Synchronous occurrence of gastrointestinal stromal tumors and other primary gastrointestinal neoplasms

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INTRODUCTION
Gastrointestinal stromal tumors (GISTs) are an uncommon mesenchymal neoplasm affecting the GI tract. The synchronous occurrence of mesenchymal tumors and other primary gastrointestinal malignancies has been rarely reported in the literature[1,2]. Most of these publications describe single case reports. We present a series of four patients, from a single institution, with GIST and a second primary neoplasm occurring synchronously. The aim of this study was to evaluate clinical and pathologic features of GISTs concomitant with other gastrointestinal malignancies.

MATERIALS AND METHODS
Patients
Between 1989 and 2005, 28 patients with primary gastrointestinal stromal tumor were treated operatively at the department of General and Gastroenterological Surgery and Nutrition, Warsaw University of Medicine. Most of the patients were women (62%). Median age of the patients at the time of presentation was 63.5 years. The primary tumor was located in the stomach (57%), small intestine (32%), large intestine (7%) and mesentery (4%). GIST was incidental in 29% of the patients. Hospital charts, operative and pathological reports were reviewed for each patient.

Methods
The histological diagnosis of all GISTs was confirmed at the department of pathology of the Warsaw University of Medicine. Specimens were fixed in 10% formaldehyde and processed routinely for paraffin embedding. 5-μm-thick sections were stained with HE. Mitoses were counted in 50 high-power fields. Malignant potential of the GISTs was stratified according to the risk categories proposed by Fletcher et al[3]. Immunohistochemistry was performed using commercially available antibodies against CD117 (polyclonal, Dako, Glostrup, Denmark) and against CD34 (monoclonal, Dako, Glostrup, Denmark).

RESULTS
GIST occurred synchronously with another gastrointestinal malignancy in four patients (14%) out of all the patients with primary gastrointestinal stromal tumor treated.
in our department. Twenty-five percent of the gastric stromal tumors and 50% of the incidental GISTs were synchronous with the second gastrointestinal malignancy. The concomitant neoplasms were also primaries. All these GISTs were located in the stomach. In 75% of the cases, GIST was synchronous with other gastric malignancies, and one patient had a coexistent gastric stromal tumor and colorectal cancer. The patients presented clinically with abdominal pain, weight loss or partial intestinal obstruction. All the patients required operation due to the symptoms as a result of the tumor and GIST synchrony. The stromal tumor was always an incidental finding during the operation. The clinical characteristics of the patient population are shown in Table 1.

The synchronous gastrointestinal stromal tumors were uniformly CD117 and CD34 positive (Figure 2) and could be classified as low and very low risk tumors for malignant potential. The histopathologic features of the synchronous GISTs are shown in Table 3.

**DISCUSSION**

Gastrointestinal stromal tumors are uncommon mesenchymal neoplasms occurring within the abdominal cavity. Most GISTs are located in the stomach and small intestine[8]. GISTs usually develop in a sporadic fashion. However, familial occurrence has also been reported[9]. In patients with Carney’s triad, GISTs may develop together with pulmonary chondroma and extra-adrenal paraganglioma[6]. Although 10% of the patients enrolled in the Polish GIST Clinical Registry had a second neoplasm[7], these were usually metachronous and occurred earlier than the GIST. Slightly above 30 cases of the synchronous occurrence of mesenchymal tumors (including GIST) and other gastrointestinal malignancy have been reported in the literature[1]. Most of these

**Table 1** Characteristics of the patient population

| No. | Age | Sex | Synchronous malignancy | Clinical presentation          |
|-----|-----|-----|-------------------------|--------------------------------|
| 1   | 63  | F   | Colon cancer            | Intestinal obstruction         |
| 2   | 77  | F   | Gastric lymphoma        | Abdominal pain                 |
| 3   | 64  | F   | Gastric cancer          | Pyloric stenosis               |
| 4   | 66  | M   | Gastric cancer          | Abdominal pain, weight loss    |

**Table 2** Pathologic features of the synchronous GISTs and other primary gastrointestinal neoplasms

| No. | GIST | Synchronous gastrointestinal malignancy |
|-----|------|----------------------------------------|
|     | Location | Size (cm)  | Type                     | Location | Size (cm)  |
| 1   | Anterior gastric wall (corpus) | 2        | Adenocarcinoma (pT4, N2, M0) | Cecum    | 10         |
| 2   | Anterior gastric wall (fundus) | 1        | Lymphoma (diffuse large B cell) | Lesser curvature at the gastric angle | 2         |
| 3   | Anterior gastric wall (corpus) | 2        | Adenocarcinoma (Lauren diffuse type (pT4, N0, M0) | Antrum   | 5         |
| 4   | Anterior gastric wall (corpus) | 1        | Adenocarcinoma (Lauren intestinal type (pT1, N0, M0) | Posterior wall at the gastric angle | 1         |

**Table 3** Histopathologic features of the synchronous GISTs

| No. | CD117 reactivity | CD34 reactivity | Tumor size (cm) | Mitotic index | Risk category for malignant behavior |
|-----|-----------------|-----------------|----------------|---------------|-------------------------------------|
| 1   | +               | +               | 2/50 hpf        | 2/50 hpf      | Low                                 |
| 2   | -               | +               | 1/50 hpf        | 0/50 hpf      | Very low                            |
| 3   | +               | +               | 2/50 hpf        | 0/50 hpf      | Low                                 |
| 4   | +               | +               | 1/50 hpf        | 0/50 hpf      | Very low                            |

1 High-power fields.
publications describe gastric stromal tumors synchronous with another gastric malignancy. We also observed such gastric tumor association in our group. In one of our patients, GIST occurred simultaneously with colon cancer. To our knowledge, only a few reports of such tumor co-occurrence have been published in the literature[8].

GISTs have been reported to occur synchronously with adenocarcinoma, lymphoma and carcinoid[1,9]. Similar to other authors, GIST was most frequently synchronous with adenocarcinoma also in our series (75%). High percentage of synchronous GISTs and other gastrointestinal tumors in our series is both surprising and difficult to explain. 14% of all the GISTs and 25% of the gastric stromal tumors developed synchronously with a second gastrointestinal malignancy. This rate of neoplasm co-occurrence is greater than twice that observed in the largest group of synchronous GISTs published by Maiorana et al[1]. In their series, 11.5% of gastric GISTs (6 cases) were associated with other gastrointestinal malignancies.

Although the synchronous occurrence of GIST and other abdominal malignancy seems to be just a coincidence, the development of these tumors may involve common carcinogenic agents. For example Sugimura et al[10] revealed that enteral nitrosoguanidine produces adenocarcinoma in rats. In contrast, simultaneous exposure to both nitrosoguanidine and acetylsalicylic acid causes synchronous development of both gastric cancer and leiomyosarcoma[11]. In conclusion the synchronous occurrence of GISTs and other gastrointestinal malignancies is more common than it has been considered. The concomitant GIST is usually discovered incidentally during the operation performed because of the other malignancy. The development of GIST and other neoplasms may involve the same carcinogenic agents.

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