Synchronous gastric gastrointestinal stromal tumor (GIST) and other primary neoplasms of gastrointestinal tract: report of two cases

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Abstract
Gastrointestinal stromal tumors (GIST) are the most common mesenchymal neoplasms of the gastrointestinal tract with a malignant potential. However, uncommonly they can be associated with synchronous tumors of different histogenesis. We herein report two cases of gastric GIST with synchronous tumors. The first case is of a 50-year-old male patient who was suspected with GIST of stomach and was incidentally found to have an associated duodenal neuroendocrine neoplasm. The second case is of a 62-year-old male who, while undergoing surgery for a primary colon adenocarcinoma, was incidentally detected to have a coexistent gastric GIST initially suspected to be a metastatic nodule. Coexistence of gastric GIST with neuroendocrine tumor is extremely rare. To the best of our knowledge this is the second case of gastric GIST coexisting with duodenal neuroendocrine tumor to be reported in the literature. Similarly, association of GIST with adenocarcinoma is uncommon. We herein analyze the pathological findings of two such cases, and we review the malignant potential of these synchronous tumors.

Keywords: Gastrointestinal stromal tumor, adenocarcinoma, neuroendocrine tumor, synchronous tumors, gastric

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Introduction
Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal (GI) tract although accounting for only 0.1-3% of all GI neoplasms. These can arise anywhere along the GI tract. The synchronous occurrence of GIST and other primary GI malignancies is uncommon [1,2].

Case reports

Case 1

A 50-year-old male presented with history of two episodes of melena and drop in hemoglobin for 3 months. Barium meal study showed an eccentric rounded impression in the gastric fundus. Additionally there was an eccentric impression on the superior wall of the duodenal bulb. Upper GI endoscopy revealed a nodular lesion in the gastric fundus with a central ulcer. Another sessile polyp of about 1 cm size was seen in the first part of duodenum (Fig. 1A, B). Both were thought to be leiomyomas endoscopically. Contrast-enhanced computed tomography (CT) of upper abdomen showed a large nodular lesion in the fundus of stomach and another small lesion in first part of duodenum.

Pathological examination
Wedge resection of gastric tumor and duodenal polypectomy was performed. Stomach showed a firm submucosal tumor measuring 4.5x3.5 cm. Overlying mucosa was focally ulcerated. Microscopically, the tumor was seen in the submucosa and wall and was composed of fascicles of spindle cells (Fig. 1C). Immunohistochemistry demonstrated positive staining for CD117 (Fig. 1D) and CD34. Tumor cells were negative for SMA and S100. Features were consistent with benign GIST (American Joint Committee on Cancer, pT2pN0pM0). Duodenal polyp showed a well circumscribed grey yellow nodule measuring 1 cm in diameter. Histology revealed a neuroendocrine tumor, grade 1 involving the duodenal wall (pT2pN0pM0). It was composed of nests and cords of round to oval tumor cells, separated by thin fibrous septae and was seen infiltrating the muscle (Fig. 1E). The cells had moderate

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measuring 3.5x2.5 cm. Right hemicolectomy also revealed extension of tumor into the ileum with multiple tumor nodules in the mesenteric and mesocolic fat (Fig. 2C). Microscopically, a moderately differentiated adenocarcinoma originating in the sigmoid colon with infiltration into serosal fat was seen (Fig. 2D), infiltrating the ileum. Multiple lymph nodes showed tumor metastasis along with metastatic omental deposits (pT4pN2pM1).

Discussion

GISTs are the commonest mesenchymal tumors of GI tract predominantly involving the stomach (50-62%), small intestine (20-30%), colon (11%) and the rectum (7%) [2]. They originate from interstitial, pacemaker Cajal cells. The percentage of GIST patients with other diagnosed neoplasms is reported to range between 3% and 33% [3]. It has not been ascertained whether the coexistence of a GIST with other unrelated syndromes or tumors is incidental or results from related pathophysiological processes [4]. The most common secondary neoplasms are GI carcinomas. Other coexistent tumors include lymphoma/leukemia, carcinomas of prostate, breast, kidney, lung, female genital tract, soft tissue and bone sarcomas, malignant melanoma and seminomas [5].

The pathological features of two cases of synchronous gastric GIST and synchronous neoplasms of GI tract are described (Table 1). The first case outlines a duodenal neuroendocrine...
Gastric GIST with second neoplasm

Tumor presenting as a polyp along with a coexistent gastric nodule diagnosed as benign GIST on histology. Synchronous GIST and neuroendocrine tumors of duodenum are extremely rare. Only 3 cases of concomitant gastric carcinoid and GIST have been reported in the literature [6,7]. Duodenal carcinoid may coexist with different types of cancer. Burke et al [8] studied 99 patients with duodenal carcinoids and found 28 patients with another malignancy. No GIST was however found coexisting with duodenal carcinoid. Cirillo reported association of gastric carcinoid and low risk GIST [7]. Pusiol et al [9] reported the first case of synchronous duodenal carcinoid and high-risk gastric GIST. In our study, which is the second case of duodenal neuroendocrine tumor with GIST, the GIST was of low grade. The second case is of a primary advanced colon adenocarcinoma and an incidentally detected gastric nodule that was initially suspected to be metastatic. This is an uncommon association [2] that can lead to diagnostic errors as the neoplasm is mistaken for a metastatic nodule particularly in a scenario of advanced carcinoma. The simultaneous appearance of GIST and another neoplasm in different parts of the GI tract is very rare. These patients have great diagnostic difficulties as the clinical features overlap.

Table 1 Summary of histopathological features of two cases of gastric GISTs with synchronous tumors

<table>
<thead>
<tr>
<th>Gastric GIST</th>
<th>Associated tumor</th>
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<tbody>
<tr>
<td><strong>Patient</strong></td>
<td><strong>Tumor size (cm)</strong></td>
</tr>
<tr>
<td>Case 1</td>
<td>4.5</td>
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<tr>
<td>Case 2</td>
<td>4.0</td>
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</tbody>
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GIST, gastric gastrointestinal stromal tumor
The etiology of synchronous occurrence of GISTs with histologically unrelated tumors still remains unclear. Some authors have postulated that they may share common carcinogenic pathways or genetic mutations with proliferation of different cell lines [10]. Given the limited number of cases of associated duodenal neuroendocrine tumors, the possibility of their sporadic occurrence is more likely. Further studies are needed to analyze the molecular and genetic mechanisms of carcinogenesis.

Awareness of occurrence and pattern of synchronous GIST and other neoplasms is important for both histopathologists and surgeons. The associated neoplasms may be both high-grade-like advanced colon carcinoma or low-grade-like well differentiated neuroendocrine tumor in this study. GIST itself can be of any grade. It may not always be possible to diagnose a coexisting tumor preoperatively. Surgeons should be alert to recognize a coexisting tumor before or during surgery and be prepared to modify the plan of surgery accordingly.

References