Gastrointestinal Stromal Tumor (GIST) Associated with Synchronous Colon Adenocarcinoma – A Case Report

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Abstract

Gastrointestinal stromal tumors (GIST) are rare mesenchymal neoplasms of the gastrointestinal tract with a malignant potential and unpredictable behavior. In the literature a few cases of synchronous development of a GIST and another neoplasia with different incidence, etiology, evolution and prognostic have been described. We report a case of a 61 year old male with a simultaneous occurrence of a GIST and a colon adenocarcinoma.

Key words

Gastrointestinal stromal tumors - GIST – adenocarcinoma – synchronous tumors – metallothioneins.

Introduction

Gastrointestinal stromal tumors (GIST) are rare mesenchymal neoplasms of the gastrointestinal tract with an incidence of 1.5/100,000/year [1, 2] typically described in adults, with a peak incidence in the sixth and seventh decades [3].

These tumors have malignancy potential, but their behavior has been difficult to predict and the co-existence of other primary gastrointestinal malignancies and GIST has been rarely reported in the literature [4]. We present a 61 year old male with a simultaneous occurrence of a GIST and a colon adenocarcinoma.

Case report

A 61 year old male was admitted complaining of asthenia, weakness, chest pain, diffuse abdominal pain, flatulence. He denied any associated gastrointestinal symptoms such as nausea, vomiting, weight loss, diarrhea, constipation, melena or hematemesis.

A duodenal ulcer, surgery for an umbilical hernia and chronic anemia were mentioned in his medical history. The patient had as comorbidities essential hypertension, ischemic heart disease, stable angina pectoris and benign prostate hypertrophy.

At physical examination, abdominal obesity with diffuse tenderness to deep palpation, leg edema, mucocutaneous pallor was detected. Laboratory tests revealed abnormal parameters (reference range in parentheses): iron deficiency anemia with hemoglobin of 7.5 g/dl (11.5–17.5 g/dl), hematocrit of 25.98% (35–52%), sideremia of 23 µg/dl (50 - 175 µg/dl), reticulocyte count of 26 ‰ (5-20‰) and a positive hemoccult test.

Upper gastrointestinal (GI) endoscopy was performed, showing an ulcerated tumor, covered with normal gastric mucosa, localized on the posterior wall of the greater curvature. Upper endoscopic ultrasonography (Fig.1) evidenced a submucosal lesion, about 36/26 mm with decreased echogenicity and inhomogeneous structure, and necrotic areas. The lesion belonged to the muscular layer.

The patient was scheduled for surgery. Intraoperatively a tumor at the posterior gastric wall (4/2.7/1.8 cm) and a tumor (about 4./6.55 cm) at the transverse colon had been detected which was infiltrative and stenosing. Gastric tumor

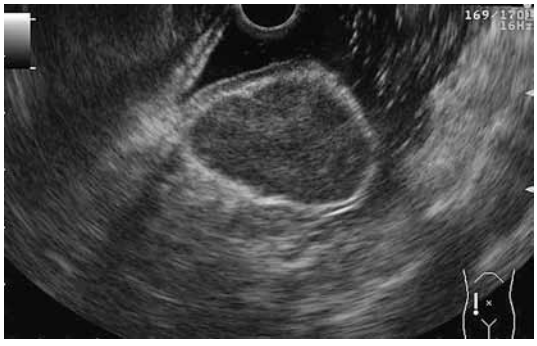

Fig 1. Submucosal lesion belonging to the muscular layer by upper endoscopic ultrasonography

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resection and enlarged right hemicolectomy with ileocolic anastomosis were performed.

The histopathological diagnosis for the submucosal nodule was fusiform GIST low-grade (G1) pT2 (Fig 2), without necrosis and atypia and the mitotic index (number of mitoses per 50 high-power fields) was 1/50 HPF (Fig 3). The immunohistochemistry indicated strong staining for c-Kit/CD117 (Fig 4) and CD34 (Fig 5), while expression of S-100 were negative.

The tumor in the colon was a well differentiated (G1) colon adenocarcinoma, with lower mucinous component pT3N1cMx (Fig 6).

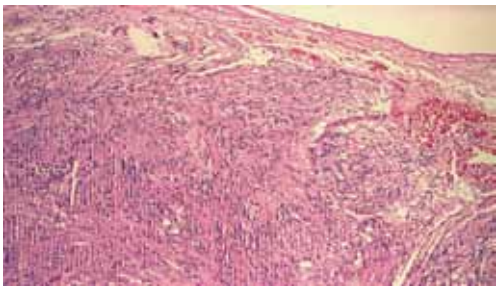

Fig 2. Fusiform low grade GIST (H&E stain x4).

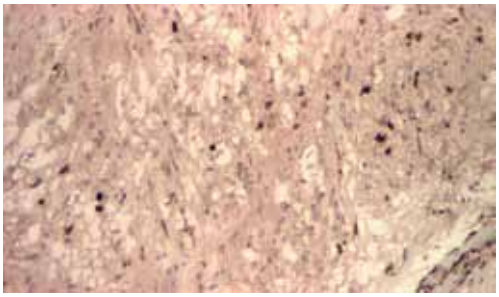

Fig 3. GIST – Ki-67 x10 (nuclear antigen associated with cell proliferation) proliferation index 3%.

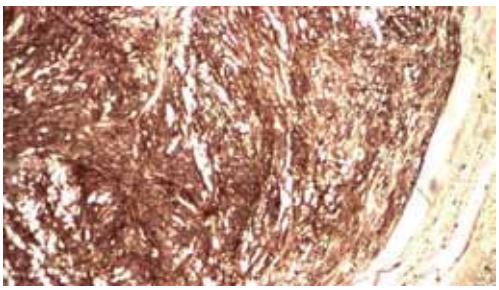

Fig 4. GIST – c-Kit/CD 117 (a type III tyrosine kinase growth factor receptor) positivity (x4).

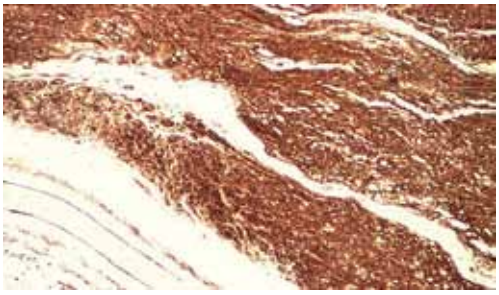

Fig 5. GIST – CD34 (myeloid progenitor cell antigen) positivity (x4).

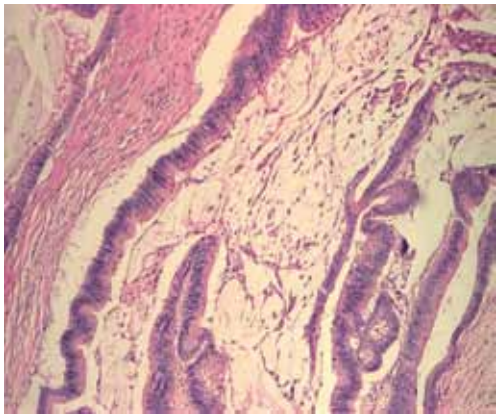

Fig 6. Colonic adenocarcinoma – mucinous areas (H&E x4).

The patient was discharged from the hospital and oral chemotherapy was initiated without any complications.

Discussion

GIST and adenocarcinomas represent distinct oncogenic entities. GISTs are the most common mesenchymal tumors of the GI tract [5] and this group of tumors represents about 0.1% to 3% of all GI neoplasms.

The mean age at presentation is over 40 and the clinical presentation is typically characterized by GI bleeding, abdominal pain, weight loss, anemia and a palpable mass [6]. The etiology may be represented by mutations in the Kit gene or PDGFRA (platelet derived growth factor receptor alpha) gene and the origin of GIST is considered to be the interstitial cell of Cajal [7].

The most common location for GIST is the stomach (52-60%), followed by small intestine (20% - 30%) and colorectum (10%) and the diagnosis is based on morphology and immunohistochemistry. Immunohistochemical stains like c-Kit/CD117 (a tyrosine kinase inhibitor) – positive in 95% [8], CD34 – positive in 40-50%, SMA (smooth muscle actin) – positive in 20-30% and S100 desmin – in about 10%, Ki67 - marker of cell proliferation [6] are necessary to make a precise diagnosis of GIST and to make the differential diagnosis between GIST and other mesenchymal tumors [7].

Surgery is typically the first step in the treatment of GIST, inclusive in patients with resectable metastatic tumors. Recurrence, metastatic disease or unresectable tumors can be treated with Imatinib (stopping cell-proliferation actions of the KIT and PDGFR tyrosine kinases) [9] .

The prognostic indicators are represented by tumor size, mitotic index, necrosis, infiltration and metastatic disease – variables that have an independent value for predicting the prognosis of patients with GIST [7].

The colorectal adenocarcinoma ranks as the fourth cause of cancer deaths worldwide and its development is a process of several stages influenced by complex interactions between host and environmental factors [10]. The histological

grade was demonstrated by many analyses to be a stage-independent prognostic factor in colorectal cancer [11].

The simultaneous occurrence of GIST and adenocarcinoma is uncommon in the literature, often the first one being detected incidentally at surgery [12].

However, in one study of 783 patients, Pandurengan et al showed that approximately 20% of patients with GIST develop other types of cancers [13] but it remains unclear if this is just an incidental coexistence or these two are related by a causal relationship.

Another study [14] demonstrated that synchronous colorectal adenocarcinoma and GIST have been more frequently reported. Due to the small number of cases, one cannot exclude an incidental relationship. Genetic pathways seem to be different for these two tumors.

Yan-Jun Liu et al found that incidental GIST coexisted most commonly with esophageal (1.13%) and gastric tumors (0.53%), less with colorectal tumors (0.03%) and has a high prevalence in males [15]. The association of a GIST with a small bowel tumor has previously been reported [16].

A possible explanation for the synchronous occurrence of these two entities is represented by the metallothioneins (MT), proteins with an increased affinity for heavy metal ions, coded by a family of 10 functional genes in human. The expression of these metalloproteins has been associated with protection against DNA damage, apoptosis, cell survival, angiogenesis and oxidative stress [17]. Metallothioneins have been reported to be overexpressed in multiple neoplasia (such as breast, ovarian, uterus, oral cavity, lung, skin and pancreas) and down regulated in other types of cancers such as gastric, colorectal, liver and central nervous system tumors [18].

Soo et al observed the nuclear expression of MT as determined by immunohistochemistry in all the GIST. Knowing that MT is correlated with cell proliferation, there is a possibility that MT may be involved in GIST proliferation [19]. Several studies have shown a direct correlation between MT and pathophysiology [20].

The particularity of the present case is represented by the synchronous appearance of a gastric gastrointestinal stromal tumor and a colon adenocarcinoma in a patient without specific manifestations and also the incidental finding of a colon tumor during laparotomy for GIST.

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