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【 CASE REPORT 】

The Capsule Endoscopy Findings in S-1-induced Enteritis with Severe Diarrhea during Adjuvant Chemotherapy for Gastric Cancer (with Video)

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Abstract:
Although S-1 chemotherapy is used widely as postoperative adjuvant chemotherapy for gastric cancer, some patients experience diarrhea during treatment. The patient was a 39-year-old woman who underwent distal gastrectomy for gastric cancer and who had started S-1 chemotherapy as postoperative adjuvant chemotherapy 1 week before her presentation. She experienced severe diarrhea immediately after starting the course of S-1 tablets. Capsule endoscopy revealed severe S-1-induced enteritis with extensive mucosal injury in the ileum and red intestinal fluid due to the oozing of blood in the ileum. After reducing the dosage of S-1, her diarrhea became milder, and she was able to continue S-1 chemotherapy.

Key words: S-1-induced enteritis, diarrhea, endoscopic findings, chemotherapy

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Introduction

Although S-1 chemotherapy, consisting of oral 5-fluoropyrimidine (5-FU), is used widely and effectively in Japan as postoperative adjuvant chemotherapy for advanced gastric cancer (1), some patients experience severe diarrhea during treatment. In a study using mouse intestine, it was found that 5-FU chemotherapy induced dysbiosis and small intestinal mucosal injury (which was caused by apoptosis) and suppressed the proliferation of intestinal cells and the expression of inflammatory cytokines (2). These complex events may cause small intestinal mucosal injury, which then results in diarrhea (2). The serum diamine oxidase activity is a sensitive indicator of gastrointestinal damage before the onset of symptoms, as demonstrated in a clinical trial of gastrointestinal toxicity in patients with gastric cancer (3). However, the endoscopic findings in the small intestine of patients with diarrhea during S-1 therapy have not been described.

In the present report, we describe the case of a patient who experienced S-1-induced enteritis with severe diarrhea while receiving S-1 chemotherapy as postoperative adjuvant chemotherapy.

Case Report

A 39-year-old Japanese woman who underwent distal gastrectomy and Roux-en-Y reconstruction for advanced gastric cancer started S-1 chemotherapy (tegafur/gimeracil/oteracil tablets, 100 mg/day) as postoperative adjuvant chemotherapy 1 week before her presentation. She experienced severe diarrhea immediately after starting the course of S-1 tablets; however, her bowel movements were normal after surgery. Her diarrhea persisted following the initiation of S-1 chemotherapy. Capsule endoscopy was performed 4 weeks later to investigate the cause.

Small bowel capsule endoscopy revealed multiple ulcers, erosions, and diffuse erythema covering the entire circumference of her terminal ileum. The intestinal fluid was red due to the oozing of blood in the intestine. There were no remarkable findings in areas other than the terminal ileum.

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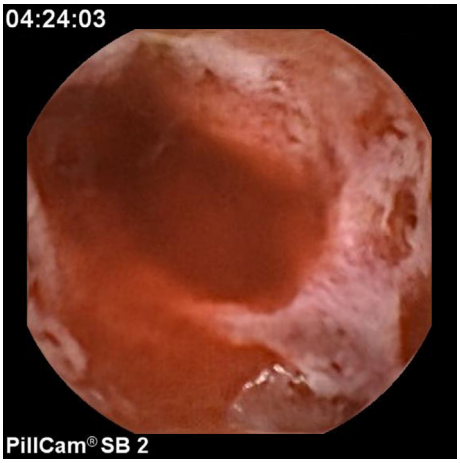

Figure. The capsule endoscopy findings included severe and extensive mucosal injury in the terminal ileum, reduced peristalsis, and red intestinal fluid, which was caused by the oozing of blood in the terminal ileum.

Peristalsis was reduced in the lesion area (Supplementary material, Figure). A blood test revealed hypoproteinemia (blood total protein level: 6.1 g/dL) and hypoalbuminemia (blood albumin level: 3.2 g/dL), although the blood test results were normal before S-1 chemotherapy. It was considered that her diarrhea was caused by S-1-induced enteritis, and the dosage of S-1 was reduced to 40 mg/day. Reducing the dosage of S-1 and the administration of intestinal regulators alleviated the diarrhea, and she was able to continue the S-1 chemotherapy. She received no non-steroid anti-inflammatory drugs (NSAIDs) or antibiotics during that period. This adjuvant chemotherapy lasted 1 year, and she has remained relapse-free for 3 years since completing the year of adjuvant chemotherapy.

Discussion

S-1 chemotherapy often causes severe diarrhea induced by intestinal mucosal injury (4). Tegafur is a prodrug of 5-FU, and gimeracil and oteracil are modulators of metabolism of 5-FU. Although oteracil was added to suppress the gastrointestinal toxicity of 5-FU by phosphorylation, it has been reported that the incidence of severe diarrhea requiring hospitalization among patients undergoing S-1 chemotherapy (7.0%) was significantly higher in comparison to those receiving conventional 5-FU via a continuous intravenous infusion (0.4%) (5). Gimeracil is an inhibitor of dihydropyrimidine dehydrogenase (DPD), which metabolizes 5-FU (6). The DPD activity varies among individuals, and the administration of gimeracil allows for a sufficient concentration of 5-FU to be maintained in patients with high levels of DPD activity (7). In contrast, patients with low levels of DPD activity may experience more severe adverse events.

In the present patient, enteritis was clearly caused by the S-1 chemotherapy, since the symptoms improved after the dose was reduced. The capsule endoscopy findings of patients with enteritis caused by anticancer drugs have not been described. Capsule endoscopy allows for the entire small intestine to be observed, even in patients with severe symptoms, and is also suitable for determining the state of the intestinal fluid and examining peristalsis. It was revealed that the current patient with S-1-induced enteritis had extensive mucosal injury in the terminal ileum, reduced peristalsis, and red intestinal fluid due to the oozing of blood. Although she had severe enteritis, her general condition did not require hospitalization. The blood test revealed only mild hypoproteinemia and hypoalbuminemia. Despite the presence of severe diarrhea, there was no tarry stool or anemia. Thus, many patients undergoing S-1 chemotherapy may have similar changes in their small intestine. It is possible that the adverse events associated with the administration of 5-FU were exacerbated by an unusually low level of DPD activity. A clinical study is necessary to determine the pathogenesis of S-1-induced enteritis and to prevent the induction of diarrhea by anticancer drugs.

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

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