Clinical Case Report

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Rectal adenocarcinoma coexisting with incidentally found microscopic gastrointestinal stromal tumor

A case report

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Abstract

Rationale: Adenocarcinoma coexists with adjacent microscopic gastrointestinal stromal tumor (micro-GIST) is rare, especially in the rectum, where the gastrointestinal stromal tumors (GISTs) have the lower incidence rate. It is easy to ignore the concurrent micro-GIST due to the untypical symptoms.

Patient concerns: A 77-year-old male patient suffered from lower abdominal pain for 20 days and presented with per rectal bleeding for 10 days. He had the medical history of hypertension and diabetes for more than 25 years.

Diagnoses: Endoscopy revealed that the patient had rectum adenocarcinoma and multiple rectum polyps. Besides, the gastrointestinal stromal tumor was diagnosed by the pathologist.

Interventions: The patient underwent surgery of laparoscopic rectum resection and prophylactic ileostomy and took 6 courses of Capecitabine tablets orally.

Outcomes: One year after surgery, the patient had no local relapse by the CT scan. However, not long after the CT examination, he died of cardiovascular disease.

Lessons: Although micro-GIST may be noninvasive and asymptomatic, it may have the potential for transforming to malignancies. More attention should be paid to the patients diagnosed with gastrointestinal malignancy coexisting with micro-GIST.

Abbreviations: GISTs = gastrointestinal stromal tumors, micro-GIST = microscopic gastrointestinal stromal tumor, CT = computed tomography.

Keywords: coexistence, GISTs, micro-GIST, rectal adenocarcinoma, synchronously

1. Introduction

Gastrointestinal stromal tumors (GISTs) are rare mesenchymal neoplasms originating from primitive cells in the gastrointestinal tract. Histologically, GISTs include spindle cell (70%), epithelioid (20%), and mixed morphology (10%). It has the characteristic cells of interstitial cells of Cajal (ICC) and occurs predominantly in the stomach (70%), small intestine (10–20%) and the colon (11%), the rectum (7%), while the esophagus is rarely involved (0.6–1%). [1]

In the recent years, the incidence of GISTs in China has increased[2] due to most GISTs incidentally diagnosed during the therapeutic procedures for unrelated diseases or microscopically found during the surgical specimen for histological examination. However, in fact, there may be a much higher incident with nearly one third of people having micro-GIST (<1 cm) without clinically relevant symptoms[3] and mostly found on the histological examination of resected specimens.

The range of patients with GISTs concurrently diagnosed with another digestive tract tumor has been reportedly from 17.1% to 37.9%.[4] However, GISTs coexisting with other neoplasms in the same lesion are rare, especially in the rectum. Reviewing the literature, only 2 reports have been described previously, we believe that this is the first time to describe a concurrent micro-GIST with an adjacent adenocarcinoma in the rectum.

2. Case report

The patient written the informed consent and this study was approved by the Ethics Committee and institutional Review Board of the second hospital of Jilin University (JDEY-2018-0045), Changchun, China.

Editor: N/A.

WX and SW have similar contribution.

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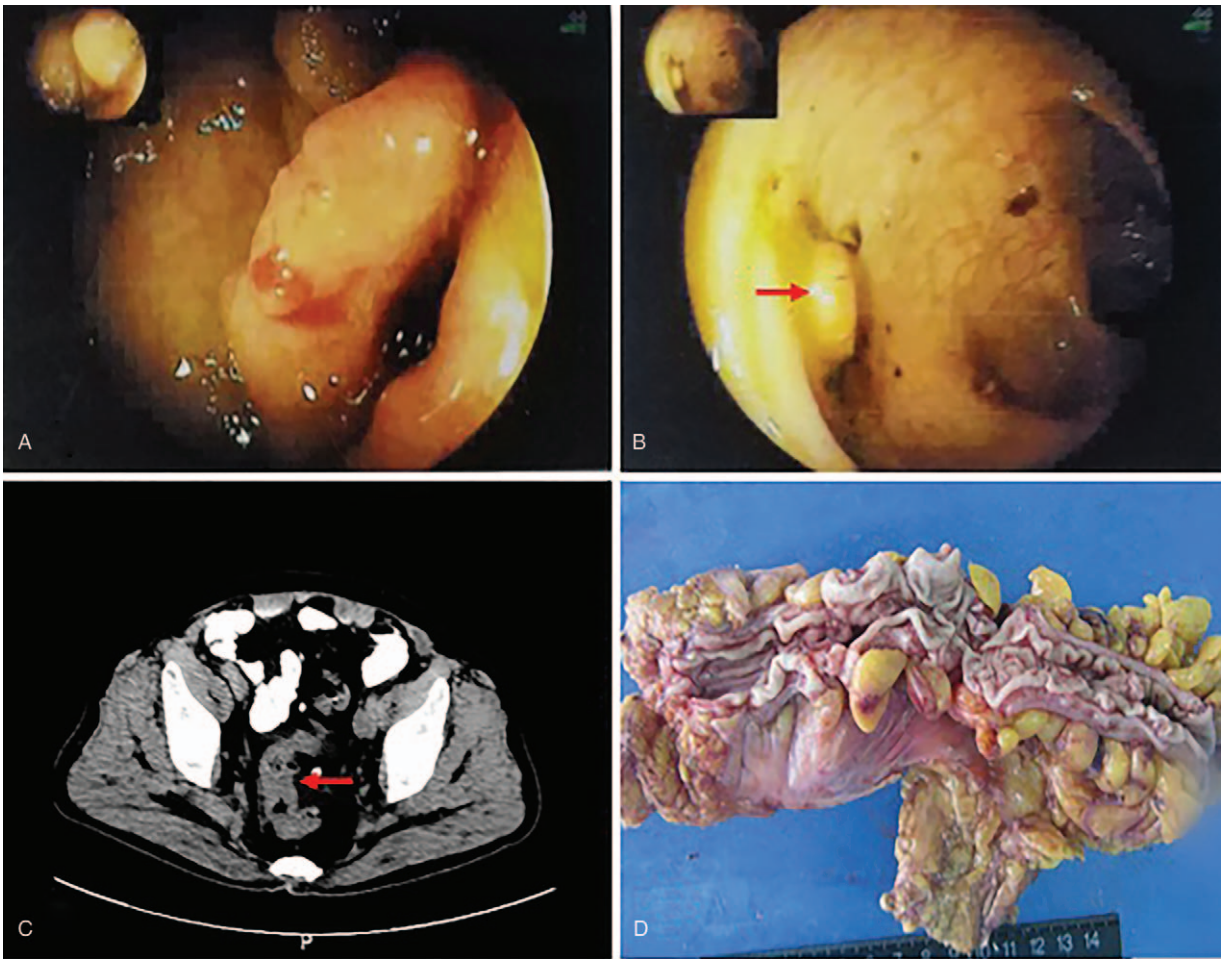

Figure 1. The images of tumor and examinations. A. The tumor showed by the endoscope. B. One of the multiple polyps found by the endoscope. C. The CT revealed the irregular mural thickening involving the rectum (red arrow). D. The resected specimen. CT = computed tomography.

In January 2017, a 77-year-old male patient visited our hospital for blood in the stool for 10 days. The local hospital colonoscopy result revealed a mass in the rectum with 10 cm from the anal verge and multiple polyps of different sizes less than 0.6 cm in diameter in the lower rectum (Fig. 1).

The biopsy pathology outcome revealed the mass with highly-moderately differentiated adenocarcinoma. The computed tomography (CT) shows an irregular mural thickening involving the rectum. No lymphadenopathy or distant metastasis was found. Tumor biomarkers, including carcinoembryonic antigen (CEA), carbohydrate antigen19-9 (CA-199) and á-fetoprotein (AFP) were all in normal range. He had the medical history of hypertension and diabetes for more than 25 years.

After comprehensive preoperative evaluation, laparoscopic rectum resection with a colorectal anastomosis and a prophylactic ileostomy were operated and the postoperative recovery was uneventful. The postoperative pathology revealed the moderately rectum adenocarcinoma (pT3N0M0). However, in the resected rectum specimen, a GIST (0.4 cm in diameter) was incidentally found and classified as spindle cell subtype by morphology characteristics (Fig. 2). According the National institutes of Health (NIH) consensus criteria (Fletcher criteria),[5] its malignant potential grade was assessed as very low risk.

The immunohistochemistry showed the PMS2 (+), EGFR (+), CDX2 (+), CD 117 (+), CD 34 (+), DOG 1 (+). Resection margins were negative and all 15 lymph nodes harvested were all negative for malignancy. The postoperative recovery of patient was uneventful. He only took oral treatment with Capecitabine tablets for 6 courses, and there was no local recurrence after 1 year of CT scan. However, not long after the CT examination, he died of cardiovascular disease.

3. Discussion

GISTs are most synchronously associated with gastric cancer[6] and also reported to occur concurrently with other cancer such as colon cancer, hepatic carcinoma and pancreatic cancer, breast cancer.[7,8] and incidence of that for esophageal or gastric cancer is 10%.[9] In 2000, Maiorana et al[10] firstly reported coexistent epithelial and stromal tumors in the stomach. Since then, it has been reported with increasing frequency that the coexistence of GISTs with gastrointestinal or other malignancies. However, the GISTs synchronously occurring with rectal cancer, especially in the same region is rare.

To our knowledge, only 2 cases of GISTs synchronously with rectal adenocarcinoma have been reported. Harshal et al[11] first reported a case of a large GIST coexisting with an adenocarcinoma

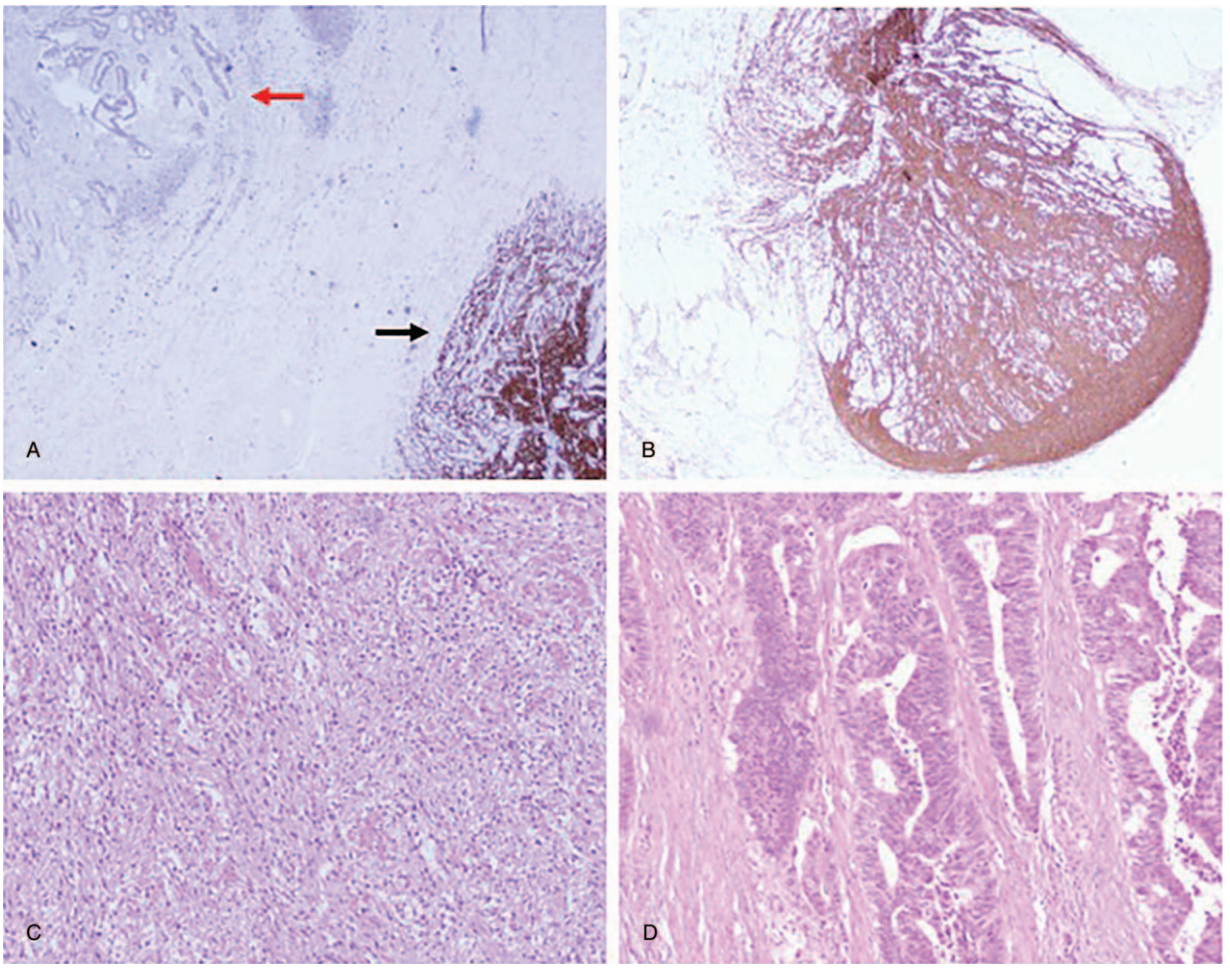

Figure 2. The images of specimen histology. A. Micro-GIST (red arrow) was adjacent to adenocarcinoma (black arrow) in low-power view. B. Strong and diffuse positivity was seen with CD34 immunostaining. C. Higher-power view of micro-GIST showed spindle cells. D. The adenocarcinoma in higher-power view. micro-GIST = microscopic gastrointestinal stromal tumor.

of the rectum, and in another case, advanced adenocarcinoma in the rectum coexisting with an incidental prostate carcinoma was reported synchronously with a large GIST by Suzuki et al.[12] In our report, synchronous occurrence of micro-GIST and rectal carcinoma are discovered incidentally as during histological examination of resected specimen.

Micro-GIST is mostly asymptomatic and presents clinically in benign or inert biological behavior. Rossi et al[13] reported that micro-GIST generally showed benign behavior irrespective of the mitotic rate. However, a few cases presented with invasive behavior, especially in those mitotic count >5/50 HPF or >10/50 HPF.[14] Although micro-GIST may be noninvasive and asymptomatic when diagnosed, it may have the potential for transforming to malignancies. Fletcher et al[5] think that at least at present time, based on the mitotic count and tumor size, it is probably not wise to use the definitive term "benign" for any GISTs.

Given to the high incidence of micro-GIST in patients with digestive tumor, endoscopy and endoscopic ultrasound are recommended in diagnosing and surveillance. Endoscopy could detect the mostly intramural tumors and early asymptomatic GISTs with submucosal protrusions < 1 cm in diameter are mostly detected incidentally during endoscopy.

In our report, the micro-GIST had chance to be mistaken as a polyp of the multiple rectum polyps found by endoscopy. Zhou et al[15] reported a case of rectal GISTs incidentally found as rectal polyps in a patient and the postoperative pathology result finally revealed the coexisting of rectal GISTs and polyps. Therefore, endoscopic ultrasound (EUS)-guided puncture to acquire the samples for cytological and histological examination was also recommended.

Once diagnosed, R0 resection should be achieved for symptomatic GISTs and for those larger than 2 cm in diameter. Because the residual GISTs may turn into growth and ulceration causing obstruction and bleeding. Furthermore, it may bring difficulties to evaluate the primary gastrointestinal tumor postoperatively. However, micro-GIST differs from clinically relevant tumors. It has an obviously lower proliferation rate pathologically and clinically, which raises the question of wait and see policy.[16] Patients with locally advanced inoperable GISTs are recommended to receive the neoadjuvant Imatinib therapy aiming to achieve secondary operability. Bonvalot et al[17] reported that the secondary excision of residual tumor had been related to a better prognosis in patients who respond to Imatinib.

GISTs seem to derive from gastrointestinal tract stem cells retaining some potential for differentiating either to mesenchymal

and epithelial lineages. CD117 and CD34 have been shown to express in these cells indicating stem cell nature. CD117 (c- kit pro-oncogene product) and CD34 (hematopoietic cell progenitor antigen) are recommended to be as the most significant markers for defining the GIST[18] and the positive rate for CD117 and CD 34 in 95% and 70%, respectively, in the GIST.[5]

Currently, the diagnostic marker DOG 1 (composing a calcium-regulated chloride ion channel) attracts much more attention and probably has even higher sensitivity than CD117, especially for CD117-negative GISTs.[19] However, some non-GISTs also could express the CD117 and DOG1, such as anorectal melanomas[20] and retroperitoneal leiomyomas.[21] Therefore, other markers such as S-100 and desmin should be taken to discriminate GISTs from schwannomas or leiomyomas. In our laboratory, we routinely perform the immunohistochemical stains for CD117, CD34, and DOG1 to identify and diagnose of GISTs (Fig. 2).

The main metastatic sites of GISTs are the liver and peritoneum. Lung and bone metastases are unusual. Although GISTs rarely metastasize to lymph nodes,[22] GISTs found during the surgery still may be mistaken as lymph node metastases, especially in the rectum, which may affect treatment decision. Laboratory examinations have no diagnostic value of GISTs metastases. Instead, CT scan combined with positron emission tomography (FDGPET/ CT)[23] is recommended to detect the metastases.

Whether the coexistence is a simple incidental relationship or a valid causal association is still unknown. Zhang et al[24] retrospectively reviewed 585 patients diagnosed with the GISTs and 32 (5.5%) had a concurrent primary digestive tract carcinoma and 28 of them (87.5%) GISTs was incidentally detected during an operation intended for a carcinoma or microscopically found by pathologists.

There are various hypotheses attempting to explain the synchronicity between the occurrences of the 2 tumors. Some researchers attributed it to the unknown carcinogens inducing the oncogenesis of stromal and epithelial cells and the simultaneous proliferation.[24] Therefore, further studies are required to clarify the genetic and molecular events of carcinogenesis and progression associating GISTs and concurrent carcinomas.

Until now, there are few literatures describing the clinical progression of micro-GIST and no a uniform guideline for clinical management of micro-GIST in the world. Given the annual incidence of clinical GISTs, only few micro-GIST may grow into a clinical size with malignant potential[25] and Zhang et al[24] reached a conclusion that carcinoma seemed to have a greater unfavorable effect than GISTs on prognosis. Therefore, it is more important to treat on the primary malignancy. Certainly, further studies to explain the genetic mechanisms accounting for the transformation of micro-GIST to clinical GISTs are needed.

Author contributions

Data curation: Wangsheng Xue, Yongbo Li, Ke Yu, Jiaqi Yu, Zeyun Zhao, Dan Jiang.
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Supervision: Mingwei Zhang, Tongjun Liu, Min Wang.
Visualization: Jiaqi Yu.
Writing – original draft: Wangsheng Xue.
Writing – review & editing: Wangsheng Xue, Min Wang.

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