Experience of 100 Surgical Cases of Encapsulating Peritoneal Sclerosis: Investigation of Recurrent Cases After Surgery

Since 1993, we have performed enterolysis for encapsulating peritoneal sclerosis (EPS) in 86 patients. Five patients died after surgery, but the remaining 81 patients achieved symptomatic improvement. However, some of the surviving patients developed symptoms of intestinal obstruction after several months, and EPS recurrence remains our greatest challenge.

In the present study, we identified factors related to recurrence by clinically comparing 47 recurrent and nonrecurrent patients that we were able to follow for more than 2 years after surgery.

In the 47 patients we followed, 11 (23.4%) experienced recurrence, and 10 of those patients underwent a second surgery. Four patients needed a third surgery. The mean time to recurrence was 15.2 months, and all patients with recurrence, except one, experienced their recurrence within 20 months. We observed no differences between the recurrent and nonrecurrent patients in follow-up period, age, history of peritoneal dialysis, use or nonuse of steroids after surgery, thickness of the submesothelial compact zone, or inflammatory cell infiltration. However, the number of microvessels was significantly higher in the recurrent patients.

Our surgical experience with EPS shows recurrence in approximately 23% of patients. The results of the present study suggest that peritoneal microvascular hyperplasia is a factor involved in recurrence, and that patients with recurrence may have an irreversible pathologic condition and may experience repeated recurrences.

Key words
Encapsulating peritoneal sclerosis, EPS, surgery, recurrence
divided by the repeated lysis of fibrin membranes with a sharp instrument (5). The surgery always starts with the adhesions that can be easily lysed. Thus, in many cases, adhesiolysis of the mesenteric side is performed first, and the encapsulated intestinal loops are lysed afterwards. If intestinal lysis is difficult, the capsules on the intestinal surface may simply be longitudinally cut; but the lesions causing intestinal obstruction must be removed. However, because the fibrin membranes are continuous with the altered peritoneum, no serosa are present, making it difficult to identify the plane of separation. Subsequent development of severe peritoneal calcification makes the adhesiolysis more difficult. Errors in the adhesiolysis procedure or careless intestinal traction can easily result in intestinal perforation.

The surgical procedure for EPS is simple in requiring only cutting and division of adhesions with surgical scissors; it can be performed by any digestive surgeon. However, it requires continuous, careful manipulation; the key to success is perseverance.

**Recurrence of EPS**

Surgery can remove the intestinal obstruction, but it does not improve peritoneal deterioration. In some patients, the capsules re-form, and EPS recurs after 6 – 12 months. In some patients with recurrence, enterolysis to remove the intestinal obstruction cannot be completed, reinforcing the severity of EPS as a complication of PD.

To identify the factors involved in recurrence, we compared 47 recurrent and nonrecurrent EPS patients whom we were able to follow for more than 2 years after initial surgery. We tracked PD duration, follow-up period, use or nonuse of steroid therapy after initial surgery, and pathology findings in the parietal peritoneum on laparotomy.

The pathology examination of the parietal peritoneum used hematoxylin and eosin stain and Masson–Noguchi modified stain. Based on the Williams classification (6), the thickness of the submesothelial compact zone of the parietal peritoneum and the degree of vascular sclerosis were evaluated on photomicrographs. Three microscopic fields were recorded for each specimen. In addition, the degree of inflammatory cell infiltration was determined, and the total number of microvessel cross-sections per peritoneal field was calculated according to the method of Numata (7):

\[
\text{relative microvessel number} = \frac{\text{total number of cross-sections}}{\text{width of peritoneal field at 3000 mm}}.
\]

Continuous data are expressed as mean ± standard deviation, and categorical data are expressed as number and percentage. Categorical data were compared using the chi-square test. Comparisons between groups were performed using the unpaired Student t-test. When the data were not normally distributed, a nonparametric analysis (Mann–Whitney test) was used. The nonrecurrent rate during follow-up was estimated by the Kaplan–Meier method. A difference was considered significant when the p value was less than 0.05.

**Results**

Table I lists our EPS patients seen to date. These patients were withdrawn from PD at a mean age of 43.9 years (range: 9 – 70 years) after receiving PD for a mean period of 120.5 months (range: 28.7 – 220.2 months). After

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Encapsulating peritoneal sclerosis (EPS) surgical cases, 1993–2005</th>
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<tbody>
<tr>
<td>Total cases (n)</td>
<td>86</td>
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<tr>
<td>Total surgeries (n)</td>
<td>112</td>
</tr>
<tr>
<td>Age at PD withdrawal [years (range)]</td>
<td>43.9 (9–69.9)</td>
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<tr>
<td>PD duration [months (range)]</td>
<td>120.5 (28.7–220.2)</td>
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<tr>
<td>Cases of EPS onset after withdrawal from PD [n (%)]</td>
<td>79 (91.8)</td>
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<tr>
<td>PD withdrawal to EPS onset [months (range)]</td>
<td>12.7 (0–64)</td>
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<tr>
<td>EPS onset to surgery [months (range)]</td>
<td>12.1 (1.0–84.0)</td>
</tr>
<tr>
<td>Cases given post-PD peritoneal lavage [n (%)]</td>
<td>27 (31.3%)</td>
</tr>
<tr>
<td>Cases with corticosteroid administration after EPS onset [n (%)]</td>
<td>66 (76.7)</td>
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* Excludes patients with EPS onset during PD.

PD = peritoneal dialysis.
withdrawal from PD, 79 (91.8%) developed EPS. After PD withdrawal, 27 patients (31.3%) underwent peritoneal lavage, and after the development of EPS, 66 patients (76.7%) received steroids. The mean time from development of EPS to surgery was 12.1 months (range: 1 – 84 months). Five patients (5.8%) died postoperatively of sepsis from intestinal perforation. In 3 patients, death occurred after a period of malnutrition and sepsis.

Of the 47 patients whom we were able to follow for more than 2 years, 11 (23.4%) experienced an EPS recurrence, 10 underwent a second surgery, and 4 required a third surgery. Except in 1 patient, the recurrence happened within 20 months of surgery, at a mean of 15.2 months (Figure 1).

Table II compares patients with and without EPS recurrence. We observed no differences in age, PD duration, period from EPS onset to surgery, period from first to second surgery, follow-up period, postoperative use or nonuse of steroids, thickness of the submesothelial compact zone, presence of the vasculopathy, or inflammatory cell infiltration. However, the number of peritoneal microvessels was significantly higher in the recurrent patients.

The number of microvessels per microscopic field was significantly higher in the patients with recurrence (Figure 2). Only 1 of the 20 patients with fewer than 10 microvessels per field had EPS recurrence, but EPS recurred in all 27 patients with more than 10 microvessels per field (Figure 3).

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Recurrent</th>
<th>Nonrecurrent</th>
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<tbody>
<tr>
<td>Age at PD withdrawal (years)</td>
<td>11</td>
<td>36</td>
</tr>
<tr>
<td>PD duration (months)</td>
<td>53±9.8</td>
<td>46.4±13.0</td>
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<tr>
<td>EPS onset to surgery (months)</td>
<td>122±55</td>
<td>113±41</td>
</tr>
<tr>
<td>Period from first to second surgery (months)</td>
<td>14.2±11.2</td>
<td>12.3±16.2</td>
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<tr>
<td>Follow up (months)</td>
<td>15.2±15.4</td>
<td>—</td>
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<tr>
<td>Corticosteroids administered after surgery [n (%)]</td>
<td>10 (91)</td>
<td>26 (72)</td>
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<tr>
<td>Peritoneal morphology</td>
<td></td>
<td></td>
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<tr>
<td>Thickness of submesothelial compact zone (µm)</td>
<td>8.7±3.6</td>
<td>11.6±6.3</td>
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<tr>
<td>Cases of vasculopathy [n (%)]</td>
<td>8 (72.7)</td>
<td>30 (85.7)</td>
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<td>Cases of infiltration cells [n (%)]</td>
<td>4 (36)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Relative microvessel numbers (n)</td>
<td>22±4.1</td>
<td>11±8.7 a</td>
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</tbody>
</table>

* p > 0.003.

PD = peritoneal dialysis.
A thorough understanding of the EPS development mechanism is necessary for EPS diagnosis. Two possible causative factors have been considered: deterioration of the peritoneum and intraperitoneal inflammation.

Peritoneal deterioration occurs as a result of long-term exposure to peritoneal dialysate or to repeated episodes of peritonitis. The pathologic characterization is peritoneal hypertrophy, degenerative sclerosis of the capillary vessels (6), and proliferative neoangiogenesis (7,8). The symptoms of EPS are initiated by adhesion of the deteriorated intestinal tracts, followed by encapsulation of the adhered lesions. Fibrin is considered to be a major component of the capsule, the deposition of which may lead to the development of EPS (9). Even in a case of early-stage PD, when peritoneal deterioration is not yet developed to a significant degree, the complications of intense bacterial peritonitis may readily lead to the development of EPS. Conversely, in a case of long-term PD with a deteriorated peritoneum, EPS may occur even after mild bacterial peritonitis. Furthermore, in a long-term case, EPS may occur by fibrin deposition without peritonitis.

In our 4-year prospective study of 1958 adult PD patients, EPS developed in 2.5%. However, the incidence increases rapidly after 8 years of PD, and prognosis is poor (10).

We use total parenteral nutrition (TPN), steroid therapy (11,12), and peritoneal adhesiolysis (5,13) to treat EPS. Improvement cannot be expected from TPN alone, and long-term TPN is associated with bacterial translocation and TPN catheter infection, resulting in sepsis and death.

Although steroids have been used in most patients, our prospective study showed that these drugs were effective in only half of the patient population (10). Steroids effectively suppress inflammation and prevent ascites and fibrin deposition, but they must be used immediately after onset to be effective (14). Timely administration of steroids terminates inflammation and prevents progression to a state of intestinal obstruction. However, delayed administration fails to prevent encapsulation leading to intestinal obstruction.

On recognizing that established EPS presents as intestinal obstruction, and that a radical cure for EPS presenting with prolonged symptoms of intestinal obstruction is enterolysis, we began performing complete enterolysis without enterectomy in 1993, and we have achieved a survival (improvement) rate of 94.2%.

Surgery relieves the state of intestinal obstruction, but it does not improve the peritoneal deterioration. As a result, re-encapsulation occurs in some patients 6 – 12 months after surgery, resulting in EPS recurrence. To avoid stimuli from surgical stress, steroids are administered before and after surgery. However, the usefulness of steroid administration is uncertain, because some patients later experience recurrence anyway. Because a second surgery facilitates oral food intake, we have performed repeat surgeries in the absence of other alternatives.

The pathologic features of EPS are peritoneal thickening and encapsulation. Encapsulation causes the main symptom of intestinal obstruction. The capsules are composed mainly of fibrin leaking from peritoneal microvessels (9), and their formation involves hyperplasia of the peritoneal microvessels (7,8). Yamamoto et al. (15) demonstrated similar findings, noting a significantly higher incidence of EPS in a group of patients with increased peritoneal permeability. Moreover, in the present study, the incidence of postoperative recurrence—that is, re-encapsulation—was significantly higher in the group with microvascular hyperplasia.

In the present study, no peritoneal equilibration test data were available from the PD course of the patients, and therefore we could not demonstrate an association between EPS and peritoneal permeability.
But the degree of microvascular hyperplasia varied between the patients with EPS. This variation may account for the development of EPS. That is, patients with mild microvascular hyperplasia may progress to EPS after some superimposed, strong, traumatic inflammation; conversely, those with marked microvascular hyperplasia may easily progress to EPS after mild stimuli.

At what point does the formation of fibrin capsules from hyperplastic microvessels end? The patient showing the most marked microvascular hyperplasia required four surgeries, all of which demonstrated encapsulation. Although 65 months have passed since PD was discontinued in this patient, we have observed no tendency toward improvement, suggesting the presence of irreversible changes.

Conclusions
Our experience with 112 surgeries for EPS in 86 patients shows that approximately 23% of patients experience recurrence and suggests that microvascular hyperplasia is involved as a factor in that recurrence. In these patients, EPS may recur repeatedly, suggesting the presence of an irreversible pathologic condition.

References

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