

Esophageal gastrointestinal autonomic nerve tumor

Esophageal gastrointestinal stromal tumors (GISTs) are less common than other tumors of the esophagus. Gastrointestinal autonomic nerve tumors (GANTs) comprise a subgroup of GISTs. These tumors are mostly located in the small intestine and stomach, whereas they rarely arise in the esophagus. In immunohistochemical examinations, staining for CD117 and CD34 is positive in these tumors, whereas smooth muscle actin staining is negative. The most important risk factors for progressive disease are the mitotic count and tumor size, and surgery is recommended for the treatment of suitable cases. In this article, we discussed the clinicopathologic features of GISTs and the treatment options in light of the literature of a patients diagnosed with esophageal GANTs.

Gastrointestinal stromal tumors (GISTs) have been reported to be anatomically located in the stomach; small intestine; colon, rectum, and appendix; and esophagus in 51-70%, 25-36%, 5-7%, and 1-3% of cases, respectively (1). Gastrointestinal autonomic nerve tumors (GANTs) comprise a subgroup of GISTs. These tumors are mostly located in the small intestine and stomach, whereas they rarely arise in the esophagus.

On computed tomography of the thorax of a 61-year-old female patient who presented to our clinic with shortness of breath and swallowing difficulty, a lesion of approximately 62 × 33 × 68 in size was observed. The lesion filled the prevertebral distance and subcarinal area from the level of the arcus aorta in the mediastinum and compressed the right and left main bronchi, and it had borders with the esophagus that could not be distinguished. A diagnosis could not be made, and as a result, transbronchial biopsy was performed. The maximum standardized uptake value on positron emission tomography-computed tomography (PET/CT) of the mass was 23.8 (Figure 1a). There was no pathologic involvement for the mass on PET/CT, and the patient

underwent right thoracotomy. The lesion, which appeared to originate from between the muscle fibers of the esophagus, was excised without complete removal of the esophageal mucosa (Figure 1b). On immunohistochemical examination of the tumor, in which microscopically spindle cells were generally organized as cellular areas, CD117 and CD34 staining was positive, and in addition to the existence of neuronal cells and S-100 positivity, staining for smooth muscle actin, desmin, and synaptophysin was negative (Figure 2). The mass was 7 cm in size with 1 mitotic count per 50 high-power fields (HPFs). The tumor was histopathologically diagnosed as a GANT, and the risk for progressive disease as intermediate.

GISTs are divided into subgroups according to their phenotypic features (2). In GANTs, tumor cells display differentiation toward neuronal structures. Long cytoplasm similar to axons, scattered microtubules compatible with neurotubules, and dense-core neurosecretory type granules are observed on electron microscopy. GANTs are also known as myenteric plexus tumors or plexosarcomas, as they resemble the autonomic myenteric plexus with this appearance (2). Staining for neural or neuroendocrine markers such as neurofilament proteins, chromogranin, and synaptophysin is usually poor.

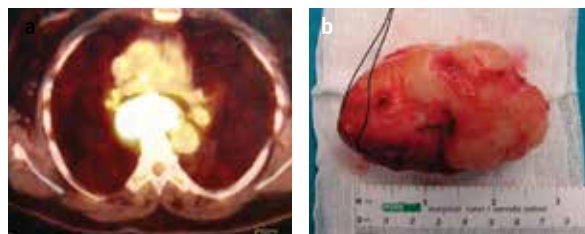


Figure 1. a, b. 2-Deoxy-2-(F-18)fluoro-D-glucose (18F-FDG) positron emission tomography-computed tomography showing a well-delineated, homogeneous, low-density mass of the esophagus, with increased 18F-FDG uptake, on cross-sectional image. Gross appearance of an esophageal gastrointestinal autonomic nerve tumor (b).

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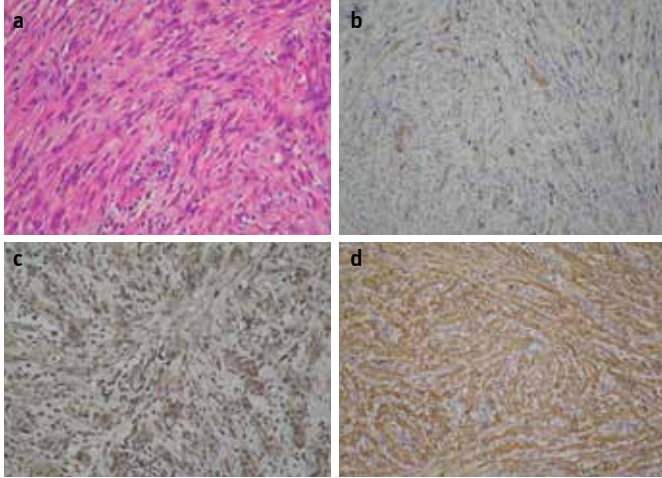


Figure 2: a-c. The cytologic features include absent mitotic activity (hematoxylin and eosin staining, $\times 400$ magnification) (a). Immunohistochemical staining showing positive immunoreactivity within tumor cells for CD34 (b). Strong CD117 immunoreactivity in a gastrointestinal autonomic nerve tumor. (c) Tumor cells are diffusely and strongly S-100 protein-positive (d).

However, the less specific neurons of neural tumors are positive for enolase, Leu-7, and S-100. Their electron microscopic features display neuronal characteristics rather than those of schwannomas. Smooth muscle cell differentiation markers are negative in these tumors. These tumors differ from schwannomas, and thus, they should be differentiated from esophageal schwannomas.

Considering the tumor size and mitotic count per 50 HPFs, these tumors are classified as having a very low, low, intermediate, or high risk for progressive disease (2). Bone, liver, peritoneal, and pulmonary parenchymal metastases have been reported in tumors with a high risk of progressive disease (1). Approximately, 10% of GISTs carry malignant characteristics (1).

The primary treatment for GISTs is excision of the tumor for those with negative surgical margins. Enucleation is the most frequently used surgical method for esophageal GISTs. Thora-

scopic enucleation is recommended for tumors smaller than 5 cm, whereas thoracotomy enucleation is recommended for tumors 5-10 cm in size. Meanwhile, esophagectomy is recommended if there is mucosal involvement (3,4). Esophagectomy is recommended also for larger (≥ 10 cm) tumors, which are more infrequent (3). The most important prognostic factors are the mitotic count and tumor size (4). Because CD117 (c-kit) receptors are expressed in GISTs, c-kit receptor inhibitors can be used for to treat these tumors. Imatinib binds to active c-kit receptors, blocking signal transmission pathways and thus inhibiting uncontrolled cell proliferation (5). Successful results have been reported, namely a 40% reduction in tumor size after 2 months of imatinib mesylate therapy at a dose of 400 mg/day, in cases diagnosed as stromal tumors in the preoperative period (5).

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