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Gastrointestinal Stromal Tumor of the Colon Mimicking Inflammatory Fibroid Polyp with a Novel 63 bp *c-kit* Deletion Mutation
- A Case Report -

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Colonic gastrointestinal stromal tumors (GISTs) are rare and behave aggressively compared to GISTs in other parts of the gastrointestinal tract. Therefore, accurate diagnosis of GISTs and their distinction from other mesenchymal tumors is important for proper patient management and follow-up. Herein, we present an unusual case of a colonic GIST mimicking an inflammatory fibroid polyp with a novel 63 bp deletion mutation in exon 11 of the *c-kit* gene, which has not previously been reported. The tumor consisted of loosely arranged spindle cells and many inflammatory cells scattered throughout the tumor. Immunohistochemically, the tumor cells were focally and weakly positive for c-kit and diffusely positive for CD34, but were negative for PKC-theta, SMA, S-100 protein, ALK-1, and desmin. Our case re-emphasizes the broad morphologic spectrum of GISTs.

Key Words : Gastrointestinal stromal tumors; Colonic polyp; *c-kit*; Mutation

Gastrointestinal stromal tumors (GISTs), characterized by gain of function mutations of *c-kit* or *PDGFRA* genes, are the most common mesenchymal tumors of the gastrointestinal tract and are believed to originate from interstitial cells of Cajal or their stem-cell like precursors.[1] Accurate diagnosis of GISTs is important because their clinical course and outcome are very different from other gastrointestinal mesenchymal tumors. Recently, we experienced a very unusual case of a colonic GIST microscopically mimicking an inflammatory fibroid polyp. Herein we report the histologic features and mutation results.

CASE REPORT

A 64-year-old male patient was transferred to our hospital for evaluation of an incidentally detected asymptomatic intraluminal mass in the ascending colon. On physical examination, there were no specific findings. Laboratory tests were within normal limits. Abdominal-computed tomography showed a 3.3 cm colonic mass with enhancement. Colonoscopic examination showed a 3.5 cm yellow polypoid mass covered with normal mucosa in the distal ascending colon. A laparoscopic right hemicolectomy with side-to-side anastomosis was performed.

Macroscopically, there was a polypoid mass measuring 4 cm in the largest diameter in the ascending colon. The tumor was well-circumscribed and was mainly located in the muscularis propria and projected into the lumen without mucosal ulceration. On cut section, the mass was pale to deep brown, and myxoid with a smooth cut surface and multiple foci of hemorrhage (Fig. 1).

Microscopically, the tumor originated from the muscularis propria and showed an expansile growth pattern with a rather well-circumscribed border between the tumor and muscularis propria. The tumor consisted of loosely arranged spindle cells and many inflammatory cells scattered throughout the tumor (Fig. 2A). Lymphocytes occasionally formed nodular aggregates without germinal centers and plasma cells dominated (Fig. 2A, B). Some eosinophils and mast cells were also noted (Fig. 2C). In addition, there were regions of low cellularity with a myxoid stroma. The spindle cells had elongated spindle-shaped nuclei with eosinophilic cytoplasm and distinct cell borders. Mitotic activity was not observed in 50 high power fields.

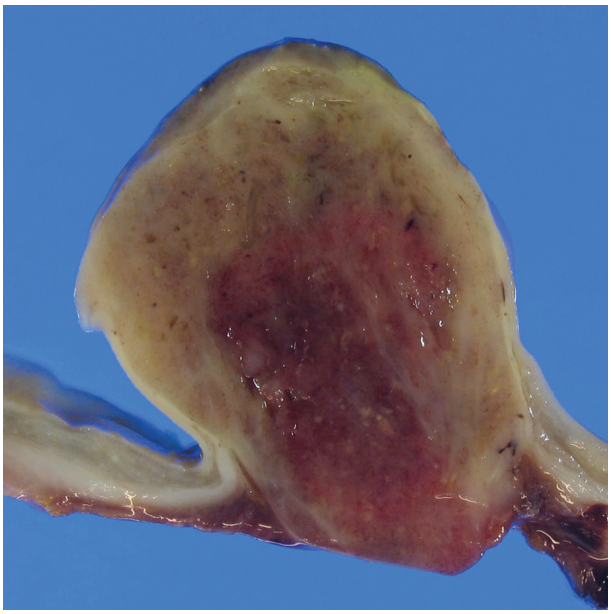

Fig. 1. Macroscopically, cut surface of polypoid mass shows a well-defined pale-brown tumor based in the muscularis propria with intraluminal protrusion.

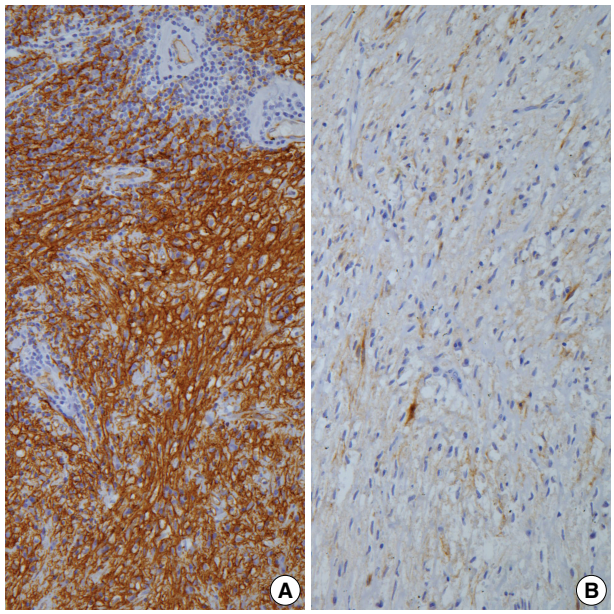

Fig. 3. Immunohistochemically, tumor cells are diffusely strong positive for CD 34 (A) and focally weak positive for c-kit (B).

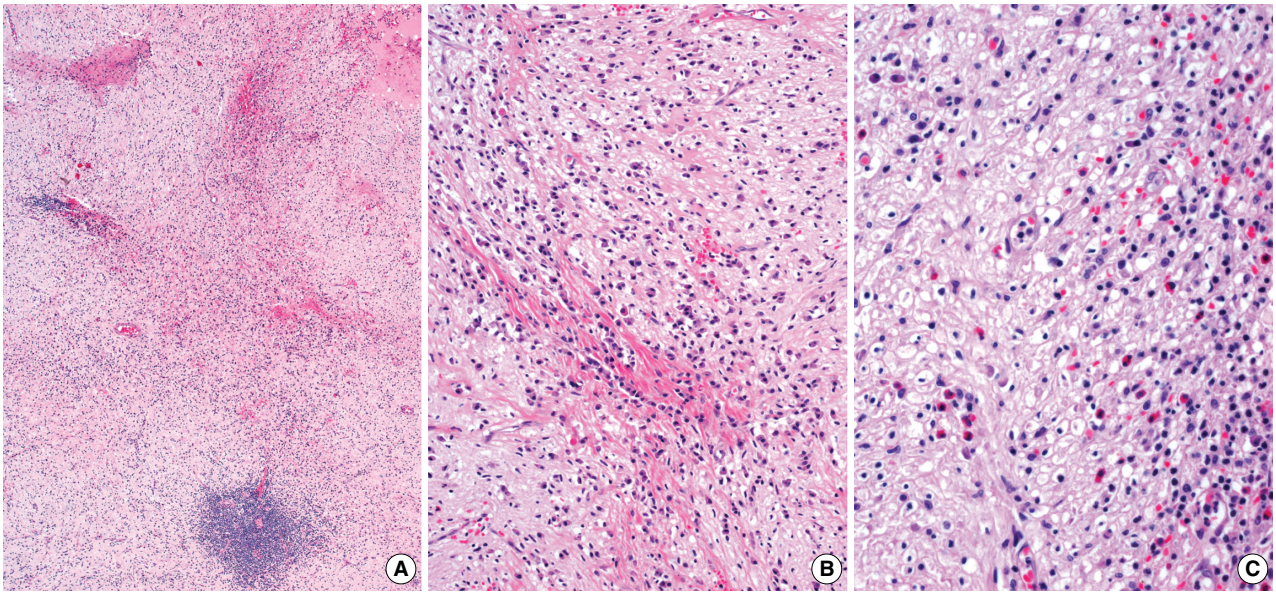

Fig. 2. (A) Low power view shows proliferation of spindle cells with infiltration of inflammatory cells throughout the tumor and focal aggregation of lymphoid cells. (B, C) High power view reveals proliferation of spindle cells and scattered inflammatory cells including lymphoplasma cells and some eosninophils in loose fibrous stroma.

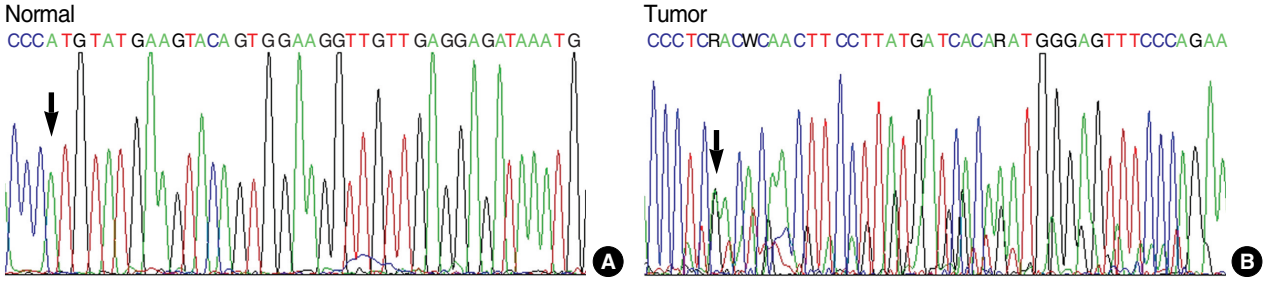

Fig. 4. With direct sequencing, a 63 bp deletion mutation starting from codon 552 of exon 11 of the *c-kit* gene is detected.

Immunohistochemical procedures were performed with primary antibodies including c-kit (polyclonal, 1:800, DAKO, Glostrup, Denmark), PKC-theta (monoclonal, clone 27, 1:100, BD Transduction Laboratories, Franklin Lakes, NJ, USA), CD34 (monoclonal, clone Qbend10, 1:50, DAKO), desmin (monoclonal, 1:50, DAKO), alpha-smooth muscle actin (SMA) (monoclonal, 1:50, DAKO), S-100 protein (polyclonal, 1:1,000, DAKO), and anaplastic lymphoma kinase-1 (ALK-1) (monoclonal, 1:40, DAKO). The DAKO EnVision™+ System was applied according to the manufacturer's instructions and diaminobenzidine was used as a chromogen. Most tumor cells were diffusely positive for CD34 (Fig. 3A), but focally and weakly positive for c-kit (Fig. 3B). Immunohistochemical stains for PKC-theta, SMA, S-100 protein, ALK-1, and desmin were all negative in the tumor cells.

Genetic analyses of exons 9, 11, 13, and 17 of the *c-kit* gene were performed using genomic DNA extracted from paraffin-embedded normal colonic mucosa and tumor tissue as previously described.[2] In exon 11 of the *c-kit* gene, a novel 63 bp deletion mutation was detected from the tumor tissue (Fig. 4). The final diagnosis was GIST with a low risk of aggressive behavior. After surgery, the patient had no evidence of a recurrence or distant metastasis during 18 months of follow-up care.

DISCUSSION

Our case showed a well-circumscribed tumor mass comprised of spindle cells with infiltration of inflammatory cells throughout the tumor. The differential diagnostic considerations included an inflammatory myofibroblastic tumor, a schwannoma, an inflammatory fibroid polyp, and a GIST. The spindle tumor cells were negative for SMA, S-100 protein, and ALK-1, but positive for CD34. The tumor cells were nearly negative for c-kit. Based on immunohistochemical studies, the possibility of a schwannoma and an inflammatory myofibroblastic tumor was excluded. The main differential diagnosis was between an inflammatory fibroid polyp and a GIST.

Inflammatory fibroid polyps are uncommon benign mesenchymal tumors that typically form ulcerated intraluminal polyps. CD34 is positive in 70-100% of cases and c-kit is typically negative.[3-5] Microscopically, inflammatory fibroid polyps are comprised of stellate-to-plump stromal cells, abundant small-sized blood vessels, and an inflammatory infiltrate dominated by eosinophils. The stromal cells tend to condense around blood vessels to form perivascular cuffs. However, the spindle cells in our case showed elongated nuclei and pale-to-pink cytoplasm with distinct cytoplasmic borders. Perivascular condensation was not observed in any portion of the tumor. Rather, fascicular, palisading, or patternless arrangements were observed. The predominant inflammatory infiltrate consisted of lymphoplasmacytes with fewer eosinophils. Moreover, although inflammatory fibroid polyps usually arise from the submucosa, the tumor in this case originated from the muscularis propria. Although the tumor was nearly negative for c-kit and showed a prominent inflammatory infiltrate, the possibility of GIST was considered. To confirm the diagnosis, genetic analysis was performed and showed a 63 bp deletion mutation in exon 11, which has not previously been reported in GISTs.

GIST is the most common mesenchymal tumor of the gastrointestinal tract. However, in the colon (excluding the rectum), it is exceedingly rare and comprises no more than 1-2% of all GISTs.[4,6-8] About 95% of GISTs in all other locations are c-kit positive.[9] However, in the colon, only about 75% of GISTs stain for this antigen. The c-kit staining pattern in our case was equivocal, but the tumor was found to harbor a mutation in the *c-kit* gene. GISTs with a prominent inflammatory infiltrate are uncommon, and only one case has been reported in a gastrointestinal autonomic nerve tumor (GANT), a variant of GISTs.[10] To our knowledge, this is the second case with this morphology and the first case with a 63 bp deletion of the *c-kit* gene.

The case reported herein re-emphasizes the broad morphologic spectrum of GISTs. Pathologists should keep in mind that

GISTs can be negative or weakly positive for c-kit, and GISTs should be included in the differential diagnosis when encountering mesenchymal tumors with an unusual histology in the gastrointestinal tract. In such circumstances, genetic analysis for *c-kit* mutations may be necessary.

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