

SYNCHRONOUS OCCURRENCE OF ILEAL STROMAL TUMOR (GIST) AND COLONIC ADENOCARCINOMA: A CASE REPORT

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Abstract

Introduction: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the digestive tract. There is an increasing number of literature reports on synchronous occurrence of gastrointestinal stromal tumors and another malignancy of distinct etiology and evolution. The most reported cases include gastric synchronous occurrence of gastrointestinal stromal tumors and adenocarcinoma and gastric gastrointestinal stromal tumors and colonic adenocarcinoma.

Case report: We present a case of a 77-old female, with synchronous cecal moderately differentiated adenocarcinoma in Stage IIA according to the TNM classification and ileal spindle cell type GIST with low malignant potential, positive for c-Kit, CD34, vimentin, Actin, and negative for S100.

Conclusion: The synchronous occurrence of small bowel gastrointestinal stromal tumors and other primary gastrointestinal malignancies has been rarely reported. There is a need of further investigations to identify the relationship between gastrointestinal stromal tumors and colorectal cancers.

Key words: gastrointestinal stromal tumors, adenocarcinoma, colon

Introduction

The synchronous existence of two different tumors in the gastrointestinal tract (GI) is uncommon. Most cases of synchronous tumors in GI involve adenocarcinomas, lymphomas, carcinoids or leiomyosarcomas of the stomach [1, 2]. Concurrent gastrointestinal stromal tumors (GIST) and adenocarcinomas are extremely rare, with very few reported cases [3–6]. Usually, the coexistence of GISTs with other primaries is discovered incidentally during GI surgery for carcinomas [7, 8].

We present a rare case of synchronous GIST of terminal ileum and cecal adenocarcinoma, both detected during the diagnostic procedure. The study was performed according to the standards of the Ethics Committee of the Medical Faculty in Skopje.

Case report

A 77-old female, presented with anemia, weight loss, intermittent abdominal pain and right abdominal mass. Colonoscopy revealed an exophytic ulcerated neoplastic mass in the cecum and abdominal CT scan showed an additional well-defined heterogeneous mass located in the ileum. The patient underwent a right hemicolectomy with lymph-node dissection and partial resection of ileum.

Histological examination after standard dissection protocol of the surgically resected specimen followed. The obtained tissue specimens were formalin fixed, paraffin embedded and analyzed with routine HE stains. Additional immunohistochemical analysis was performed with c-Kit, vimentin, CD34, Actin and S100.

The cecal mass measuring 6×3 cm was identified and diagnosed as a moderately differentiated adenocarcinoma, Stage IIA according to the TNM classification. Another bulging tumor, located 15 cm proximal to the ileocecal valve was found in the intestinal wall of the ileum measuring 2.5×2 cm. It was well circumscribed, covered with intact intestinal mucosa.

Histopathological examination revealed a stromal cell neoplasm composed of bland uniform spindle cells with a low mitotic index; < 5 mitotic figures/50HPFs.

After performed immunohistochemistry the neoplasm was diagnosed as low malignant risk GIST, positive for c-Kit, CD34, vimentin, Actin, and negative for S100.

The cecal carcinoma was not CD117 positive.

Seven months after the operation the patient is alive, undergoing chemotherapy.

Discussion

Coexistence of a GIST and adenocarcinoma at two separate locations in the gastrointestinal tract is extremely uncommon [9]. These tumors represent distinct oncological entities. Adenocarcinoma is the most common malignancy in the gastrointestinal tract whereas GIST is a rare disease, with an incidence of 10–20 per 1 million cases [10]. There is no association between GIST and tumors of other histological types except in patients with Neurofibromatosis type I, Carneys triad and familial GIST [9, 11].

GIST is a rare, non-epithelial neoplasm arising primarily from mesenchymal tissues in the alimentary tract and the abdomen [1]. GISTs arise from interstitial cells of Cajal and their precursors of the GI and represent about 0.1–1.0% of all malignant neoplasms of the gastrointestinal tract [12, 13].

Most of the GISTs arise in the stomach (50–62%), the small intestine (20–30%), the colon (11%) and the rectum (7%), while the esophagus is rarely involved (0.6–1%) [14–17]. They also have been found in other locations such as the omentum, mesentery and retroperitoneum [18].

GISTs are usually well circumscribed, surrounded by a pseudocapsule and their size is in the range from a few millimeters to 35 cm, with a median size of between 5 cm and 8 cm.

Microscopically, most of the GISTs consist of spindle-shaped cells (70%), but some GISTs consist of rounded cells (epithelioid type, 20%) or a mixture, but they can also be pleomorphic [13].

According to the consensus report of GIST by Terada and Fletcher [19, 20], the malignant potential of GIST depends on tumor size and mitotic counts. In very low malignant risk groups, tumor size is less than 2 cm and mitotic counts are less than 5 per 50 high power fields (HPFs). In low malignant risk groups, tumor size is $2 \text{ cm} < 5 \text{ cm}$, and mitotic counts are $< 5/50$ HPFs. In intermediate risk groups, tumor size is $5 \text{ cm} < 10 \text{ cm}$, and mitotic counts are $< 5/50$ HPFs. In high risk groups, tumor size is $> 10 \text{ cm}$, and mitotic counts are $> 10/50$ HPFs [19, 20].

GISTs are distinguished from other mesenchymal tumors by their unique expression of c-Kit protein (CD117) [1, 17]. The most important markers for defining GISTs are CD117 (c-Kit protein) and CD34 (hematopoietic cell progenitor antigen). The majority of GISTs are usually positive for CD117 (near 95% of cases), CD34 (positive in 70–80% of cases), smooth muscle actin (positive in 40% of cases), S-100 (positive near 5% of cases), and desmin (positive in approximately 2% of cases) [8, 19].

Surgery has so far been the only effective treatment for GIST [6]. Recently, however, imatinib mesylate, a selective tyrosine kinase inhibitor, has shown activity in GISTs expressing CD117 [1].

The concomitant GI stromal tumor is usually discovered incidentally during diagnostic procedure, endoscopy or radiographic studies or surgery performed for other malignancies [21, 22].

Although the coexistence of GIST with other tumors is rare and they tend to be small, asymptomatic, and occur in low-risk patients, GIST still causes problems for the surgeon, the oncologist, and the pathologist [1, 23]. Surgical plans may need to be changed due to the incidental discovery of an unexpected tumor during surgery and appropriate sampling and thorough examination of the samples should be performed, especially in the case of small GISTs such as that in our case. Sufficient sampling is required to allow the diagnosis of suspicious metastatic/recurrent lesions during follow-up [1].

GISTs have been reported to occur synchronously mostly with adenocarcinoma; nevertheless there are reports of synchronicity with lymphomas and carcinoid tumors [14].

Various hypotheses have been proposed regarding the simultaneous development of GI stromal tumor and colorectal adenocarcinoma [24]. The vast majority of GISTs (80%) are associated with mutations of the proto-oncogene c-Kit, a growth factor receptor of the tyrosine kinase subclass III family, normally expressed in a variety of human tissues including the interstitial cells of Cajal. Approximately 5–7% of GISTs have a constitutively activating mutation in Platelet-Derived-Growth-Factor (PDGFR α) that stimulate the growth of various cell types, particularly in connective tissue, and the remainder (15%) of tumors have no mutations in either KIT or PDGFR α [13, 24].

Occurrence of sporadic CRC is associated with mutations of APC, DCC, p53, K-ras, DNA mismatch repair genes and with chromosomal and microsatellite instability (85% and 15%, respectively)

Some authors have described a correlation between c-Kit expression and colorectal cancer (CRC) but there is lack of evidence of the key role of c-Kit in the development of colorectal cancer [25].

Conclusions

The synchronous occurrence of small bowel GIST and other primary gastrointestinal malignancies has been rarely reported. There is a need of further investigations to identify the relationship between GIST and colorectal cancers. A possible neoplasm of different histological origin has to be excluded in any detected case of GIST.

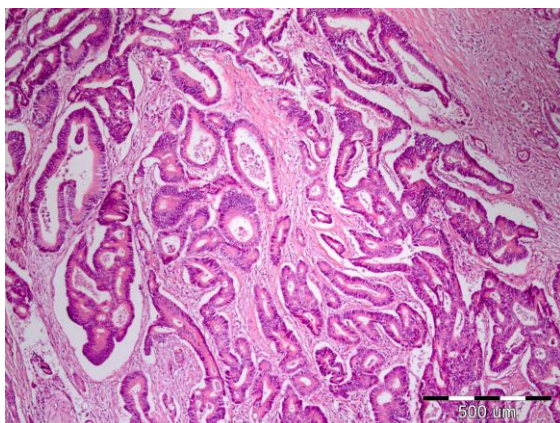


Figure 1 – Moderately differentiated cecal adenocarcinoma (HE. 10 × 4)

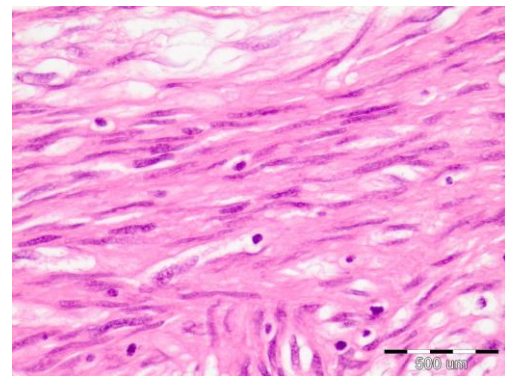
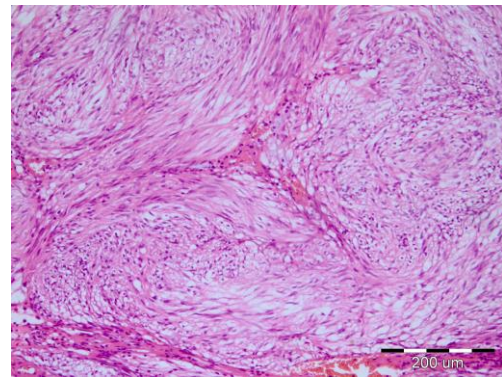


Figure 2 – Spindle cell type ileal GIST. (HE.4 × 10) a) The neoplasm shows interlacing fascicles of bland, uniform spindle cells with pale eosinophilic cytoplasm and low mitotic rate (10 × 10) b) High power view of the same neoplasm (10 × 40)

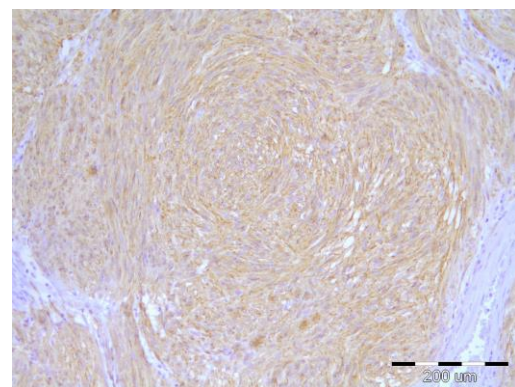


Figure 3 – GIST - Strong positivity for CD117 (10 × 10)

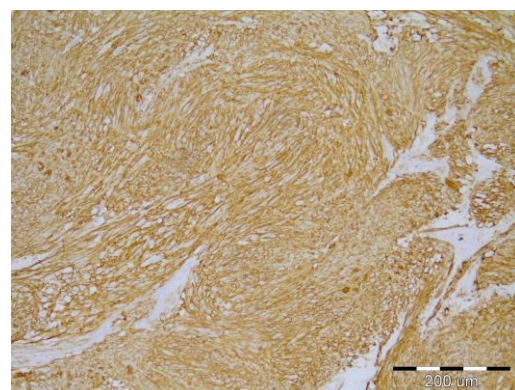


Figure 4 – GIST – Strong positivity for CD34 (10 × 20)

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Резиме

СИНХРОНО ЈАВУВАЊЕ НА ИЛЕАЛЕН СТРОМАЛЕН ТУМОР (ГИСТ) И АДЕНОКАРЦИНОМ НА КОЛОН – ПРИКАЗ НА СЛУЧАЈ

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Вовед: Гастроинтестиналните стромални тумори (ГИСТ) се најчести мезенхимални тумори на дигестивниот тракт. Бројот на објавени

случаи на истовремено јавување на гастроинтестинални стромални тумори и други малигни процеси со различна етиологија и еволуција е во пораст. Најголем број од публикуваните случаи прикажуваат синхронно јавување на гастроинтестинален стромален тумор и аденокарцином на желудник, како и гастроинтестинален стромален тумор на желудник и аденокарцином на колон.

Приказ на случај: Прикажуваме случај на жена на возраст од 77 години, со синхронно јавување на цекален умерено диференциран аденокарцином на цекум во стадиум ПА, според TNM-класификацијата, и илеален ГИСТ со вретеновидни клетки со низок малиген потенцијал, позитивен на c-Kit, CD34, виментин, актин и негативен на S100.

Заклучок: За истовремено јавување на гастроинтестинални стромални тумори на тенкото црево и други примарни малигни процеси на гастроинтестиналниот тракт ретко е објавувано. Постои потреба од понатамошни испитувања за да се утврди врската помеѓу гастроинтестиналните стромални тумори и колоректалните карциноми.

Клучни зборови: гастроинтестинален стромален тумор, аденокарцином, колон.