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Case Report

SYNCHRONOUS TUMORS OF THE STOMACH: A CASE REPORT OF MIXED GASTROINTESTINAL STROMAL TUMOR AND ADENOCARCINOMA

Abstract

Synchronous or metachronous gastric tumors composed of adenocarcinoma and gastrointestinal stromal tumor (GIST) are very rare and have seldom been reported in the literature. We present a case of an elderly man with synchronous gastric adenocarcinoma and GIST of the stomach. The adenocarcinoma presented as an ulcerated transmural tumor measuring 12 x 11 x 2 cm protruding from the lumen, occurring synchronously or metachronously with a 0.7 cm sized intramural nodular lesion, 1.5 cm proximal to the distal border of the resection, and was diagnosed as a gastrointestinal stromal tumor. The increasing tendency for gastric tumours to be synchronous or metachronous may be due to the change in biological behavior of tumors or causal environmental factors. Whether this association has any effect on survival is yet unknown. The important thing however, is to completely resect the lesions, as in single gastric carcinoma cases.

Key Words: Aged; Stomach neoplasms/surgery; Gastrectomy.

Olgu Sunumu

SENKRON MİDE TÜMÖRÜ: MİKS GASTROİNTESTİNAL STROMAL TÜMÖR VE ADENOKARSİNOMA OLGUSU

Öz

Adenokarsinoma ve miks gastrointestinal stromal tümörden oluşan senkron mide tümörü çok nadir görülen ve literatürde de nadir rastlanan bir durumdur. Bu yazıda ileri yaşta bir hastada, adenokarsinoma ve miks gastrointestinal stromal tümörün birlikte olduğu senkron mide tümörü olgusu sunulmaktadır. Olgu, 12x11x2 cm boyutlarında, transmural büyüyen ve lümenden protrüde olan, ülsere adenokarsinoma ile beraberinde 0.7 cm çapında, intramural yerleşimli, nodüler yapıda ve distal rezeksiyon sınırının 1.5 cm proksimalinde saptanan miks gastrointestinal stromal tümörden oluşmaktaydı. Senkron mide tümörü sıklığında artma eğilimi, değişen çevresel faktörler ve buna paralel olarak değişen biyolojik tümör davranışına bağlı olabilir. Ancak bu ilişkinin sağkalım üzerinde bir değişikliğe yol açıp açmadığı açık değildir. Önemli olan gastrik kanser olgularında olduğu gibi, lezyonların komplet olarak rezeksiyonudur.

Anahtar Sözcükler: Yaşlı; Mide kanseri/cerrahi; Gastrektomi.

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INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common gastrointestinal mesenchymal tumor, accounting for 1–3% of malignant gastric tumors. Gastric adenocarcinomas account for approximately 95% of all malignant gastric tumors (1). Dual gastric tumours may be synchronous if they arise simultaneously from the stomach or metachronous if they arise one following the other from the stomach, and are both rare. Most of them are composed of adenocarcinoma and lymphoma or adenocarcinoma and carcinoid tumor. Collision gastric tumors that are composed of adenocarcinoma and gastrointestinal stromal tumor (GIST) are exceedingly rare and have seldom been reported in the literature (1-3). We present a case of either a synchronous or metachronous occurrence of gastric adenocarcinoma and GIST of the stomach.

Case Report

A 78-year-old man was admitted to our hospital with complaints of anorexia, abdominal distension, hematemesis and weight loss of about 8% of total body weight over 2 months. The initial abnormal laboratory data included a hemoglobin level of 7 g/dl (normal 14.0–17.5 g/dl), a mean corpuscular volume of 59.6 fL/red cell (normal: 80–97 fL/red cell) and an albumin level of 32 g/dl (normal 35–54 g/dl). The investigated tumor markers included AFP, CEA, CA–19–9, and all were found to be within the normal ranges.

Ultrasonography of the abdomen demonstrated gastric thickening of the corpus and antrum, measuring 15 mm. Computed tomography of the abdomen with intravenous contrast demonstrated irregular gastric thickening at corpus inferior and antrum, measuring 12 mm, and perigastric reticular density signs and multiple lymph-nodes with diameters less than 1 cm.

Esophagogastroduodenoscopy revealed an infiltrative lesion at the corpus lesser curvature of the stomach, near the cardia. Endoscopic examination suggested gastric cancer. Multiple biopsies were carried out and gastric signet cell-adenocarcinoma was diagnosed by histopathological examination.

The patient underwent total gastrectomy with Roux-en-Y esophagojejunostomy and D2µ Lymph node dissection. During the operation, **a transmural tumor** was found to be located on the gastric corpus lesser curvature, directly invading the liver segments 3 and 4. Therefore, the surgical procedure was completed with non anatomic liver resection. Postoperative course of the patient was uneventful and he was discharged 10 days postoperatively. He is still alive now without any recurrence.

RESULTS

Pathological Findings

The gross specimen consisted of a large ulcerated protruding transmural tumor measuring 12 x 11 x 2 cm invading the adipose tissue and the liver. Simultaneously, a 0.7 cm sized intramural nodular lesion, 1.5 cm proximal to the distal border of the resection was observed.

Microscopically, desmoplasia of the tumor was moderate. Tumor was extending to the adipose tissue adjacent to liver capsule, with no parenchymal invasion. Perineural, neural and vascular invasion were observed (Figure 1). A GIST measuring 8 mm was detected in the nodular lesion. The GIST borders were determined on submucosal and muscular layers. Microscopically spindle cells were seen. No mitotic figures were noted (Figure 2). Immunohistologically, the cells of the tumor were diffusely and strongly (90%) positive for CD34 but were rarely and weakly positive (5%) for CD117. No immunoreaction was observed with S–100, actin and desmin. GIST was accepted to confer low grade risk according to diameter, proliferative activity, necrosis and cytologic atypia of tumor.

DISCUSSION

In 1983, GISTs were described as tumors of the gastrointestinal tract and mesentery, characterized by a specific histological and immunohistochemical pattern (4). These tumors occurred at a median age of 60 years in most series, with a

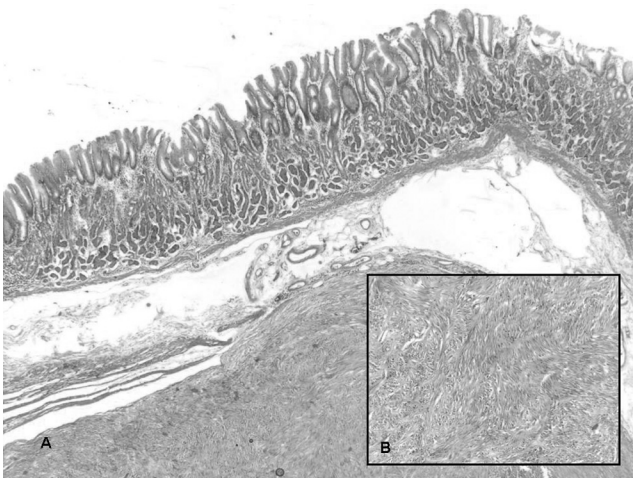

Figure 1— Perineural, neural and vascular invasion.

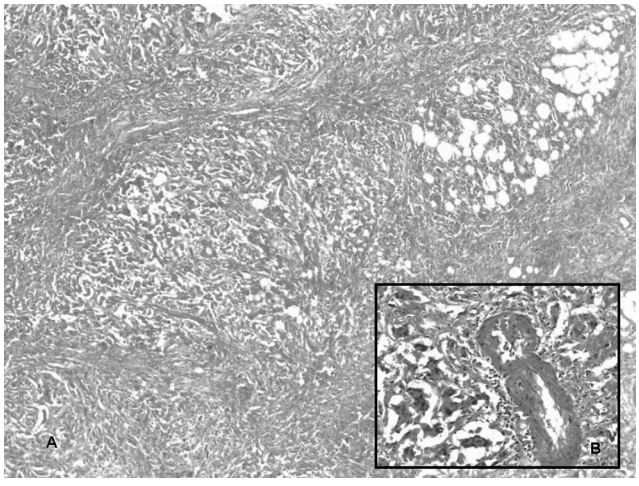

Figure 2— GIST borders and spindle cells.

slight male predominance. Subsequently, GIST was shown to exhibit typical activating mutations of the KIT or PDGFRA protooncogenes, which are the likely causal molecular events of GIST (5).

The coexistence of GISTs with other neoplasms has been widely addressed in literature. Notably, the percentage of patients with a GIST in whom other neoplasms were diagnosed ranges between 2.95 and 33.33%. Agaimy et al. found 444 (9.3%) cases of secondary malignancies among 4777 patients with GIST in their literature review (6). Most common secondary neoplasms were colorectal cancer, prostate cancer, and neoplasms derived from lymphoid tissue. They reported 17 (2.1%) cases of pancreatic cancer diagnosed among 813 patients with GIST and other neoplasms (7). In their analysis of serial sections of 100 surgically resected cases of gastric cancer, Kawanowa et al. demonstrated a high incidence of microscopic GISTs in the stomach (35%) (8).

Literature review by Uchiyama et al. only showed 15 cases of synchronous gastric epithelial tumors and GISTs in the stomach (1). Since this literature search showed only one publication by Lee et al., our case represents the seventeenth case in literature (Table 1).

In our case, the GIST had a very low risk of aggressive behavior based on histology and size. Our case was asymptomatic and was found incidentally during surgery. Liszka et al. showed that among patients with a GIST accompanied by other neoplasms, 16 of 22 (72.7%) were found incidentally du-

Table 1— Summary of Previous Synchronous Gastric Epithelial Tumors (ETs) and Gastrointestinal Stromal Tumors (GISTs) in The Stomach. Adapted from Uchiama et al.'s article (1).

Case	Source	Year	Sex/Age	Size, gross appearance of ETs	Histology	Size, gross appearance of GIST
1	Maiorana et al	2000	F/81	4.0 cm, Vegetant	Adenocarcinoma	5.0cm, Intramural
2	Maiorana et al	2000	F/79	2.0 cm Erosion	Adenocarcinoma	6.0 cm, Submucosal
3	Maiorana et al.	2000	M/75	4.0 cm, Ulcerated	Adenocarcinoma	5.0 cm, Submucosal
4	Maiorana et al.	2000	F/79	1.2 cm, Ulcerated	Adenocarcinoma	5.0 cm, Subserosal
5	Maiorana et al	2000	M/79	2.0 cm, Ulcerated	Adenocarcinoma	0.6 cm, Subserosal
6	Maiorana et al.	2000	M/69	0.6 cm, Sessile polyp	Carcinoid	5.0 cm, Submucosal
7	Andea et al	2001	F/73	0.6 cm, Nodule	Carcinoid	1.2 cm, Submucosal
8	Kaffes et al	2002	M/78	Unknown, slightly raised	Adenocarcinoma	1.5 cm, Serosal nodule
9	Liu et al.	2002	M/70	8x5x3cm, Ulcerative	Adenocarcinoma	8 x 5 x 3 cm, Ulcerative
10	Bircan et al	2004	M/71	5.7 cm, Ulcerovegetative	Adenocarcinoma	0.5 cm, Subserosal
11	Bircan et al.	2004	M/77	7.5 cm, Vegetative	Adenocarcinoma	0.6 cm, Submucosal
12	Wronski et al.	2006	F/64	5.0 cm, Unknown	Adenocarcinoma	2.0 cm, Intramural
13	Wronski et al.	2006	M/66	1.0 cm, Unknown	Adenocarcinoma	1.0 cm, Intramural
14	Lin et al	2006	F/70	1.7x1.4 cm, Depressed	Adenocarcinoma	1.1x0.8x0.7 cm, Sessile polyp
15	Uchiyama et al	2006	M/74	1.5x1.5 cm, IIa + IIc	Adenocarcinoma	0.8 cm, Extramural
16	Fang-Yi Lee	2007	M/82	9 cm, Ulcerative	Adenocarcinoma	1.5 cm,Intramural
17	Present Case	2008	M/78	12 cm, Ulcerative	Adenocarcinoma	0,7 cm, intramural

ring surgery and two of 22 (9,1%) were found incidentally on autopsy (7). Importantly, the proportion of symptomatic and incidentally found GISTs among patients with other tumors in a population-based study was reversed. It is not yet established whether the coexistence of a GIST with other, unrelated syndromes or tumors is incidental or results from related pathophysiological processes (7,9,10,11).

Synchronous or metachronous tumors rarely develop in the stomach. Occurrence of adenocarcinoma admixed with gastric lymphoma, carcinoid, leiomyosarcoma or rhabdomyosarcoma, as well as adenoma admixed with a sarcomatous stromal component were described in single case reports. Among reports of carcinosarcoma of stomach, none have described collision tumor with a GIST and adenocarcinoma. So far, only one case report of synchronous tumor in the stomach consisting of adenocarcinoma and leiomyoma have been documented (3).

The admixture of gastric epithelial and stromal tumors raised the question of whether such an occurrence is a simple incidental association or whether the two lesions are connected by a causal relationship. It is possible that a single carcinogenic agent may interact with two neighboring tissues, inducing development of tumors of different histological types in the same organ. The compound N-methyl-N'-nitrosoguanidine can induce gastric adenocarcinoma after oral administration in rats. If combined with other agents, which alter the gastric mucosa barrier (such as non-steroidal anti-inflammatory drugs), leiomyosarcoma can be induced in association with the epithelial tumor. However, there is no evidence to show that these compounds play an important role on human gastric malignancy. We anticipate that the stomach may have been influenced by the same unknown carcinogen, resulting in simultaneous proliferation of different cell lines (epithelial and stromal cells) especially in the elderly. A potential pluripotent stem cell could also be the initial target of the carcinogen or causal influence, however further serial studies are needed to clarify these possibilities (2).

In conclusion, the literature review has shown that synchronous tumors of stomach remains uncommon with only 16 previously reported cases. It is important to consider the possibility of synchronous tumors in patients with a seperate lesion within the stomach. The reason for the increase in tendency of such lesions in the stomach, their natural history and the effect of their associations on survival remains unknown. Although found incidentally, it is important and sufficient to completely resect the lesions surgically.

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