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A case of spontaneous intestinal perforation following cytotoxic therapy of a primary multiple malignant lymphoma

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ABSTRACT

We report a case of diffuse large B cell lymphomas in the small intestine with perforative peritonitis. A 55-year-old man presented with the chief complaint of spontaneous back pain and was diagnosed as having multiple primary malignant lymphoma of the small intestine with a metastatic vertebral tumor after undergoing a complete medical examination. The patient thereafter underwent chemotherapy accompanied by radiotherapy. After the third week of medication was completed, the patient started complaining of severe abdominal pain. Abdominal computed tomography revealed free air. An emergency laparotomy confirmed a diagnosis of perforative peritonitis. Multiple white nodules were observed in the small intestine approximately 10 cm to 280 cm from the ligament of Treiz. The site of perforation correlated with one of the nodules. Partial resection of the small intestine was performed. Histological examinations revealed an abscess and inflammation of the serous side of the intestine, and no malignant cells. These findings suggested that the thickened wall of the ulcer may have been the result of the chemo-radiotherapy and thus was considered to be the cause of the perforation. We recommend that caution should be taken in case of perforation, because an excellent outcome after surgical intervention depends on an early diagnosis and prompt exploration. Ryukyu Med. J., 23(1,2) 39~43, 2004

Key words: diffuse large B cell lymphoma, perforative peritonitis, small intestine

INTRODUCTION

Spontaneous perforation of the gastrointestinal tract is an uncommon but life-threatening complication of systemic chemotherapy for malignant lymphoma. We herein report a case of spontaneous intestinal perforation associated with cytotoxic therapy and steroid treatment of malignant lymphoma.

CASE

A 50-year-old man was admitted to the department of orthopedics of our hospital with back pain and numbness. Examination revealed that the pain and numbness below the T10 level were due to a metastatic vertebral tumor (Th 6~7) in January 1999. He was transferred to the Internal Medicine department and was diagnosed as having intestinal malignant lymphoma (diffuse large B cell type) based on the findings of a general examination and pathological findings of biopsy specimens.1) (Fig.1, 2) After three cycles of combined chemotherapy with Cyclo-BEAP (70 mg of Adriamycine day 1,3,5, 1500 mg of Cyclophosphamide day 1,5, 70 mg of Endoxan day 3, 15mg of Bleomycm day 5 and 40 mg of Pledonisolone everyday) and 30 Gy of radiotherapy, he suddenly began to experience abdominal
Lymphoma of the small intestine with perforated peritonitis

Fig. 1 Barium meal radiography of the small intestine revealed multiple lesions of filling defects with a smooth surface in the ileum.

Fig. 2 Histology of the biopsied specimen from the ileum showing diffuse pleomorphic lymphoid cells (left: H-E). The lymphoma cells stained positively for L26 (right) but negatively for UCHL1, bcl-1, bcl-2 and keratin.

Fig. 3 Pathological findings of the resected specimen showed a severe inflammation with foreign body and abscess formation on the serous side at the perforation (left). No carcinoma cells were detected in the resected specimen includes multiple nodular areas (right).

pain and showed evidence of peritonitis. A computed tomography scans revealed pneumoperitoneum. At emergency laparotomy, a small perforation of the jejunum with multiple areas of macroscopic lymphomatous involvement was found. A resection of the small intestine, including the perforation and multiple nodular areas, was thus performed. Histological findings, a severe inflammation with foreign body and abscess formation on the serous side of the small intestine, and no carcinoma cells were detected, confirmed a spontaneous perforation of the jejunum. (Fig. 3) In addition, there were no carcinoma cells in the multiple nodular areas. He recovered from his illness 22 days after the surgical procedure and thereafter underwent an additional combined chemotherapy. He is presently being treated on an outpatient basis and has shown no evidence of the disease as of March 2002.

**DISCUSSION**

Primary malignant lymphoma of the small intestine is a rare disease. The percentage of primary small intestinal involvement reported in literature ranges from 20% to 40% of malignant small intestinal tumors and less than 1% of gastrointestinal malignant tumors. In studies concerning primary malignant lymphoma of the small intestine, NHL (non-Hodgkin's lymphoma) is relatively rare representing approximately 7% of extranodal lymphomas. The age group most frequently affected is 50 years and beyond in Japan. Also, there is just a slight predominance for the male sex (about two thirds of the patients were males). In addition, perforations occur in 8% to 47% of all cases. Therefore, we cannot disregard the incidence of a perforation.

Some types of intestinal lymphoma are known to be highly sensitive to chemotherapy and radiotherapy.
Several studies have reported an increased survival following adjuvant radiotherapy or chemotherapy. Therefore, operative approaches are not considered to be more advantageous than conservative treatment in gastric lymphoma cases. A study has shown that patients with small bowel lymphomas have a lower complete or partial remission rate than those with gastric lymphomas. Furthermore, when a lymphoma invades the walls of the intestine or shows an ulcerative lesion, and is effectively treated with chemotherapy, tumor necrosis with perforation is a potential complication.

In patients with primary malignant lymphomas of the small intestine, the diagnosis is difficult because most of the patients do not present with typical symptoms and physical findings until either the disease progresses or the tumor becomes enlarged. Previous studies have reported the morbidity and mortality of gastrointestinal perforation to be high. However, almost all cases reported the spontaneous perforation as the first symptom, with most of the cases having a severe preoperative condition.

From April 1985 through April 1999, 45 patients with primary gastrointestinal malignant lymphomas were admitted to our surgical division. The tumor sites were as follows: stomach (42, 93.3%), small intestine (2, 4.44%), and colon (1, 2.22%). Three cases had perforations (6.7%); all 3 were males from 55 to 58 of an age. However, the patient discussed in this study was the first to demonstrate a perforation of the small intestine. The data obtained in our previous cases corresponds to the findings of other investigators.

A pathological examination revealed that lymphoma cells could not be detected from tissue specimens from all sites in this patient. The findings of this patient thus differ from those of most other previous reports, therefore the perforation was considered to be due to tumor lysis of the small intestine.

Controversy remains in literature regarding the need for surgical debulking. Some investigators have argued that the physical removal of as much tissue may reduces the risk of complications due to chemotherapy or radiotherapy, such as hemorrhage or perforation, while others have argued that this is not the case. However, almost all these reported cases were treated or diagnosed chiefly by surgical resection. The latter opinions therefore were probably due to the high proportion rate of patients with evidence of MALT (mucosal associated lymphoid tissue) type gastric lymphoma, since the survival of such patients was high in this series. One major difference regarding our case was that the patient was diagnosed without the surgical approach and received chemo-radio therapy.

It has been recently reported that perforation has been found not to be an independent prognostic factor based on a multivariate analysis. However, in fact, when a spontaneous perforation occurs in patients receiving systemic chemotherapy, they may deteriorate and severe endotoxin shock can easily occur due to immunodepression. Therefore, spontaneous gastrointestinal perforation is a potentially lethal complication of anti-lymphoma therapy. An excellent outcome can be expected for surgical intervention in a patient who is diagnosed and is indicated to undergo chemotherapy, as in our case, when an early diagnosis and prompt exploration is performed, and when resection of the tumor with an ulcer is done before chemotherapy. It is possible that the risk of the above described lethal complication may be decreased this way.

In conclusion, a resection of such lesions before chemotherapy and/or radiotherapy should thus be considered for patients having intestinal lymphomas with ulceration. In addition, we recommend that patients who complain of abdominal pain should be checked for the presence of perforation if they are receiving chemotherapy or radiotherapy for lymphoma, because tumor necrosis with perforation is one potential complication of these therapies. An excellent outcome after surgical intervention in such cases is attributed to an early diagnosis and prompt exploration.

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REFERENCES


