Appendiceal perforation with intra-abdominal free air due to metastatic appendiceal carcinoma from gastric carcinoma

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Abstract

A 54-year-old woman with advanced gastric cancer underwent emergency laparotomy following diagnosis of digestive tract perforation with peritonitis. Abdominal roentgenography showed intra-abdominal free air, and laboratory tests showed significant inflammation. Intraoperatively, a perforation approximately 1 mm in diameter was confirmed in the appendix wall. Macroscopically, there were no definite findings of metastasis and peritoneal dissemination from gastric cancer. Appendectomy was performed after diagnosis of appendiceal perforation due to acute appendicitis. Light microscopic examination of the resected appendix showed that gastric carcinoma cells predominantly infiltrated from the appendiceal serosa to the muscular layer of the appendix wall. Only appendectomy was performed, and the patient was then treated with an anticancer drug for primary gastric cancer.

Metastatic appendiceal carcinoma is rare but several cases of metastatic appendiceal carcinoma from gastric cancer have been reported. We report the first case of appendiceal perforation with intra-abdominal free air due to metastatic appendiceal carcinoma from gastric cancer.

Introduction

Metastatic appendiceal carcinoma is rare, and it can complicate acute appendicitis with severe inflammation and perforation. Among 34 cases of metastatic appendiceal carcinoma from gastric cancer have been reported in the Japanese literature, there have been no reports of this being associated with intra-abdominal free air. Here, we report the first case of appendiceal perforation with intra-abdominal free air due to metastatic appendiceal carcinoma from gastric cancer and discuss this rare case.

Case Report

A 54-year-old woman with advanced gastric cancer was admitted to our hospital for examinations before an operation. Endoscopy revealed an ulcerative lesion, with foci of necrosis and hemorrhage, at the greater curvature, extending from the antrum to the body of the stomach. Gastric biopsy revealed a poorly differentiated adenocarcinoma. An upper gastrointestinal radiological study, which was performed according to the General Rules of the Japanese Gastric Cancer Association (JGCA), revealed type 4 gastric cancer.

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FIG. 1 Abdominal roentgenography showed intra-abdominal free air in the right subphrenic space (arrow).

FIG. 2 Macroscopic appearance of the resected appendix, showing perforation about 1 mm diameter in the appendix wall.

Five days after hospitalization, she had experienced lower abdominal pain with Blumberg sign and high grade fever. Laboratory tests showed significant inflammation (white blood cells [WBC], 16,000/ul; C-reactive protein [CRP], 40.69 mg/dl). The serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19-9) were within normal limits. Abdominal roentgenography showed intra-abdominal free air, and the remainder of the barium was used for upper gastrointestinal radiological study in the intestinal tract (Fig. 1). Accordingly, perforation with peritonitis was diagnosed, and an emergency laparotomy was performed. Intra-operative findings, revealed serious yellow ascites and a significant amount of fibrin components in the surrounding appendix and pouch of Douglas. There were no definite findings of metastasis and peritoneal dissemination from gastric cancer. The mesoappendix was thick and edematous, and perforation approximately 1 mm diameter was confirmed in the appendix wall. Macroscopically, invasion of gastric cancer to the serosa of the gastric wall was confirmed, but no perforation was revealed. Moreover, there was

FIG. 3A A low-magnification photomicrograph of perforation site of the resected appendix (H & E, ×10).

FIG. 3B Atypical cells similar to gastric carcinoma cells were seen in the appendix wall at a higher magnification (H & E, ×400).

FIG. 3C Immunohistochemical staining for cytokeratin (CAM5.2) shows diffuse positive in the atypical cells (×400).
no other intestinal perforation. Only appendectomy was performed after diagnosis of appendiceal perforation due to acute appendicitis. Macroscopic findings of the resected appendix were as follows, length of the appendix was about 5 cm, and perforation about 1 mm in diameter contralateral to the mesoappendix was confirmed (Fig. 2). Mucosa of the resected appendix was intact, and no neoplasm was revealed by macroscopic examination. Light microscopic examination showed that atypical cells similar to gastric carcinoma cells predominantly infiltrated from the appendiceal serosa to the muscular layer of the perforated appendix wall (Fig. 3a-b). These atypical cells showed positive granules in the cytoplasm when periodic acid-Schiff (PAS) staining was performed. Immunohistochemical staining, revealed that the atypical cells were strongly positive for cytokeratin (CAM5.2) (Fig. 3c) and CEA. After operation, the cytology of intra-operative ascites was strongly suspicious for gastric cancer cells. As a consequence of these pathological and cytological findings, these atypical cells were diagnosed to be metastatic appendiceal carcinoma from gastric cancer. The mechanism of metastasis to the appendix from gastric cancer was considered to be peritoneal dissemination. The postoperative course was been good, and she was subsequently treated with an oral anticancer drug (1 M tegafur-0.4 M gimestat-1 M otastat potassium, TS-1: 100 mg/day) for primary gastric cancer with peritoneal dissemination from December 25, 2004. The patient remains alive 12 months after the operation, and careful follow-up is being performed.

Discussion

Cancer metastasis to the appendix is very rare. Gillesse et al.20 studied 37 cases, in 1987, and six of these had the primary cancer in the stomach. In Japan, there were 52 reported cases of cancer metastasis to the appendix, as best we could determine on searching, between January 1979 and October 2004; and in these cases, the primary lesions were gastric cancer in 32 cases (61.5%)12-13, lung cancer in 9 (17.3%)10, gallbladder cancer in 4 (7.7%)10, breast cancer in 4 (7.7%)10, liver cancer in 110, colon cancer in 1, and pancreas cancer in 1. A clinical pathological study of 32 reported cases of metastasis of gastric cancer to the appendix, in Japan, revealed that the age of onset ranged from age 34 to 81 years (average, 62.3 years); the gender mix was 24 men, eight women (Table 1). As to the onset mechanism, onset of acute appendicitis after resection of gastric cancer was the most common, in 16 cases (50.0%), followed by discovery of gastric cancer at surgery for acute appendicitis, in 9 cases (28.1%); onset of acute appendicitis before surgery for gastric cancer, in 4 cases (12.5%), including this case, and finding the metastatic appendiceal carcinoma through appendectomy during surgery for gastric cancer, in 3 cases (9.4%). As to the appendix itself, gangrenous appendicitis or perforation was also found in 17 cases. As best we could determine, each primary gastric cancer was an advanced state, and the histological types were well-differentiated tubular adenocarcinoma (tub1) and moderately differentiated tubular adenocarcinoma (tub2) in 14 cases, and poorly

| Table 1 Summary of cases with metastatic appendiceal carcinoma from gastric cancer reported in Japan |
|----------------------------------|------------------|------------------|
| Male : Female | 24 : 8 |  |
| Age (years) | mean : 62.3 (range, 34-81 years) |  |
| Onset mechanism |  | Findings of the appendix |
| Acute appendicitis after resection of stomach cancer | 16 (50.0%) | Gangrenous appendicitis or perforated 17 (53.1%) |
| Discovery of stomach cancer at surgery for acute appendicitis | 9 (28.1%) | Phlegmonous appendicitis 3 (9.4%) |
| Acute appendicitis before surgery for stomach cancer | 4 (12.5%) | Catarhal appendicitis 0 |
| Finding the metastatic appendiceal carcinoma through appendectomy during surgery for stomach cancer | 3 (9.4%) | Normal 1 (3.1%) |
| Others | 6 (18.8%) |  |
| Unknown | 5 (15.6%) |  |
| Primary gastric cancer |  | Histology of the gastric cancer |
| Early state | 0 | tub 1 or tub 2 14 (43.8%) |
| Advanced state | 28 (87.5%) | por or sig 10 (31.3%) |
| Unknown | 4 (12.5%) | unknown 8 (25.0%) |
| Mechanism of metastasis to the appendix |  | Operation |
| Peritoneal dissemination | 12 (37.5%) | Appendectomy 27 (84.4%) |
| Lymphogenous | 8 (25.0%) | Cecalectomy 2 (6.3%) |
| Hematogenous | 2 (6.3%) | Ascanectomy 1 (3.1%) |
| Unknown | 10 (31.3%) | Unknown 2 (6.3%) |

* tub 1 : well differentiated tubular adenocarcinoma * tub 2 : moderately differentiated tubular adenocarcinoma  * por : poorly differentiated adenocarcinoma  * sig : signet ring cell carcinoma
differentiated adenocarcinoma (por) and signet ring cell carcinoma (sig) in 10 cases, showing no significant difference. Regarding the mechanism of metastasis to the appendix, peritoneal dissemination was the most common, in 12 cases (37.5%), including this case, lymphogenous metastasis occurred in 8 cases (25.0%), hematogenous metastasis occurred in 2 cases (6.3%), and the route of metastasis was unknown in 10 cases.

As the mechanism of metastasis of gastric cancer to the appendix in this case, primary gastric cancer invaded the serosa of the gastric wall; cytodiagnosis of ascites was strongly suspicious for gastric cancer cells, and cancer infiltration was noted from the appendiceal serosa side to the muscularis; as such, the mechanism was considered to be disseminated metastasis. Cancer metastasis to the appendix is known to cause an internal pressure increase and stasis, because cancer invasion blocks the appendiceal lumen, resulting in serious appendicitis. In this case, histopathological findings did not show tumor invasion to the appendiceal mucosa, and the membrane surrounding the perforation site was maintained, such that the findings did not actually indicate acute appendicitis that could cause perforation. The cause of occurrence of perforation was considered to be lowered immunological function due to the tumor-bearing state, accompanied by direct invasion of stomach cancer from the appendiceal serosa and cancerous peritonitis. Further, a speculated possibility was the thinning of walls of appendiceal diverticula, etc., because the appendiceal perforation site was pin-point in size, but a histopathologically definitive diagnosis could not be obtained.

This case is very rare in that intra-abdominal free air was generated with perforation of the vermiform appendix. Generally, intra-abdominal free air is unlikely to be generated with appendiceal perforation due to appendicitis. The reason is that, in appendicitis that causes perforation, the appendiceal lumen becomes blocked due to edema of appendiceal mucosa or fecal calculus, which blocks patency to the colon, and gas in the intestinal tract is not released into the abdominal cavity. Another reason is that the perforation site is quickly sealed over with greater omentum. In this case, perforation was caused by cancer invasion from the appendiceal serosa side, histopathological findings of appendicitis were few, and the appendiceal lumen was maintained. Also, the perforation site was contralateral to the mesoappendix, and it could not be easily sealed over. These factors can be considered to have caused the generation of intra-abdominal free air.

In this case, a possibility of gastrectomy at the same time as an appendectomy was considered, but the primary lesion, which was gastric cancer, had invaded the serosa; and, considering the possibility of non-radical surgery due to peritoneal metastasis, stress to the patient due to emergency surgery, and safety, only an appendectomy was performed. The prognosis of peritoneal dissemination of stomach cancer is poor, but there are some reports that TS-1 is effective to peritoneal dissemination of stomach cancer. In this case, the patient was treated TS-1, and careful follow up has performed. After encountering this case, our view is that when a patient with cancer, or a history of surgery for a malignant tumor, has peritonitis or acute appendicitis-like symptoms, it is important to conduct as complete an intra-abdominal search during surgery as possible, and to select an optimal surgery method, always keeping in mind the possibility of cancer metastasis to the appendix. We consider it is also important to conduct histopathological testing on the removed appendix, in order not to miss cancer metastasis to this organ.

References


腹腔内遊離ガスを生じた胃癌虫垂転移による虫垂穿孔の1例

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【要旨】 転移性虫垂癌はまれな疾患であり、穿孔を伴う重篤な虫垂炎を呈することが多い。本邦において胃癌の虫垂転移例の報告が散見されるが、腹部内遊離ガスを生じた虫垂穿孔例は認められない。今回われわれは、腹部内遊離ガスを生じた胃癌虫垂転移による虫垂穿孔の1例を経験したので文献的考察を含め報告する。症例は54歳、女性。胃癌の診断にて術前聴覚目的のため入院となる。入院時より腸部を中心とした腹痛を認め、徐々に増強。入院後5日目より発熱および腹膜刺激症状を伴った下腹部痛を認め、血液生化学所見にて白血球16,000/ul、CRP 40.69と高度の炎症反応を認めた。腹部単純X線検査にて腹部内遊離ガス像を認め、消化管穿孔および腹膜炎の診断にて緊急開腹術を施行した。腹腔内には淡黄色の腹水とダグラス囊および虫垂周围には著明な膿苔の付着を認めた。虫垂周囲には浮腫および肥厚と虫垂壁には径1mm大の穿孔部を認めた。急性虫垂炎による虫垂穿孔の診断にて虫垂切除術およびドレナージ術を施行した。病理組織診断にて、摘出した虫垂壁の穿孔部にPAS染色陽性の細小異型細胞を認め胃癌の転移に矛盾しない所見であった。本症例は、摘出標本観察および病理組織所見において虫垂内癌は保たれており、さらに虫垂粘膜部の炎症は軽度で穿孔を伴うほどの急性虫垂炎の所見に乏しいため、癌膜側からの癌細胞転移・浸潤が虫垂穿孔による腹腔内遊離ガスを誘発したものと考えられた。

＜Key words＞ 虫垂、胃癌、急性虫垂炎、転移性癌