is reasonable to treat with prednisolone at 0.5-1.0 mg/kg/d for 1 mo and taper over the course of a year[78]. Absence of improvement after 1 mo may be considered a treatment failure and we recommend stopping steroids and considering alternative therapy such as tamoxifen or surgery. In the absence of data, other immunosuppressive medications should be reserved for patients with additional indications such as organ transplantation or strong contraindications to surgery.

Anti-fibrotics

Immunosuppression alone may not be effective in those patients who have already developed signficant fibrosis (Stage 3). Tamoxifen is a selective estrogen receptor modulator (SERM) with strong anti-fibrotic properties related to inhibition of TGF-β, an important cytokine in the fibrosis process[79]. Its successful use in EPS was

Table 3 Summary of studies of interventions in encapsulating peritoneal sclerosis

	Design	Patient population	Treatment	Outcome	Comments
Kuriyama 2001	Retrospective case-control	*n* = 11 Japan PD patients Age - 49.1 yr 27% female	**Steroids** Prednisolone Dose - 0.5 mg/kg/d Duration - NS *n* = 5 **Control** TPN-alone *n* = 6	**Steroids** All remained alive at 1-3 yr after diagnosis. **Control** All died of EPS-related complications within 8 mo of diagnosis.	All control patients were diagnosed prior to 1997 and all who received steroids were diagnosed after 1997.
Kawanishi 2004	Prospective cohort	*n* = 48 Japan PD patients Age - 54.7 yr 25% female	**Steroids** - Prednisolone Dose - 10-40 mg/d Methylprednisolone Dose - 0.5-1.0 g/d Duration – NS *n* = 39 **Surgery** Total enterolysis *n* = 12 **Control** TPN-alone *n* = 3	**Steroids** Recovery - 38.5% Surgery - 15.4% Mortality - 31% **Surgery** Recovery - 58.3 % Mortality - 33% **Control** Recovery - 0% Mortality - 66%	Six steroid patients underwent surgery. Surgical treatment consisted of total enterolysis.
Maruyama 2008	Retrospective case series	*n* = 79 Japan PD patients	**Steroids** Prednisolone Dose – 2.6-60 mg/d Duration - 1-36 mo *n* = 79	**Steroids** Mortality – Stage 2 – 3.6% Stage 3 – 14.3% Stage 4 – 25%	Did not compare to a control group.
Balasubramanian 2009	Retrospective case series	*n* = 111 United Kingdom PD patients Age - 52.0 yr 53% female	**Steroids ± immunosuppression** *n* = 7 **Tamoxifen** *n* = 17 **Tamoxifen + steroids ± immunosuppression** *n* = 8 **Surgery** Adhesiolysis (*n* = 5) jejunostomy (*n* = 1) Small bowel resection (*n* = 1) Ileal-transverse colon bypass (*n* = 1) **Control** No specific drug therapy (*n* = 46)	**Steroids ± immunosuppression** Median survival 7 mo **Tamoxifen** Median survival 15 mo **Tamoxifen + steroids ± immunosuppression** Median survival 14 mo **Surgery** Median survival 17 mo **Control** Median survival 13 mo	Dose and duration of medications not specified. Numerous patients received combinations of therapies. Immunosuppression consisted of azathioprine, cyclosporin, tacrolimus, mycophenolate mofetil, or sirolimus. Unable to analyze statistically due to heterogeneity in groups.
Korte 2011	Retrospective survival analysis	*n* = 63 Netherlands PD patients Age 43.4 yr 50% female	**Tamoxifen** Dose - Dose 10 mg/d to 20 mg twice daily Duration – at least 4 wk *n* = 24 **Control** No tamoxifen *n* =39	**Tamoxifen** Mortality rate - 45.8% **Control** Mortality rate - 74.4%	None underwent surgery in either group. Patients in both groups received steroids, which was not analyzed separately other than noting a trend towards improved mortality in the tamoxifen group.
Kawanishi 2011	Retrospective case series	*n* = 181 Japan PD patients	**Surgery** Total enterolysis *n* = 181	**Surgery** Recurrence – 25.4% Surgical mortality – 7.7% Overall mortality – 35% 0/17 with Noble plication experienced recurrence at 8 mo	Heterogeneous operation types. Those after April 2007 received Noble plication.
Ulmer 2013	Retrospective case series	*n* = 26 Netherlands PD patients Age 54 yr 11% female	**Surgery** Peritonectomy and enterolysis (PEEL)	**Surgery** Major morbidity - 31% Reoperation – 17% Recurrence – 10% Surgical mortality – 10%	8 patients received steroids, 1 tamoxifen, and 1 tacrolimus pre-operatively.

PD: Peritoneal dialysis; EPS: Encapsulating peritoneal sclerosis.

first described by Allaria *et al*[80] in 1999. Similar to corticosteroids, evidence for tamoxifen is limited to observational studies in PD patients (Table 3).

A retrospective Dutch study reported a significant difference in mortality (45.8% *vs* 74.4%, $P < 0.05$) with tamoxifen at 130 mo of follow-up with a trend towards

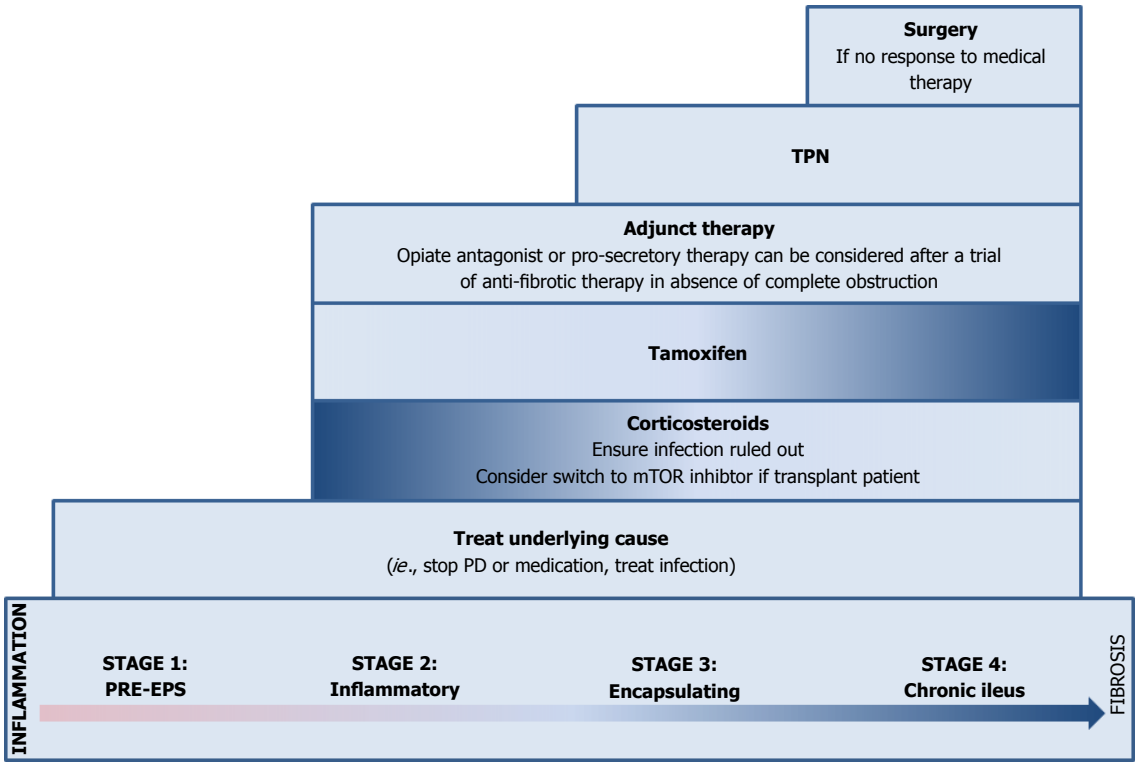

Figure 3 Therapeutic and management approach for encapsulating peritoneal sclerosis. Treatment strategies should be tailored to each patient, depending on the extent and stage of EPS. In all stages, especially during the early stages, the underlying cause should be identified and treated or removed. During the earlier stages (Stage 1-2), the pathophysiology tends to be more inflammatory and the degree of sclerosis tends to be minimal. Thus, after infection has been ruled out, corticosteroids may be of benefit. In the later stages (Stage 3-4), more advanced sclerosis may be present, and patients may start exhibiting signs and symptoms of partial or complete bowel obstruction. In treating abdominal pain, opioids should be avoided. However, this may not always be possible and thus opiate antagonists are recommended in this setting. Tamoxifen plays an increasing rule in the later stages. If poor oral intake or malnutrition is present, total parenteral nutrition may be required. If symptoms are severe and there has been no response to medical therapy, surgical intervention may be considered. EPS: Encapsulating peritoneal sclerosis.

improved survival on survival analysis after adjusting for calendar time, use of corticosteroids, and use of parental nutrition[81]. In contrast, a retrospective study of PD patients from the United Kingdom (UK), did not find any survival benefit with tamoxifen (median 15 mo) compared to no therapy (12 mo) although it was limited by significant treatment heterogeneity[55].

The dose and duration of tamoxifen treatment is not well-defined. Most studies use between 10-40 mg daily. The Dutch EPS Registry suggests starting with 20mg BID[78]. A clinical response is typically seen within 1-6 mo[11,14,82]. Treatment should be continued for at least a year and tapered off thereafter as long as the underlying condition is controlled and the patient has had an adequate clinical and radiologic response. Resolution may be seen in form of clinical improvement and/or evidenced by resolution of peritoneal thickening on follow-up imaging. Potential side effects of tamoxifen including deep venous thrombosis, stroke, hot flashes and endometrial carcinoma should be discussed prior to initiating therapy[83].

Surgical treatment of EPS

Given the time-consuming, hazardous, and technical nature of surgical techniques for EPS, surgery is recommended only in patients who have failed conservative, medical therapy and, if possible, in centers with experience in such operations. Surgical techniques vary from those with curative intent, such as enterolysis (ablation of fibrotic tissue and lysis of adhesions), to those aimed at addressing a specific complication such as limited lysis of adhesions or resection of perforated or ischemic bowel. The former techniques are preferred. They have lower frequency of symptom recurrence, but are time-consuming, often technically difficult, and carry a risk of bowel injury[84-86].

In a 17-year review of 239 cases in one center in Japan, in which enterolysis alone was primarily employed, mortality was 35.4% (7.7% attributed to post-operative complications and 18.2% to persistent EPS-related complications)[87]. During initial experience, 25.4% required a second operation for persistent obstructive symptoms[85], but after institution of Noble plication (suturing of the intestines to each other) in addition to enterolysis, this improved to 12.3%[88]. More recent experience in other institutions is also encouraging with only 10% requiring reoperation after peritonectomy and enterolysis (PEEL) and 10% mortality at 1 year[86]. Continuation of steroids or tamoxifen post-operatively may reduce recurrence[89].

Dysmotility

While the primary driver of obstructive symptoms in EPS is mechanical and related to adhesions and constriction

within the encapsulating peritoneum, we hypothesize dysmotility may also play a role both through disruption of the myenteric plexus by fibrosis and increased endogenous opioids from activated lymphocytes inhibiting both propulsive motor and secretory activity in the gut[66,90,91]. Successful use of methylnaltrexone to combat inflammation-associated dysmotility has been described in anti-Hu-associated intestinal pseudo-obstruction[92]. We suggest use of a μ-opioid antagonist and a guanylate cyclase C agonist in patients who remain symptomatic, but have already been started on appropriate anti-fibrotic therapy (Figure 3).

CONCLUSION

Encapsulating peritoneal sclerosis is a rare, but devastating condition associated with high morbidity and mortality. A high index of suspicion is warranted in patients with unexplained recurrent symptoms of bowel obstruction. A careful history should be obtained to identify patients with known risk factors. EPS can be divided into primary (idiopathic) or secondary. Implicated triggers may include medications, infections, chronic mechanical or chemical irritation, especially in patients on peritoneal dialysis, or in various other chronic, inflammatory diseases (cirrhosis, history of organ transplant, gynecologic or rheumatologic conditions). Diagnosis is clinical, and can be confirmed by x-ray or laparotomy. Treatment should be directed at the underlying condition, optimizing nutrition, and corticosteroids or tamoxifen alone-or in combination-depending on disease state and contraindications. In patients who have failed conservative medical therapy, surgical enterolysis should be considered.

Prior studies have been limited by inconsistent definitions and staging of EPS, and all treatment studies have been observational with variable dosage, duration of treatment, and outcomes. Since treatment may vary based on disease stage, future studies should appropriately document disease stage when assessing treatment. Long-term longitudinal data from past case series may shed more light on the natural history of EPS and mortality benefits of certain treatments. A gap in knowledge still exists in our understanding of the underlying pathogenesis of EPS and fibrosis, and will need to be bridged in order to develop effective therapies.

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