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*Case Report*

# Plexiform myxoid gastrointestinal stromal tumor: a potential diagnostic pitfall in pathological findings

Bo Li[1], Qing-Fu Zhang[2], Yu-Nan Han[3], Ling Ouyang[1]

*[1]Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang 110004, People's Republic of China; [2]Department of Pathology, College of Basic Medical Sciences and The First Affiliated Hospital of China Medical University, Shenyang 110001, People's Republic of China; [3]Department of Breast Surgery, The First Affiliated Hospital of China Medical University, Shenyang 110001, People's Republic of China*

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**Abstract:** Gastrointestinal stromal tumors (GISTs) have a rather wide morphologic spectrum. Here, we report a rare variant plexiform GIST in gastric antrum. Microscopically, the tumor showed plexiform or multinodular growth pattern, proliferation of spindle cells, presence of epithelioid cells, and abundant myxoid stroma with thin-walled blood vessels. The histologic features were similar to plexiform fibromyxoma. The typical characteristics of immunohistochemistry (positive for CD34, DOG-1 and CD117) confirmed the final diagnosis of GIST. This is a rare case of myxoid GIST characterized by a plexiform growth pattern.

**Keywords:** Gastrointestinal stromal tumors, plexiform fibromyxoma, c-KIT mutation

## Background

Gastrointestinal stromal tumors are the most frequent mesenchymal tumors in gastrointestinal tract. Their behavior is driven by specific KIT- or PDFGRA-signaling [1]. Histologically, the tumor cells were comparatively monotypic with spindle cells (86%), epithelioid cells (5%), or mixed patterns (9%). Some histologic variants were recognized among the spindle tumor cells (palisaded-vacuolated, storiform, organ-like, perivascular collar-like, sclerosing and sarcomatous patterns). Such variants may also be recognized among epithelioid tumor cells (sclerosing, dyscohesive, diffuse hypercellular and sarcomatous patterns), which might have abundant myxoid stroma and hyaline degeneration [2]. However, myxoid GISTs which present with plexiform growth pattern were rare reported in older patients. In this paper, we report a case of this unique variant of GISTs and emphasize that it can be a potential pitfall for confusing with a plexiform fibermyxoma.

## Case presentation

A 71-year-old Asian woman who presented with a one-year history of black stool. The patient was shock ten days ago, her blood pressure was 75/55 mmHg and hemoglobin was 50 g/l. At that time, the patient visited at a local hospital and received a gastroscope and an enteroscopy examination. The gastroscopy demonstrated a 4.5*4.0 cm tumor located at gastric angle, lesser curvature and anterior/posterior wall of the stomach, which was stiff by their surface texture, roughness, erosion and friable at the apex. The enteroscopy showed three polypous state upheavals at 30 cm-50 cm distance from the anal verge, the tumors were about 0.3*0.3 cm-0.6*0.6 cm at large. And 45 cm distance from the anal verge observed a 0.8*0.8 cm mucosa thickening. Then the patient went to our hospital from her locality and performed some other examination. Whole abdomen plain and enhancement CT computed tomography (CT) scanning showed a under stomach mucosa solid mass which was about 6*5 cm and located at the side of greater curvature of the gastric antrum. The CT value was about 22 Hu. Enhanced CT scanning displayed the lesion with uneven enhancement and the CT value was about 38 HU. No retroperitoneal lymph nodes, liver and peritoneum was seen abnormal. Upper gastrointestinal opacification showed filling defect at the gastric antrum and

**Table 1.** Reagents and conditions used for immunohistochemistry

| Antibody | Clone | Dilution | Source | Results |
|---|---|---|---|---|
| CK (pan) | AE1/AE3 | Ready to use | Fuzhou Maixin Biology, Fouzhou, China | - |
| Vimentin | SP20 | Ready to use | Fuzhou Maixin Biology, Fouzhou, China | + |
| CD117 | A4502 | 1:100 | Dako, Carpinteria, CA, USA | + |
| DOG1 | K9 | 1:100 | Dako, Carpinteria, CA, USA | + |
| CD34 | QBEnd/10 | 1:100 | Dako, Carpinteria, CA, USA | + |
| SDHB | CL0349 | 1:100 | Sigma-Aldrich, MO, USA | - |
| Actin (SMA) | RB-9010 | 1:100 | Dako, Carpinteria, CA, USA | - |
| desmin | D33 | 1:100 | Dako, Carpinteria, CA, USA | - |
| S-100 | 4C4.9 | 1:100 | Dako, Carpinteria, CA, USA | - |
| β-Catenin | DO-7 | 1:75 | Dako, Carpinteria, CA, USA | nucleus- |
| Ki67 | MIB-1, | Ready to Use | Fuzhou Maixin Biology, Fouzhou, China | 2%+ |
| CD10 | MX002 | Ready to Use | Fuzhou Maixin Biology, Fouzhou, China | - |
| CgA | SP12 | Ready to Use | Fuzhou Maixin Biology, Fouzhou, China | - |
| Syn | RM-9111 | 1:75 | Fuzhou Maixin Biology, Fouzhou, China | - |
| CD68 | KP1 | Ready to Use | Fuzhou Maixin Biology, Fouzhou, China | - |
| NF1 | 31G7 | 1:50 | Invitrogen, Inc., Carlsbad, CA, USA | - |
| ALK | ALK-1 | 1:100 | Dako, Carpinteria, CA, USA | - |

Abbreviations: CK-Pan, pan-cytokeratin; SDHB, succinate dehydrogenase B; CgA, chromogranin A; Syn, synaptophysin; NF1, neuronespecific enolase 1; ALK, anaplastic lymphoma receptor tyrosine kinase.

shallow stomach angle. The contour of greater and lesser gastric curvature were smooth. No abnormal was seen in other parts from esophagus to ileocecal junction. The patient had five-year history of hypertension and diabetes mellitus. And she had a history of adenomyosis at the age of 67 but without surgical procedures. She denied coronary heart disease, neurofibromatosis, pulmonary chondroma and paraganglioma. Serum levels of tumor markers included carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9) and carbohydrate antigen 125 (CA125), which were all within normal limits. The tumors were totally excised by a distal partial gastrectomy. The patient had no recurrence after 14 months of surgical treatment without imatinib treatment.

## Materials and methods

The tissue was fixed in 10% buffered formalin and processed as routine for paraffin embedding, paraffin sectioning, and staining with hematoxylin-eosin. Immunohistochemical stains were performed by using the streptavidin-peroxidase procedure (Ultrasensitive, MaiXin Inc, Fuzhou, China) under the instructions of manufacturer. The antibodies were shown in **Table 1**. All series included positive and negative controls were included and evaluated through appropriate procedure.

*Pathologic findings*

Histologically, at low magnification, the tumor was located in the submucosa without intruding into the mucosa (**Figure 1A**) and exhibited multiple myxoid nodules (**Figure 1B**). The nodules were in the remaining gastric muscular propria and had a pushing border even extending to the layer of the muscularis (**Figure 1C**). The plexiform nodules have three main characterizes included spindle cells, mucinous extracellular matrix and thin blood vessels (**Figure 1D**). The spindle cells were similar to myofibroblastic cells. They had indistinct cytoplasm and cellular borders with the presence of nucleoli and occasional intracytoplasmic perinuclear vacuoles. In some regions, the nodules were composed of scattered clusters of epithelioid cells which seemed consistent with epithelioid GIST (**Figure 1E**), some signet ring cells were found (**Figure 1F**). Nuclear atypia was mild in nuclear enlargement, and the tumor cells had a low mitotic activity (<1 mitoses/50 high-power fields). No coagulative necrosis, perineural invasion, or vascular invasion were found.

*Immunohistochemical findings*

The spindle cells and epithelioid cells were typically immunoreactive for vimentin, CD34 (**Figure 2A**), c-KIT (**Figure 2B**) and Dog1 (**Figure**

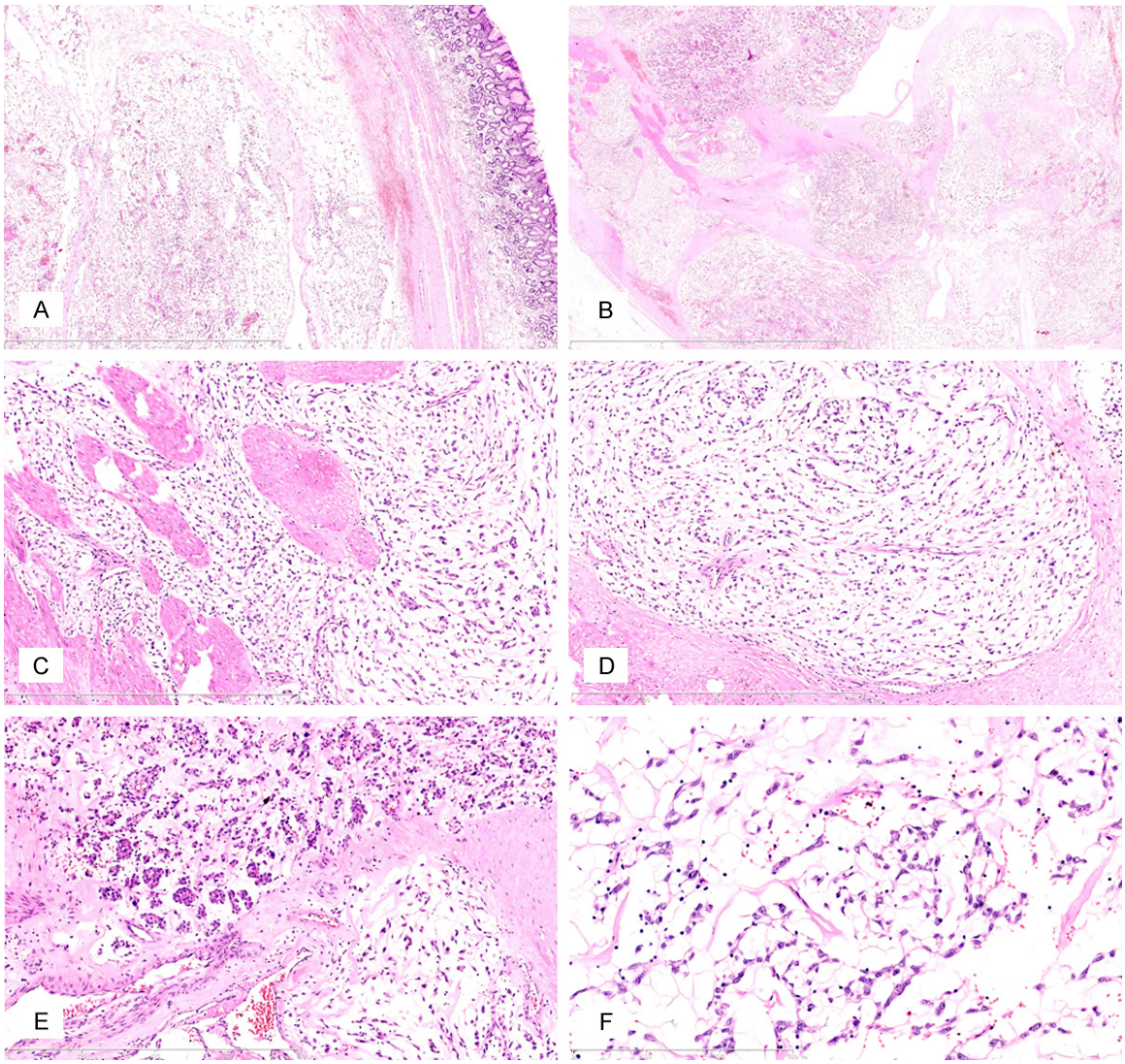


**Figure 1.** Hematoxylin and eosin staining. A. Low-power view demonstrates a multilobulated mass within the muscularis propria (original magnification ×25). B. The tumor exhibits a plexiform growth pattern with entrapment of smooth muscle fibers at the periphery (original magnification ×12.5). C. The nodules infiltrative to the muscularis (original magnification ×100). D. Tumor nodules are composed of a rich myxoid stroma, uniform spindle cells and delicate capillary (original magnification ×100). E. The tumor cells exhibited scattered clusters of epithelioid cells (hematoxylin-eosin, original magnification ×100). F. Some cells presented with signet ring cells (original magnification ×200).

**2C**), but negative for SDHB (**Figure 2D**), Actin (SMA), Desmin, S-100, Cytokeratin (pan), CD10, NF1, CD68, ALK and Neuroendocrine markers (CgA and Syn). No nuclear β-Catenin positivity could be found. The Ki-67 labeling index was about 2%.

## Discussion

GISTs, a subgroup of gastrointestinal mesenchymal neoplasms, may originate from interstitial cells of Cajal (ICC) or their stem cell-like precursors [3]. High mitosis count, large tumor size, non-gastric location, rupture, and male sex were independent adverse prognostic risks of patients with operable GISTs [4]. GISTs have a broad spectrum of morphological variants. There have been several literatures reporting that histologic subtypes were important prognostic features [5]. Patients of GISTs with epithelioid or mixed histology had a higher risk of 5-year recurrence, compared to those with spindle-cells histology [6]. Hou YY [7] showed that morphologic features of perivascular

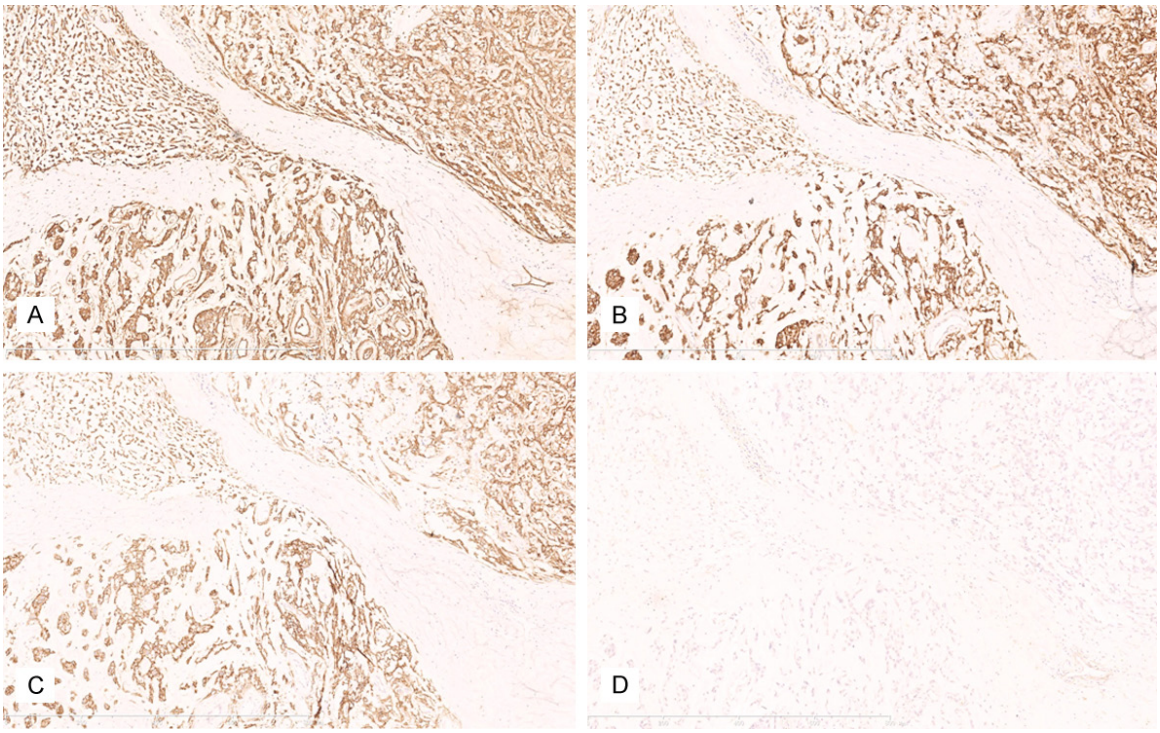


**Figure 2.** Immunohistochemical analysis. A. Immunohistochemical staining for CD34 showing strong positivity in the tumor cells and vascular endothelial cells (original magnification ×100). B. Tumor cells were diffusely positive for CD117 (c-Kit) protein (original magnification ×100). C. DOG1 immunohistochemistry shows strong cytoplasmic staining in the tumor cells (original magnification ×100). D. The tumor cells were negative for SDHB (original magnification ×100).

growth pattern to be associated with malignancy. Several recent results suggest that myxoid epithelioid GISTs are closely correlated with the platelet-derived growth factor receptor alpha (PDGFRA) gene mutation [8]. In this case, GISTs were composed of the mixed spindle and epithelioid cells within myxoid matrix and exhibited plexiform growth pattern. It was categorized by intermediate-risk according to the modified National Institutes of Health (NIH) consensus classification system. The patient had no recurrence after 14 months of surgical treatment, suggesting this unusual morphologic variation may having no close correlation with tumor malignant biological behavior.

Plexiform growth patterns have been described as a particular structure variants in various mesenchymal tumors, including neurofibromas [9], schwannomas [10], plexiform fibrous histiocytomas [11], plexiform fibermyxomas [12] and so on. Plexiform fibromyxomas are new gastric mesenchymal tumors recently described in the WHO classification of tumors in the digestive system [13]. The clinical manifestations of plexiform fibromyxomas are similar with the GISTs, which are apparently specific location in the gastric antrum or the duodenal bulb. The histology indicated a plexiform growth pattern composed of spindle cells, fine small vessels and the myxoid matrix [12]. The tumor cells had limited atypia and mitotic activity lower than 5/50 high-power fields. Plexiform fibromyxomas were always positive for vimentin, actin (SMA) and variably for CD10, and were always negative for CD34, c-KIT, DOG1, Desmin, and S-100 protein, without c-KIT or PDGFR-a mutations were present [14]. This current case was presented with submucosal of gastric antrum, histological characteristics similar to plexiform fibromyxoma. However, in immunophenotype, the positivity for c-KIT, DOG1, CD34 plus negativity for actin (SMA) and CD10 help excluding plexiform fibromyxomas. Immunohistochemical stains are also helpful in differentiating plexiform GISTs from other myxoid and fibromyxoid gastric neoplasms, such as plexiform neurofibromas (S-100 negative), plexiform schwannomas (S-100 negative), plexiform fibrohistiocytic tumors (CD68 negative), inflammatory myofi-

broblastic tumors (actin (SMA) and ALK negative). The lack of a prominent mixed inflammatory components distinguished our case from inflammatory fibroid polyps.

Plexiform growth pattern has been reported in some succinate dehydrogenase (SDH)--deficient GISTs. SDH-deficient GISTs often occur exclusively in the stomach, show predilection to young females, and have rarely been diagnosed in older patients [15]. In this case, immunohistochemical staining showed SDHB-negative expression. In addition, genetic mutation analysis exons 9, 11, 13, 17 of the C-Kit gene and exons 12, 18 of the PDGFRA gene did not detect any type of mutation in the present case (data not show). These results strongly support a diagnosis of SDH-deficient GIST.

## Conclusions

In summary, this report emphasizes that plexiform growth pattern is an unusual variable pathological features of myxoid GISTs and it is a challenging to make a diagnosis by histologic features. Pathologists should be aware of this phenomenon, avoiding misdiagnosing the disease as plexiform fibromyxomas.

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## Disclosure of conflict of interest

None.

**Address correspondence to:** Dr. Ling Ouyang, Department of Obstetrics and Gynecology, Shengjing Hospital of China Medical University, Shenyang 110004, People's Republic of China. E-mail: ouyang1964@163.com

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