

Small Bowel Perforation Caused by Metastasis from an Extra-Abdominal Malignancy: Report of Three Cases

NORIHITO ISE¹, HITOSHI KOTANAGI¹, MAYAKO MORII¹, OUKI YASUI¹, MASANAO ITO¹, KENJI KOYAMA¹, and MASATO SAGESHIMA²

¹Department of Surgery and ²Department of Clinical Pathology, Akita University School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan

Abstract Small bowel perforation is rarely caused by metastasis from an extra-abdominal malignancy. This report describes three cases of small bowel perforation that occurred secondary to a metastatic tumor. The first case involved a 72-year-old man with malignant lymphoma of the larynx that had been treated with chemo- and radiation therapy; the second involved a 70-year-old man with rhabdomyosarcoma of the mediastinum that had been treated with radiation therapy; and the third involved a 41-year-old man with lung carcinoma that had been treated with surgery 10 months prior to perforation. Each patient presented with acute abdominal pain, had X-ray findings of free air in the abdomen, and underwent limited emergency surgery. Wedge resection and closure of the ileum was performed for the first patient and partial bowel resection with the creation of an intestinal stoma was performed for the second and third patients. In each case, the histologic findings of the resected specimens were consistent with the extra-abdominal primary tumors. Although the patients recovered sufficiently to begin eating and moving about, all three died of cancer or cancer-related complications within 45 days of surgery. We conclude that surgeons should be aware of the poor prognosis of such patients and perform only the minimal surgery required.

Key words Small bowel perforation · Metastatic tumor · Malignant lymphoma · Rhabdomyosarcoma · Lung cancer

Introduction

Metastasis to the small intestine can cause various symptoms, such as obstruction, malabsorption, hemorrhage, and perforation, but intestinal obstruction is the most common.^{1,2} The most common metastases to invade the small bowel are of gastrointestinal or gynecologic origin, such as those arising from the colon, uterine cervix, or ovaries.² On the other hand, small intestinal perforation occurring secondary to a metastatic tumor, especially from an extra-abdominal malignancy, is rare.^{3,4} As a result, the pathogenesis and surgical treatment of this entity has received little attention and is poorly understood. We report herein three cases of small bowel perforation that occurred secondary to a metastatic tumor from an extra-abdominal malignancy. One of these three cases involved an ileal perforation resulting from metastatic rhabdomyosarcoma of the mediastinum which, to the best of our knowledge, has never been reported.

Case Reports

Case 1

A 72-year-old man with a diagnosis of malignant lymphoma (B-cell type) of the larynx was admitted to our hospital in December 1991 to undergo electron beam therapy and chemotherapy with steroids for metastatic cervical nodes. Early in February 1992, he presented again with acute abdominal pain and rebound tenderness. X-ray films revealed free air in the abdomen. He was transferred to our department where emergency surgery was performed. Laparotomy disclosed the presence of purulent fluid containing bile juice in the peritoneal cavity. An ileal perforation, 1 cm in diameter, was found 30 cm proximal to the ileocecal valve. Grossly, no evidence of a tumor was found in the peritoneal cavity.

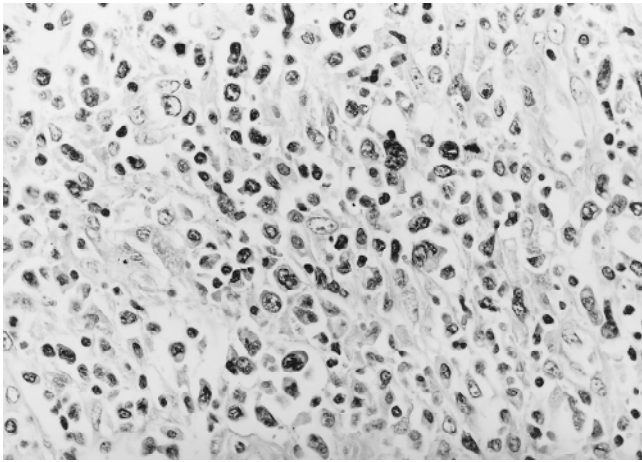


Fig. 1. Histologic findings of the resected specimen from case 1. The infiltration of atypical lymphoid cells was found around the ulcer (H&E, $\times 400$)

Under the suspected diagnosis of ileal involvement from malignant lymphoma, we performed a wedge resection and closure of the perforated ileum. The resected specimen contained a “punched-out” ulcer with perforation, and histologic examination revealed the infiltration of lymphoma cells around the perforation site (Fig. 1). The patient’s postoperative course was uneventful; he recovered sufficiently to begin eating and move about. On the 24th postoperative day, he was transferred to a medical ward for further treatment of the malignant lymphoma; however, jaundice of unknown origin developed soon after the transfer. His liver function deteriorated and eventually failed without any response to treatment. He died 17 days after the transfer.

Case 2

A 70-year-old man presented to a local hospital with a sore throat and was diagnosed with tonsillar carcinoma. He was referred to our hospital for radiation therapy in late March, 1999. On admission, chest X-ray films revealed a 10-cm tumor in the anterior mediastinum. Tumor biopsy disclosed rhabdomyosarcoma, and the patient was given radiation at 61 Gy to the affected tonsil and the mediastinum. In early May, he complained of a headache and a brain computed tomography (CT) scan disclosed a metastatic tumor, 3 cm in diameter, in the left occipitoparietal region, for which radiation therapy was begun. On May 30, 1999, he experienced severe abdominal pain and X-ray films revealed free air under the diaphragm. He was transferred to our department where emergency surgery was performed. Laparotomy revealed purulent ascites in the peritoneal cavity. A tumor in the mesentery, $10 \times 8 \times 6$ cm in size,

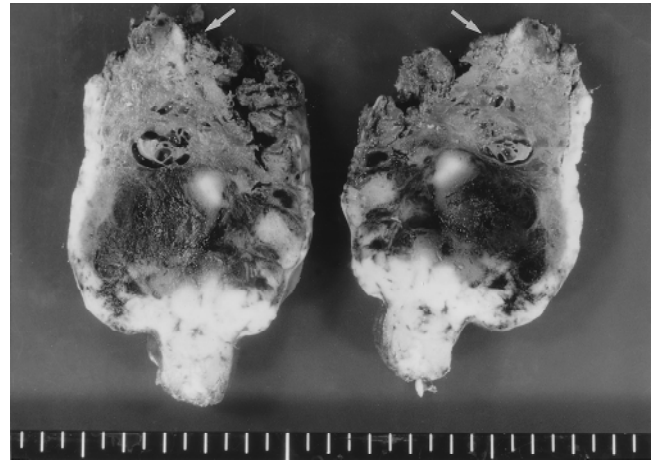


Fig. 2. Resected specimen from case 2. Cut surface of the mesenteric tumor showed a variety of components, including a cystic area, a medullary area, and a necrotic area, with bleeding. The ileum was compressed by the tumor (*arrows*)

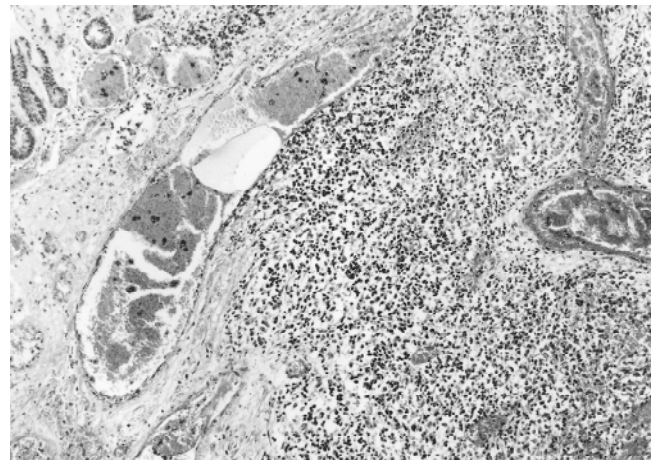


Fig. 3. Histologic findings of the resected specimen from case 2. The intramural infiltration of sarcoma cells with bleeding and necrosis was observed. The infiltrating cells were consistent with rhabdomyosarcoma (H&E, $\times 100$)

had caused free perforation of the ileum 100 cm proximal to the ileocecal valve. No liver or peritoneal tumor involvement was found. The part of the ileum with the tumor was resected, and an ileostomy was created. Cross section of the tumor showed a variety of components, such as cystic areas, medullary areas, and necrotic areas, with bleeding. The ileum was compressed by the tumor (Fig. 2). Histologic examination of the ileum revealed intramural cell infiltration and bleeding with necrosis. It was suggested that the perforation of the ileum had been forced by compression of the tumor (Fig. 3). The tumor consisted of polygonal and spindle cells with eosinophilic cytoplasm positive for periodic acid-Schiff stain. Immunohistochemical analysis revealed that



Fig. 4. Intraoperative findings in case 3. One of the mesenteric tumors had caused a free perforation of the jejunum (*arrow*)

some of these cells were also positive for myoglobin and desmin. S-100 protein, nonspecific enolase, α -smooth muscle actin, epithelial membrane antigen, and keratin were not detected. These findings were consistent with a mediastinal tumor. The histologic diagnosis was metastatic rhabdomyosarcoma. On the 14th postoperative day, the patient was transferred to the Department of Radiology to undergo further radiation therapy for the metastatic brain tumor; however, he died of pneumonia 15 days later.

Case 3

A 41-year-old man underwent a right upper lobectomy for large cell carcinoma of the lung in September 1998, 2 months following which metastatic tumors were found in his adrenal glands. Treatment with anticancer drugs was initiated, which failed to inhibit the tumor growth. In June 1999, the patient experienced abdominal pain, and an X-ray showed free air in the abdominal cavity. He was transferred to our department where emergency surgery was performed. Laparotomy revealed purulent ascites and several mesenteric tumors, 5–7 cm in diameter (Fig. 4). One of the tumors had caused a free perforation of the jejunum 120 cm distal to the Treitz ligament. Multiple liver metastases and para-aortic lymph node metastases were observed. A 17-cm portion of the jejunum containing the mesenteric tumor was resected and a double-barreled jejunostomy was created. Histologic examination revealed that cancer cells, which were consistent with large cell carcinoma of the lung, had infiltrated into the jejunal wall via lymphatic vessels (Fig. 5). The patient was transferred to a hospice facility on the 19th postoperative day in a stable condition, but died of cancer 26 days later.

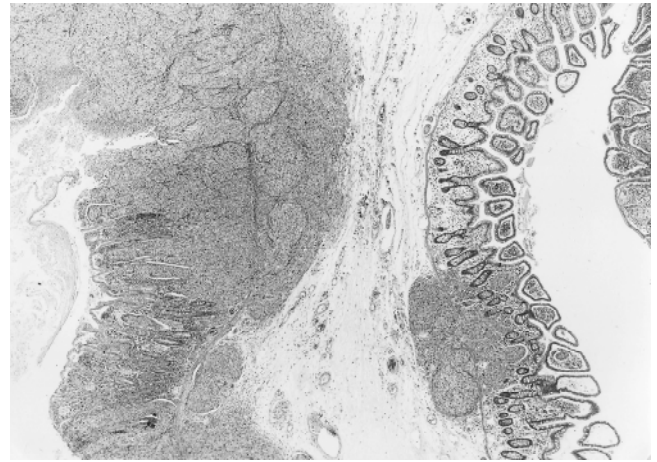


Fig. 5. Histologic findings of the resected specimen from case 3. Extensive infiltration of anaplastic carcinoma cells into the small bowel wall was observed with necrosis. Tumor cells filled the lymphatic vessels. These observations were consistent with large cell carcinoma of the lung (H&E, $\times 10$)

Discussion

The most common extra-abdominal sites from which small bowel metastases are reported to occur are the skin (melanoma) and the lung. We found 478 cases of such metastases to the small bowel: 216 from melanoma of any part of the body surface,^{5,6} 162 from lung cancer,^{1,2,7–9} and the remaining 100 from malignant lymphoma,^{10,11} testicular tumor,¹² breast cancer,¹³ salivary gland tumor,¹⁴ esophageal cancer,¹⁵ and pulmonary rhabdomyosarcoma.¹⁶ Small bowel perforation occurred in 121 (25.3%) of the 478 cases.^{1,2,5–9,11} Our search of the Japanese literature revealed only 44 cases of small bowel perforation caused by metastatic lung cancer.^{7,8,17} Of 129 cases of metastatic bowel tumors reported by Ushio et al.,¹⁷ 12 (9.3%) involved metastasis to the small bowel from extra-abdominal malignancies: 10 from cancer of the lung, 1 from a melanoma of the leg, and 1 from a testicular cancer. Small bowel perforation occurred in only two of the ten patients with lung cancer.

We were not able to find any report of small bowel perforation due to metastatic rhabdomyosarcoma. In our case 2, the mediastinal tumor was thought to be the primary lesion, based on the chronologic appearance of the lesions, the lack of any reports of rhabdomyosarcoma of the small bowel, and the fact that metastasis would not develop in the mediastinum but would develop in the liver if the mesenteric tumor were primary. Richie et al. reported 12 cases of metastatic bowel tumors from extra-abdominal sites,³ including one case of metastasis from embryonal rhabdomyosarcoma in the

neck. That patient had presented with clinical signs of intestinal perforation, but only microscopic perforation was found in the resected bowel. To the best of our knowledge, our case 2 is the first reported case of small bowel perforation that occurred secondary to metastatic rhabdomyosarcoma.

Hermann et al. reported that of 366 patients who were not diagnosed with gastrointestinal involvement at any time during the course of non-Hodgkin's lymphoma, 156 (46%) were later found to have gastrointestinal involvement at postmortem examination.¹⁰ Furthermore, of 813 patients with non-Hodgkin's lymphoma, only 31 (4%) showed clinical symptoms secondary to the gastrointestinal involvement. In these 31 patients, lymphoma cells involved the stomach in 20 patients, the small intestine in 3, the large intestine in 2, and several organs in 6. Clearly, small bowel perforation secondary to metastatic malignant lymphoma, as seen in our case 1, is a rare clinical event.

In describing the pathogenesis of bowel perforation secondary to metastatic carcinoma, Leidich et al. reported that mural replacement by tumor cells occurred after hematogenous or lymphatic metastasis, followed by necrosis.¹ Kaneda et al. described another three mechanisms of intestinal perforation, namely, ischemia of the intestine due to embolization of a metastatic tumor, increased intraluminal pressure due to intestinal obstruction, and necrosis of metastatic tumors due to chemotherapy.¹⁸ According to Wada et al., the most common factor attributing to bowel perforation in patients with malignant lymphoma is the use of systemic chemotherapy and steroids which induces tumor necrosis in the intestine.¹¹ Systemic chemotherapy with steroids had been given to our case 1; however, instead of any intensive necrosis around the perforation site, we found ulceration surrounded by lymphoma cells. We believe that the bowel perforation in case 1 occurred following the infiltration of lymphoma cells into the bowel wall through the lymphatic vessels. The mechanical action of the bowel resulted in mucosal ulceration, the depth of which increased gradually with the depth and degree of lymphoma cell infiltration, until eventually, with the increase in intraluminal pressure, the bowel wall ruptured.

In our cases 2 and 3, the metastatic tumor was found in the mesentery, suggesting that a mesenteric tumor directly invaded and compressed the adjacent bowel, causing necrosis of the bowel wall and, eventually, bowel perforation. We are unable to explain how the metastatic tumor grew so large in the intestine and mesentery in these patients. To clarify the mechanism, it might be necessary to examine the expression of cell adhesion molecules and growth factors, which are reported to be closely related to cancer metastasis and the growth of such tumors.

Shiraishi et al. reported seven cases of bowel perforation due to a metastatic tumor: two from lung cancer, three from malignant lymphoma of the larynx and lung, one from cervical cancer, and one from pleural mesothelioma.¹⁹ All of these metastases were found to be hematogenous, and were isolated and located exclusively in the ileocecal region. In our cases 1 and 2, the route of metastasis from the primary tumor to the small bowel or mesentery may have been hematogenous; however, in case 3, cancer cells apparently metastasized to the small bowel via a lymphatic route, as shown in Fig. 5. None of our metastatic tumors were isolated in the ileocecal region. Shiraishi et al. were unable to demonstrate an exact mechanism through which metastasis targeted the ileocecal region via a hematogenous route. We believe it is possible that cancer can metastasize via any route and to any part of the intestine.

Although patients with bowel perforation must undergo emergency surgery, obviously when it is caused by a metastatic tumor, their prognosis is extremely poor. Shiraishi et al. reported only one patient who survived for more than 5 years after resection of a perforated ileum resulting from metastasis of malignant lymphoma of the larynx, and six patients who died of cancer or cancer-related complications within 6 months.¹⁹ Bowel perforation secondary to metastasis from extra-abdominal malignancy is thought to occur in the late terminal stage of cancer. Even when metastatic tumors exist in the bowel, patients may live a little longer if bowel perforation does not occur, as the stress resulting from both the perforation and the necessary surgery cuts their life short. When considering the best operative course for patients with bowel perforation resulting from a metastatic tumor, it may be most appropriate to partially resect the bowel including the perforated lesion and create a stoma to avoid the possibility of anastomotic insufficiency.

In conclusion, surgeons should be aware of the poor prognosis of patients with bowel perforation secondary to metastatic tumor and, to promote their quick recovery, perform the least stressful operation necessary. In addition, we recommend further investigation of the mechanism of bowel perforation and mechanism of metastasis to the intestine from extra-abdominal malignancies. Such studies might reveal that some metastatic tumors within and/or adjacent to the bowel should be resected prophylactically before perforation occurs.

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