Surg Today
Jpn J Surg (1996) 26:508–512

SURGERY TODAY

Case Reports

Synchronous Lymphoma and Adenocarcinoma Occurring as a Collision Tumor in the Stomach: Report of a Case

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Abstract: We report herein the rare case of a 71-year-old man who was initially operated on under the diagnosis of advanced gastric cancer, but was subsequently found to have synchronous lymphoma and early adenocarcinoma of the stomach, confirmed by postoperative pathological examination. The patient had a history of lymphoma of the left tonsil, and histologically the gastric lymphoma was observed to be of the non-Hodgkin's, diffuse, large-cell type. Conversely, the gastric cancer was early well-differentiated tubular adenocarcinoma of type 0-IIa, according to the Japan Gastroenterological Endoscopy Society classification. The two tumors had collided at the fornix. The relationship between these two tumors is analyzed and the most appropriate methods of diagnosis and treatment are discussed.

Key Words: lymphoma, adenocarcinoma, collision tumor

Introduction

The majority of malignant tumors of the stomach are carcinomas, whereas sarcomas are relatively rare. In fact, lymphoma accounts for only 1%–5% of all malignant tumors of the stomach according to various reports.[1–5] Thus, the synchronous development of carcinoma and lymphoma in the stomach is extremely rare. Although gastric cancer is the most common cancer in Japan, only 34 cases of coexisting adenocarcinoma and lymphoma have been reported,[6–8] and only 6 cases from outside Japan have been documented in the English literature.[9–14] This report describes the case of a patient found to have synchronous lymphoma and early adenocarcinoma of the stomach occurring as a collision tumor.

Reprint requests to: N. Nishino
(Received for publication on Nov. 18, 1994; accepted on Jan. 5, 1996)

Case Report

A 71-year-old man was referred to our department in November, 1985, with a 6-week history of fatigue and loss of appetite. His weight had decreased by 5 kg over the 3 months prior to admission. A medical history revealed that he had been diagnosed as having lymphoma of the left tonsil 2 years earlier, for which he had received local irradiation with 44.8 Gy of cobalt-60 to the neck, as well as COP chemotherapy consisting of cyclophosphamide + vincristine + prednisone. Following this treatment, complete remission had been achieved. Histologically, the tonsillar tumor was confirmed to be stage IIa medium cell non-Hodgkin's lymphoma.

Physical examination revealed that the patient's general condition and nutritional status were good, and that his cardiorespiratory status and abdominal findings were normal. No lymph nodes were palpable. Laboratory studies, including a full blood count, hemogram, liver function tests, renal function tests, and urinalysis were normal, except for slight anemia with a Hb of 11.3 g/dl and a red blood cell count of $360 \times 10^4/\mu l$. The tumor markers CEA, α-FP, and CA 19-9 were within the normal range and a chest X-ray was also normal. An upper gastrointestinal contrast study demonstrated a large irregular mass in the fornix, and gastroscopy showed an irregular giant mass in the fornix extending to the cardioesophageal junction. There were several areas of ulceration and erosion over this irregular mass (Fig. 1a). A total of five biopsy specimens were taken from the part of the tumor near the cardia, and although three of these specimens demonstrated well-differentiated adenocarcinoma, there were no findings suggestive of lymphoma (Fig. 1b). Abdominal echography and computed tomography (CT) revealed a right renal cyst, but there was no evidence of liver metastasis or lymphadenopathy. Based on pathological examination of the biopsy specimens, a preoperative diagnosis of

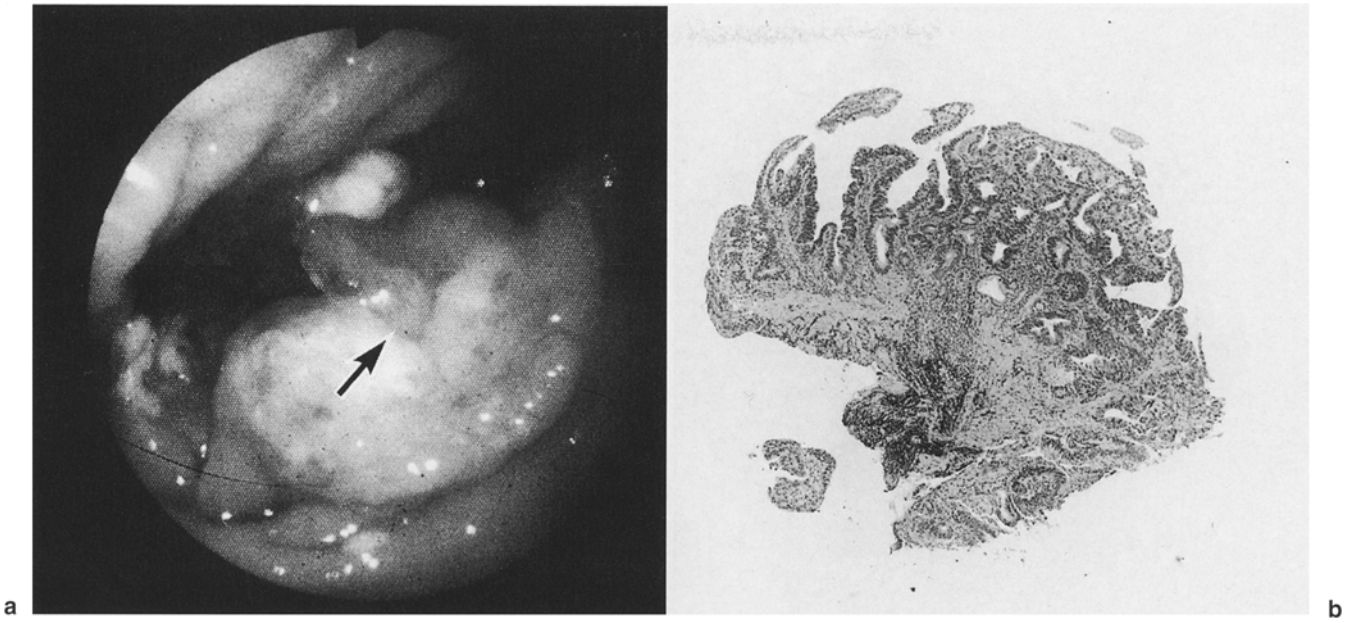

Fig. 1. a Gastroscopy findings showing an irregular giant tumor with several areas of ulceration and erosion (*arrow*) in the fornix extending to the cardioesophageal junction. **b** Well-differentiated adenocarcinoma was seen in a biopsy specimen. There was no evidence suggestive of lymphoma. (H&E ×10)

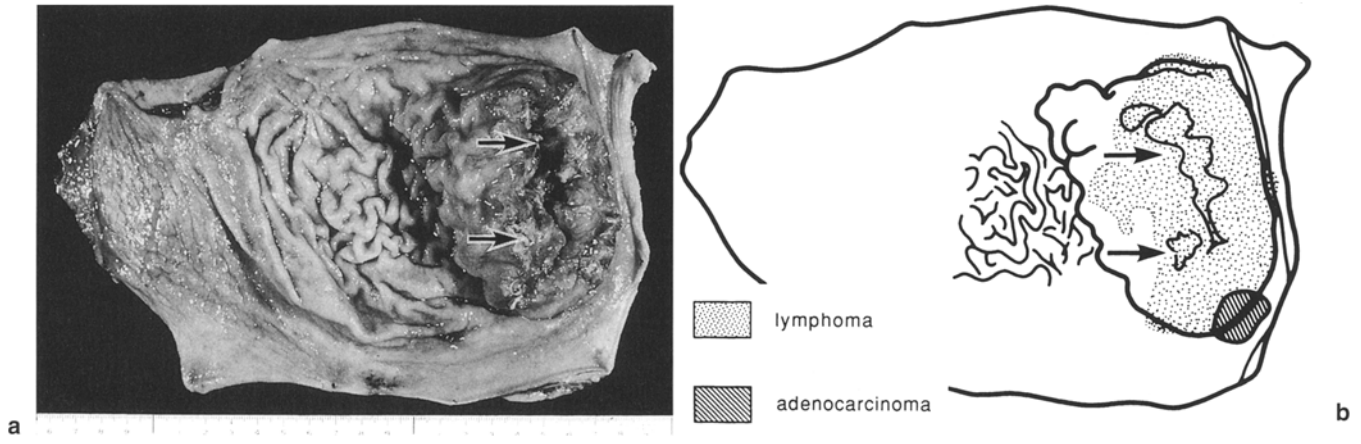

Fig. 2. Photograph of the resected specimen and schematic diagram. Pathological analysis showed the coexistence of a lymphoma and an adenocarcinoma. No protruding adenocarcinoma was recognized macroscopically. *Arrows* show the ulceration

advanced cancer of the stomach was made and a laparotomy was performed.

Surgical exploration of the abdomen revealed direct invasion of the gastric tumor into the spleen, and while neither peritoneal dissemination nor macroscopic metastasis to the liver were observed, the regional lymph nodes were found to be enlarged. Therefore, a total gastrectomy, splenectomy, omentobursectomy, and regional lymphadenectomy were performed. Examination of the resected stomach showed an irregular elevated lesion with a diameter of 7 cm in the fornix featuring a large, shallow ulcer; however, no protruding adenocarcinoma was recognized in the macroscopic specimen (Fig. 2). On microscopic examination, the coexistence of adenocarcinoma and lymphoma was clearly observed (Fig. 3a). The lymphoma was of the non-Hodgkin's, diffuse, large-cell type (Fig. 3b), which had invaded the spleen (Fig. 3c), but no lymph node involvement was seen. The monoclonality of the lymphoma was evaluated using a T-cell (UCHL 1) or B-cell (L26) marker. The lymphoma cells were stained by L26 but not by UCHL 1, confirming that it was a B-cell lymphoma. Conversely, the gastric cancer was early well-differentiated tubular adenocarcinoma (Fig. 3a) of

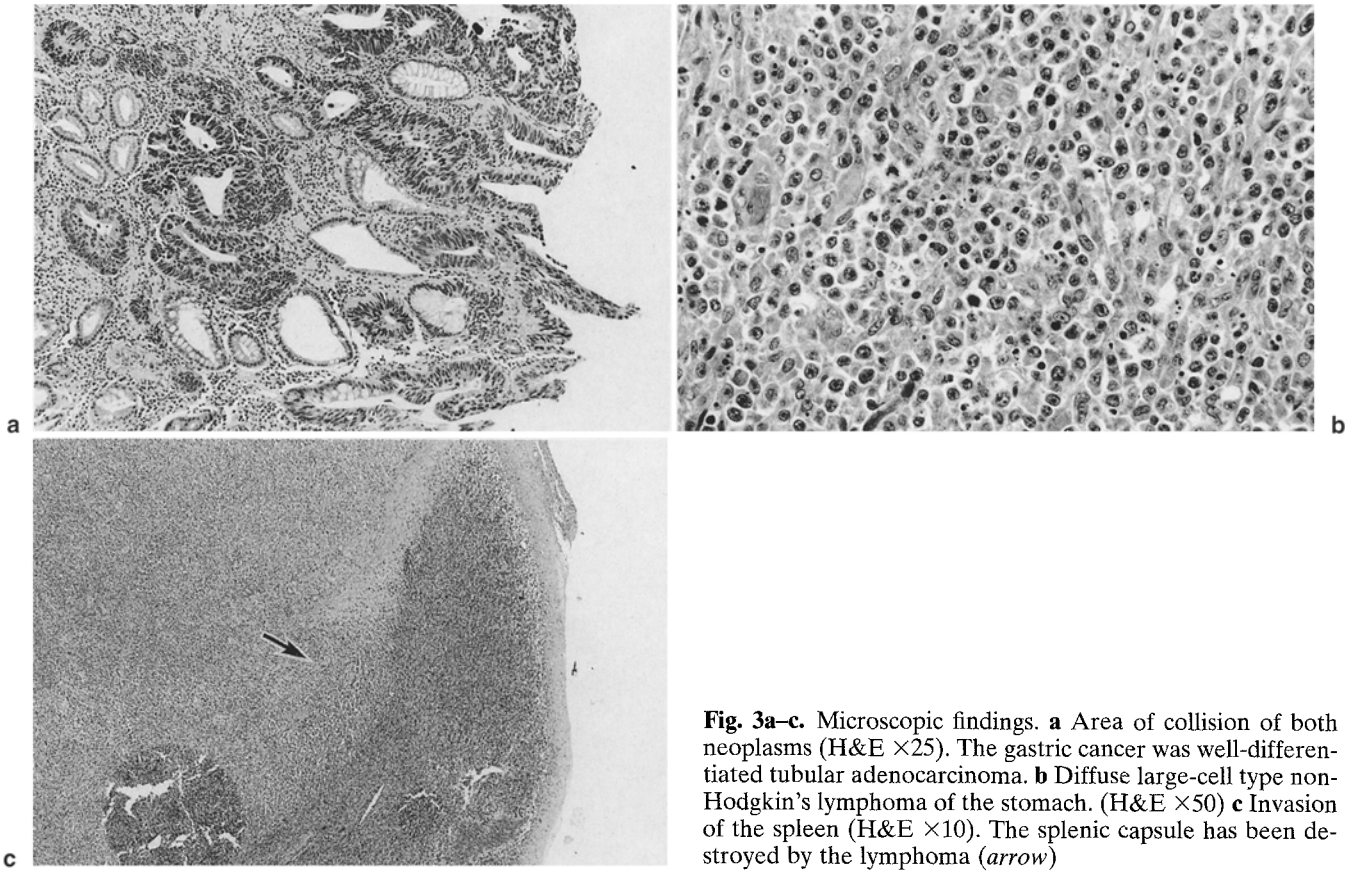

Fig. 3a–c. Microscopic findings. **a** Area of collision of both neoplasms (H&E ×25). The gastric cancer was well-differentiated tubular adenocarcinoma. **b** Diffuse large-cell type non-Hodgkin's lymphoma of the stomach. (H&E ×50) **c** Invasion of the spleen (H&E ×10). The splenic capsule has been destroyed by the lymphoma (*arrow*)

type 0-IIa, according to the classification of the Japan Gastroenterological Endoscopy Society. No nodal involvement by carcinoma was observed. Thus, a final pathological diagnosis of synchronous lymphoma and adenocarcinoma was established. Following an uneventful postoperative course the patient received a course of COP, and there has been no evidence of recurrence of either tumor in the 120 months since his operation.

Discussion

Synchronous carcinoma and lymphoma of the stomach is extremely rare, with only 40 cases having been reported in total in the Japanese and English literature.[5–14] Our patient was found to have an adenocarcinoma and lymphoma collision tumor of the stomach 2 years after complete remission of a tonsillar lymphoma had been achieved. However, we believe that the gastric lymphoma may have been a second primary lymphoma rather than metastasis because when lymphoma of Waldeyer's ring recurs in the stomach, systemic metastasis is usually detected, whereas this was not seen in our patient. Moreover, the tumor of Waldeyer's ring in our patient was a diffuse, medium-cell lymphoma, while the stomach tumor was a diffuse, large-cell lymphoma. Nevertheless, it remains uncertain whether the patient had primary or recurrent lymphoma, although there have been no previous reports of synchronous recurrent lymphoma and carcinoma of the stomach.

The operation performed consisted of total gastrectomy, splenectomy, omentobursectomy, and regional lymphadenectomy. At laparotomy, locoregional lymphadenopathy was seen, but pathological examination showed no evidence of either nodal metastasis of the carcinoma or involvement by the lymphoma. Although the gastric carcinoma was an early lesion limited to the mucosa, the lymphoma had invaded the spleen; however, a curative operation was carried out, and the patient has survived without any signs of recurrence for 120 months as of the time of writing.

Planker et al.[12] and Kasahara et al.[7] made detailed reviews of the Western and Japanese literature, respectively. According to these reviews, synchronous adenocarcinoma and lymphoma of the stomach[6–8,11] usually demonstrate the following characteristics:

1. The lymphoma is larger than the adenocarcinoma.

2. Advanced cancer is less common than early cancer, whereas the lymphoma is usually advanced.
3. The adenocarcinoma is usually well differentiated.
4. It is difficult to diagnose simultaneous carcinoma and lymphoma preoperatively, except when independent tumors exist.

Interestingly, all four of these characteristics were demonstrated in our patient. Severe intestinal metaplasia was also recognized, and based on the possibility that well-differentiated adenocarcinoma may originate from intestinal metaplasia in the gastric mucosa, Kasumi et al.[6] suggested a relationship between lymphoma and intestinal metaplasia of the stomach. However, the results of the pathological analysis of the tumor from our patient did not confirm any relationship between the intestinal metaplasia and the lymphoma.

Recently, much attention has been focused on disorders of the immunoregulatory system because of the increasing incidence of lymphoma caused by HTLV-III/LAV, which also causes AIDS.[15] However, there were no findings of HTLV-III/LAV infection in our patient. Planker et al.[12] suggested a causal relationship between the synchronous development of adenocarcinoma and lymphoma. According to their hypothesis, carcinomatous changes may arise either as a result of chronic irritation of the gastric mucosa, causing chronic immunological depression, or the two tumors may develop independently by the same carcinogenic mechanism. Kasumi et al. speculated that the existence of lymphoma tended to cause the development of well-differentiated adenocarcinoma in the adjacent gastric mucosa.[6] Interestingly, there are several reports on the coexistence of leiomyosarcoma and carcinoma.[16,17] Maeda et al. recently reported two cases of coexistent lymphoma and adenocarcinoma of the stomach, and mentioned the possible etiologic role of reactive lymphoid hyperplasia (RLH);[5] however, RLH was not recognized in our patient.

When the coexistence of adenocarcinoma and lymphoma is demonstrated, the lymphoma is usually at an advanced stage; therefore, the prognosis of these patients chiefly depends on the stage of the lymphoma. Unfortunately, in most cases, only the carcinoma is diagnosed preoperatively. In our patient as well, only the carcinoma was diagnosed preoperatively from pathological examination of the biopsy specimens, although this may have been because the biopsy sites happened to be in the part of the tumor where the carcinoma was present. However, a correct preoperative diagnosis is required to determine the appropriate therapy. The preoperative diagnostic accuracy for gastric lymphoma by biopsy has been reported at 64%,[18] whereas preoperative diagnosis of carcinoma is not difficult. To improve the preoperative diagnostic accuracy, more precise knowledge about the endoscopic and roentgenographic features of lymphoma is necessary. There are various types of lymphoma including infiltrative, ulcerative, nodular, polypoid, and combined. Furthermore, lymphoma tumors are often a large or spongy mass, unlike carcinoma. Thus, if gastric lymphoma is suspected by endoscopy or roentgenography, a large number of biopsy specimens from different sections of the mass, with repeated biopsies from the deeper parts, should be taken.

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