To the Editor:

We would like to report the observation of a similar case as described by Takahashi and collaborators.1 It concerns a 61-year-old man presenting an episode of hematemesis after nonsteroidal anti-inflammatory drugs. The gastroscopy was planned and showed a multinodular antral wall. During this procedure, biopsies were taken but were noncontributive. An echo-endoscopy was then performed. The clinician described a multinodular hypoechogenic lesion of 37 mm. A second biopsy was taken, showing a myxoid lesion, but no precise diagnosis was obtained. A partial gastrectomy was performed including the antrum and the pylorus. The gross examination of the specimen of 8 cm of length revealed a well-circumscribed polycyclic and gray translucent tumor of 37 mm that focally eroded the mucosa. Histologic examination of the thickened wall showed multiple myxoid nodules infiltrating the muscularis propria, which were also present at the serosa surface and in the insertion of the epiploon. These nodules consisted of bland-looking spindle cells, separated by abundant myxoid stroma (Fig. 1). Vascularization was made of numerous small thin blood vessels. There was no evidence of mitotic activity. These nodules were fairly well circumscribed, but not encapsulated. No inflammation or desmoplastic tissue reaction was seen.

The tumor cells were positive for vimentin, smooth muscle actin, but were negative for desmin, CD34, CD117, S100, and epithelial membrane antigen. The patient is doing well 6 months after the surgery and the control endoscopy performed 3 months later did not revealed any residual tumor.

We believe that plexiform angiomyxoid myofibroblastic tumor of the stomach indeed represents a distinctive gastric tumor.

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REFERENCE

1. Takahashi Y, Shimizu S, Ishida T, et al. Plexiform angiomyxoid myofibroblastic tumor of the stomach. *Am J Surg Pathol.* 2007;31:724–728.

REPORT OF CASES

Case 1 was a 19-year-old woman presenting with a mass in the stomach. Distal gastrectomy was performed and showed a 4.5 × 3.5 × 3 cm lobulated tan-white mass with a glistening cut surface in the antrum. The tumor involved submucosa, muscularis propria, and subserosa, and the serosal surface was studded with multiple polypoid projections of the tumor.

Case 2 was a 46-year-old man who presented with upper gastrointestinal

FIGURE 1. Histologic appearance of the multilobular tumor (hematoxylin and eosin staining, original magnification × 80).
bleeding. Endoscopy revealed an ulcer in the gastric antrum with a deeply infiltrating mass detected by ultrasound. The patient underwent distal gastrectomy. The specimen showed a 3.5 cm finely lobulated tan-white mass transmurally involving the gastric wall and associated with an overlying 1 cm ulcer.

Microscopic examination of the both lesions demonstrated virtually identical findings. The tumors grew in an irregular multinodular plexiform fashion, widely dissecting the entire thickness of the stomach wall (Fig. 1A). They consisted of a relatively hypocellular spindle cell proliferation. The tumor cells were disposed randomly or in a vaguely fascicular fashion, separated by an abundant myxoid stroma rich in capillary-sized vessels (Fig. 1B). Areas of delicate collagenization were noted, particularly in the center of the tumor nodules (Fig. 1C). No necrosis or vascular invasion was seen. The constituent cells showed oval dark nuclei with smooth contours and had indistinct cytoplasmic borders. Rarely, cells with blunted nuclear ends and thin long eosinophilic cytoplasmic extensions were seen, reminiscent of smooth muscle cells. Mitotic figures were not appreciated in case 1, and rarely noted (<1/50 high-power field) in case 2. Immunohistochemically, the tumor cells were negative for CD117, platelet-derived growth factor receptor α (PDGFRA), CD 34, and S-100 protein. Case 1 was also negative for epithelial membrane antigen, collagen type IV, laminin, estrogen receptor, progesterone receptor, and CD10. Case 2 was negative for AE1:AE3 and bcl-2. The majority of the tumor cells in both cases labeled for HHF-35 and SMA in dense cytoplasmic pattern, whereas focal staining for desmin was noted. In case 2, a subset of tumor cells was also immunopositive for caldesmon and calponin. The Ki-67 labeling index in case 2 was less than 1%. No mutation was identified in either case in KIT (exons 9, 11, 13, and 17) or PDGFRA (exons 12 and 18) by direct sequencing using paraffin-embedded tissue. There is no recurrence or metastasis in the short-term follow-up in each case, at 9 months (case 1) and 4 months (case 2) after the procedure.

**DISCUSSION**

The tumors we describe here closely resemble the reported cases

![Figure 1](image-url)
with regard to location, growth pattern, cellular architecture, cytologic features, and immunoprofile, and we believe they all represent the same entity. As was discussed in the previous report, the main differential diagnostic consideration included gastrointestinal stromal tumor (GIST), peripheral nerve sheath tumor, and leiomyoma. The plexiform dissecting growth pattern is highly unusual for a GIST, and immunonegativity for CD117 and PDGFRA departs from the typical immunoprofile of GIST. Furthermore, activating mutations in either KIT or PDGFRA were not identified in any of the tumors. Morphologic findings, as well as S-100 and epithelial membrane antigen negativity speak against peripheral nerve sheath origin. Despite immunohistochemical evidence of focal myogenic differentiation, the morphologic appearance is not typical of leiomyoma, and a significant minority of the tumor cells is not reactive to any muscle markers. We are aware of a few examples of leiomyoma with unusual growth patterns arising in the gastrointestinal tract. Those tumors were composed of intersecting fascicles of long spindle cells with classic smooth muscle cell cytolgy, different from those of the cases reported in this letter. Thus, we agree with Takahashi et al that this tumor does not seem to represent any of the well-characterized entities, and warrants special recognition.

Three additional points could be made about this rare neoplasm based on our observations in the current cases. First, our case 1 is the first example of this tumor to occur in a female. Unlike those cases affecting males, differential diagnosis in this case also included a low-grade endometrial stromal sarcoma (LGESS) because of the similar dissecting plexiform growth pattern so characteristic of this gynecologic neoplasm. Although typically a highly cellular uterine tumor, LGESS can metastasize to the gastrointestinal tract, including the stomach. Moreover, the morphologic spectrum of LGESS has recently been broadened to include a myxoid variant, which consists of a hypocellular myxoid proliferation closely simulating the histologic appearance of the tumor we are describing. The absence of a history of a gynecologic tumor, and the total lack of immunoreactivity for estrogen receptor, progesterone receptor, and CD10 helped exclude this possibility.

Second, our cases show focal fibrosis, frequently in the form of delicate collag enization in the center of tumor nodules. In places, the tumors show frank diffuse fibrosis. This spectrum of fibrous, fibromyxoid, and myxoid stromal appearance was not emphasized in the original article, and the recognition of this distinctive pattern may help identify new examples of this entity.

Third, both of our cases support the impression of the previous authors that some tumor cells might possess the potential to differentiate toward smooth muscle cells. Unlike their examples, which were completely negative for desmin, a subset of the tumor cells in our cases was strongly immunoreactive for this marker. In addition, the staining pattern of HHF-35 and SMA was dense and cytoplasmic akin to smooth muscle cells, in contrast to subcutaneous "tram-track" pattern as seen in typical myofibroblasts. Furthermore, a minority of the neoplastic cells showed cytologic features reminiscent of smooth muscle cells, with nuclei having blunted ends and long eosinophilic cytoplasmic extensions. The "myofibroblastic" designation was originally employed because of the lack of typical smooth muscle cytology, negative staining for desmin in their examples, and compatible ultrastructural features. This label would not be totally accurate for the present cases, which exhibit more features of smooth muscle differentiation rather than typical profiles of myofibroblasts. It is noteworthy that their case 2 demonstrated ultrastructural attributes similar to those of smooth muscle cells.

In summary, we report 2 additional cases of a plexiform myxoid mesenchymal neoplasm of the distal stomach, which showed focal smooth muscle differentiation. The biologic behavior of this tumor is largely unknown, due to its rarity and insufficient follow-up. Although it appears benign in a purely morphologic sense, we suspect that the plexiform growth pattern may be associated with a risk for local recurrence if the tumor were to be incompletely resected.

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Plexiform Angiomyxoid Myofibroblastic Tumor of the Stomach

In Response:
We thank Dr Galant et al and Dr Yoshida et al for presenting new cases of plexiform angiomyxoid myofibroblastic tumor of the stomach—a tumor entity that was first described by us in the year 2007. Plexiform angiomyxoid myofibroblastic tumor of the stomach is characterized by a plexiform growth pattern, proliferation of cytologically bland spindle cells, and myxoid stroma that is rich in small vessels. The immunohistochemical