

Synchronous Jejunal Gastrointestinal Stromal Tumor and Primary Adenocarcinoma of the Colon

Ramakrishnan Ayloor Seshadri · Shirley S. Singh · Ranganath Ratnagiri

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Abstract Synchronous gastrointestinal stromal tumors (GIST) and primary epithelial cancers of the gastrointestinal tract is an uncommon occurrence. We report a case of jejunal GIST which was detected incidentally in a patient during surgery for carcinoma of the sigmoid colon. The uncommon association of such synchronous tumors prompts a search for a common molecular pathway for carcinogenesis in gastrointestinal epithelial and stromal tumors.

Keywords Gastrointestinal stromal tumors · carcinoma colon · c-KIT · multiple primary neoplasms

Introduction

Gastrointestinal stromal tumors (GIST) are mesenchymal tumors arising from the wall of the gastrointestinal tract that are associated with constitutional activation of c-kit, a growth factor receptor with tyrosine kinase activity. They are usually isolated tumors, but can occur as part of syndromes like neurofibromatosis-1 or Carney's triad [1, 2]. Although synchronous occurrence of GISTs of stomach and other digestive tract cancers have been reported frequently,

GISTs of small bowel have been rarely reported to occur synchronously with other malignancies.

Case Report

A 68 year old gentleman who presented with altered bowel habits was diagnosed to have primary adenocarcinoma of the sigmoid colon. After evaluation, he underwent sigmoid colectomy. During laparotomy, he was found to have a 2.5 cm subserosal nodule in the antemesenteric border of the distal jejunum for which a resection of the jejunum with macroscopic negative margins was done (Fig. 1). There was no peritoneal or liver metastasis.

Histopathological examination of the sigmoid colectomy specimen revealed a mucin secreting adenocarcinoma, grade 3 (pT3 N1) (Fig. 2). The jejunal lesion turned out to be a submucosal gastrointestinal stromal tumor (spindle cell type) with 20 mitoses per 50 high power fields (Fig. 3). Immunohistochemical studies on the jejunal tumor showed positive staining for CD 117 (c-kit), smooth muscle actin, CD 34 and S-100 protein (Fig. 3). The patient is disease free one year after surgery.

Discussion

Synchronous second malignancies have been reported to occur in 13–14% of patients with GISTs [1, 2]. Although gastrointestinal carcinomas are the most common among these, other malignancies include hematological malig-

R. A. Seshadri (✉) · S. S. Singh · R. Ratnagiri
Cancer Institute (WIA),
Adyar,
Chennai 600020, India
e-mail: ram_a_s@yahoo.com



Fig. 1 Specimen photograph of the incidentally detected jejunal nodule

nancies, carcinoid tumors, melanoma, soft tissue sarcoma, cancers of the breast, kidney, prostate and female genital tract [1, 2]. GISTs are also known to be associated with neurofibromatosis-1 and Carney's triad [2]. The location of the GIST as well as the epithelial malignancy in most cases is the stomach, but carcinoma of the colon has also been reported to occur synchronously in patients with small bowel GISTs [1, 2]. In a majority of cases, the GIST is detected incidentally at the time of laparotomy for the primary adenocarcinoma [2]. All the stromal tumors in one report had a low malignant potential with an average size of 1.5 cm [2].

The synchronous occurrence of these tumors may probably be a coincidence [1, 2], although the role of a common carcinogenic agent has also been suggested [2]. Dietary carcinogens like nitrosamines are known to be a

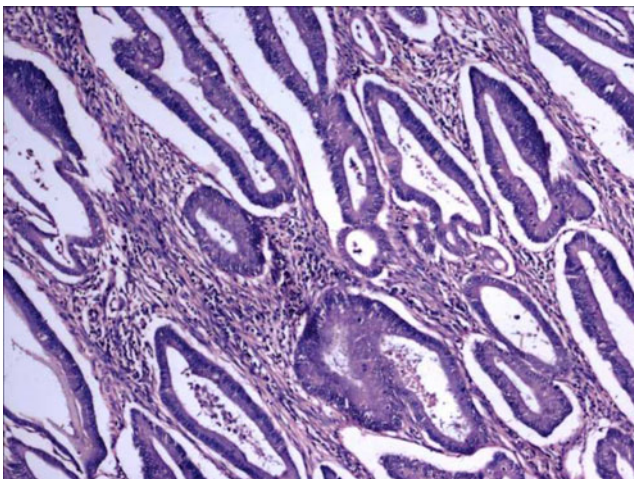


Fig. 2 Photomicrograph showing adenocarcinoma of the sigmoid colon (H&E, 20×)

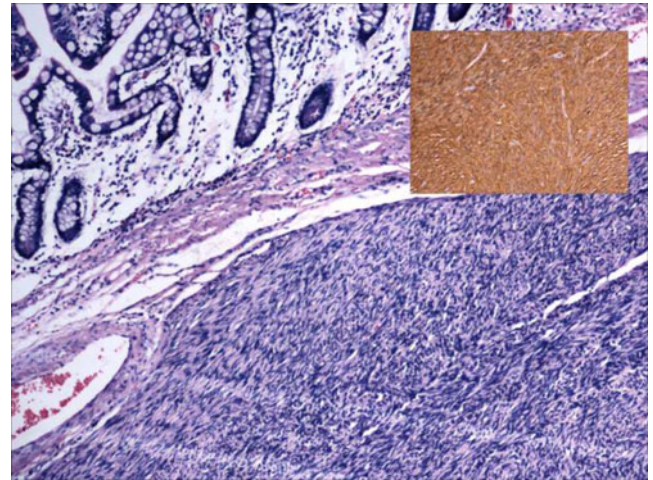


Fig. 3 Spindle shaped cells of GIST adjacent to normal jejunal mucosa (H&E, 20×). Inset shows immunoreactivity to c-kit (40×)

significant risk factor for development of various gastrointestinal adenocarcinomas and other cancers in humans [3]. Experimental studies in rats have shown that nitrosamines like N-methyl-N'-Nitro-N-nitrosoguanidine can cause adenocarcinomas as well as leiomyosarcomas (when combined with acetyl salicylic acid or stress) of the digestive tract [4]. Therefore, a common dietary carcinogen could be linked to the development of both epithelial and stromal tumors of the gastrointestinal tract.

Similarly, a common molecular pathway may underlie the development of GIST and colorectal adenocarcinoma. Constitutional activation of the c-KIT protooncogene is responsible for the development of GISTs. The role of the KIT tyrosine kinase receptor in the development of colorectal carcinoma has also been studied previously. Bellone G et al [5] have demonstrated expression of both the KIT protein and its ligand—the stem cell factor—in a small proportion of colorectal adenomas and carcinomas. They have also found that patients with expression of KIT by their tumors had a poor clinical outcome, suggesting an aberrant signaling of the KIT pathway in these lesions. Thus, we hypothesize that the KIT mediated cell signaling pathway may be a common pathway in the development of synchronous GIST and colorectal adenocarcinoma. However, further studies on the role of the KIT receptor in the pathogenesis of colorectal cancers will be required before any firm conclusions can be drawn.

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