Synchronous Occurrence of Advanced Adenocarcinoma with a Stromal Tumor in the Stomach: A Case Report

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Abstract

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms of the digestive tract. Synchronous occurrence of a gastrointestinal stromal tumor with a tumor of different histogenesis is very rare and has been documented in the literature mainly in case reports. We present the case of a 78-year old female patient who underwent surgery for an advanced gastric carcinoma during which a gastric stromal tumor was incidentally discovered. A review of the literature is also conducted on the extremely rare synchronous occurrence of malignant tumors of different histogenesis in the stomach.

Key Words

Gastric adenocarcinoma – gastrointestinal stromal tumor – synchronous occurrence

Introduction

Gastrointestinal stromal tumors (GISTs) are the most common non epithelial tumors of the digestive tract, accounting for only 1% of all gastrointestinal malignancies [1,2] and for 5.7 % of all sarcomas [3]. They strongly express the KIT (CD117) protein, a type III tyrosine kinase receptor encoded by the c-kit proto-oncogene [4-6]. GISTs have been reported in the literature to coexist with tumors of different histogenesis such as adenocarcinomas, carcinoids, MALT lymphomas and Burkitt’s lymphomas [7-11], as well as with different mesenchymal tumors [12-15]. This paper reports a rare synchronous occurrence of a stromal tumor with an advanced adenocarcinoma in the stomach, in a 78 year old female.

Case presentation

A 78 year old female was admitted to our department complaining of a progressively worsening epigastric pain of three weeks duration, nausea and vomiting. She also complained of an 8 kg weight loss during the last two months prior to admission. She did not have any significant medical history. On clinical examination a mild upper abdominal tenderness was apparent and a small mass was palpated in the epigastrium. Blood count test revealed anemia, while liver function tests and serum electrolytes were normal. Chest and abdominal X-rays were unremarkable, while abdominal CT scan showed thickening of the gastric wall. Esophagogastroduodenoscopy revealed an ulcerative mass in the gastric antrum measuring approximately 5cm x 6cm, located 4cm proximally to the pylorus. Histological examination of the biopsies revealed fragments of a poorly differentiated intestinal type gastric adenocarcinoma.

An exploratory laparotomy followed and the patient underwent total gastrectomy with esophagojejunal Roux-en-Y reconstruction and splenectomy. During gastrectomy a well defined nodular lesion measuring 1cm was palpated 3cm proximally to the adenocarcinoma in the lesser curvature. Histological examination of the whole resected stomach confirmed the presence of a poorly differentiated intestinal type adenocarcinoma located in the antrum measuring 6.5cm x 5.5cm (Fig. 1). The tumor was infiltrating the full thickness of the gastric wall and extended to the serosal fat of the lesser curvature. Five of the 15 resected lymph nodes were found to contain metastases.

Histologically, the second lesion of 1cm diameter consisted of spindle to ovoid-shaped mesenchymal cells arranged in interlacing bundles or sheets. Those cells demonstrated cyanophilic or eosinophilic cytoplasm and single elongated nuclei with moderate level of pleomorphism, and mitotic activity (5-7 mitoses per/10HPF) (H&E stain). Chromatin was predominantly finely granular. Perinuclear vacuolization was also observed. Immunohistochemical analysis was performed for the identification of the tumor’s origin. CD 117 (c-kit protein) was moderately to strongly positive demonstrating a combined membranous and diffuse
but immunohistochemical staining for CD 117 has never been confirmed [8]. Although in most of the reported cases, as well as in our case, the coexisting tumors were located in different sections of the stomach, cases with collision tumors have also been reported [18]. In most cases the coexisting epithelial tumor is a poorly differentiated intestinal type gastric adenocarcinoma while atrophic gastritis, chronic active gastritis, intestinal metaplasia or helicobacter pylori infection can also be present [4,8-11,14].

Only Maionara et al reported a series of six cases of synchronous occurrence of GISTs with gastric adenocarcinoma in five patients and one with carcinoid tumor [7]. All these cases stained positive for vimentin, four stained positive for CD34, while stain for S-100 was focally positive and SMA and desmin were negative. There was no information about c-kit staining. In our case, CD 117 staining was moderately to strongly positive, CD 34 protein was positive, whereas S-100, desmin and SMA demonstrated negative or very weak reactivity. The coexisting stromal tumors are usually very small and are detected incidentally during surgery, as in our case. Sanchez et al reported an incidence of 0.8% of incidentally finding small GISTs in patients who underwent laparoscopic Roux-en-Y gastric bypass [19].

Various hypotheses have been made for the synchronous occurrence of a GIST with other tumors of different histogenesis. In earlier Japanese literature a few cases of coexistence of gastric leiomyoblastoma, leiomyoma or leiomyosarcoma, with gastric cancer have been reported, cytoplasmic staining pattern. Additionally, CD 34 protein was observed to be positive (membranous stain), whereas S-100, desmin and SMA demonstrated negative or very weak reactivity (Fig. 1).

Resection margins as well as spleen and omentum were free of disease. The postoperative course was uneventful. Following surgery the patient received adjuvant chemotherapy, but unfortunately died of progressive disease 14 months later.

Discussion
The term GIST was introduced by Mazur and Clark in 1983 in order to indicate a distinct heterogeneous group of mesenchymal neoplasms of spindle or epithelioid cells of varying differentiation [16]. These tumors had been designated in the earlier literature as leiomyomas, leiomyosarcomas, leiomyoblastomas and schwannomas but with the implementation of the immunohistochemical stains and electron microscopy in recent years they have been recognized as a distinct pathological entity [17].

Despite the great progress made in recent years in understanding the molecular biology of GISTs, little is yet known about their rare synchronous occurrence with tumors of different histogenesis. In earlier Japanese literature a few cases of coexistence of gastric leiomyoblastoma, leiomyoma or leiomyosarcoma, with gastric cancer have been reported, but immunohistochemical staining for CD 117 has never been confirmed [8].

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histogenesis. Gene mutations or influenced neighboring stomach tissues by the same carcinogen could be causative factors [7,11].

Apart from the above mentioned theories, simple coincidence could also be the case, especially in geographical regions that have high incidence rates of gastric surgery [7,9]. Regarding the Helicobacter pylori infection, although it has been implicated as a carcinogen in the stomach, there is no evidence that links it with GISTs development [14]. Although the coexistence of those tumors (intestinal type gastric adenocarcinoma and GIST) is a very rare event, it seems that there is a combined genetic deregulation involved in this carcinogetic process. Furthermore, high grade (poorly differentiated) neoplasms associated with high risk GISTs, due to the criteria of size and mitotic count, must be analyzed for the definition of their genetic profile.

Conclusions

The synchronous occurrence of a gastrointestinal stromal tumor with a tumor of a different histogenesis is very rare, and little is known about this association. Coexisting GISTs are in most cases very small, asymptomatic tumors and are detected incidentally during surgery for another reason. Thorough investigation of the peritoneal cavity during laparotomies is essential. Surgery is the mainstay treatment. Further molecular biology studies are required, in order to explain the simultaneous development of tumors of different histotypes.

References