Original Article

Schwannoma of stomach: a clinicopathologic study of 12 cases

Li-Ping Tao¹, Er-Jiong Huang¹, Peng Li², Yong-Yong Lu³

Departments of ¹Gastroenterology, ²Pathology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China; ³The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, Zhejiang Province, China

Received December 13, 2017; Accepted January 8, 2018; Epub March 1, 2018; Published March 15, 2018

Abstract: We analyzed clinicopathologically 12 gastric schwannomas. Patient ages ranged from 41 to 79 years (mean, 52 years; median, 59 years). They variably presented with gastric discomfort, bleeding, or rarely gastric outlet obstruction and many were incidental findings during other medical procedures. The maximum tumor diameters ranged from 1.0 to 5.4 cm (mean, 3.5 cm; median 3.8 cm). The typical histologic features included spindle cells with micro-trabecular architecture, focal nuclear atypia, and peritumoral lymphoid cuff. Median mitotic count was 1/50 high-power field. No malignant variants were recognized, and follow-up did not reveal recurrences or metastases. Immunohistochemically, all tumors were positive for S100 and SOX10, and most were also GFAP positive, whereas CD34 and NF were rarely positive. All tumors were negative for cytokeratin AE1/3, HMB45, c-kit, DOG1, smooth muscle actin, desmin, and synaptophysin. None of the tumors showed gastrointestinal stromal tumor-specific KIT or PDGFRA mutations. Gastric schwannoma is a distinctive form of peripheral nerve sheath tumor and it should be distinguished from gastrointestinal stromal tumor and other mesenchymal tumors of the gastrointestinal tract, especially clear cell sarcoma and metastatic melanoma.

Keywords: Schwannoma, stomach, S100 protein, SOX10, prognosis, differential diagnosis

Introduction

Schwannomas of the gastrointestinal tract (GIT) are rare tumors, with the stomach being the most common location [1]. The tumors occur in middle age to late adulthood with a peak in the sixth decade of life. Most are benign and asymptomatic but nevertheless, the potential for malignant transformation does exist and is directly related to the size of the tumor. Surgical resection is the treatment of choice. The histologic appearance of gastric schwannoma is essentially very similar to their soft tissue counterpart, namely, a proliferation of spindle cells with vague nuclear palisading with variably myxoid stroma [2]. In addition, gastric schwannomas are characterized by the presence of lymphoid tissue surrounding the lesions. Voltaggio et al. [3] reported 51 cases of gastric schwannoma, the largest series of immunohistochemically documented cases of this entity to date. In this study, we analyzed 12 gastric schwannomas clinically, histologically, immunohistochemically, and genetically, including follow-up data and further confirmed the benign nature of this tumor without malignant variants.

Materials and methods

All 12 cases were retrospectively collected from the archive in the authors’ institutions from 2006 to 2016 when electronic surgical pathology records were available. Clinical information was retrieved from the electronic medical records and follow-up information was obtained by chart review. The hematoxylin-and-eosin slides of all cases were reviewed and immunohistochemical studies using the avidin-biotin-complex immunoperoxidase technique were performed. The following commercially available antibodies were used in all 3 cases: cytokeratin AE1/AE3, S100, smooth muscle actin (SMA), SOX10, CD34, HMB45, GFAP, des-
Schwannoma of stomach

min, synaptophysin, c-kit, DOG1, and neurofilament (NF). Heat-induced epitope retrieval in an EDTA buffer was used for all antibodies. Detection was performed using Ventana detection system and automation with diaminobenzidine as the chromogen.

Mutation analysis for gastrointestinal stromal tumor (GIST)-specific KIT and platelet derived growth factor receptor alpha (PDGFRA) mutation “hot spots” was performed as previously described [4]. Briefly, tumor DNA samples were obtained from formalin-fixed and paraffin-embedded tissue and were polymerase chain reaction amplified; and the purified polymerase chain reaction products were sequenced directly.

Results

Patient ages ranged from 41 to 79 years (mean, 52 years; median, 59 years). There were 3 men and 9 women, with a male to female ratio of 1:3. Gastrointestinal bleeding was seen in 3 patients. Other complaints included epigastric pain or discomfort (n=2) and weight loss due to gastric outlet obstruction (n=1). Six patients were asymptomatic and came to medical attention for unrelated diseases. One patient was identified on computed tomography as part of follow-up examination after colon cancer diagnosis. None of the patients had a history of NF1 or NF2 syndrome. The surgical treatment included partial gastrectomy (n=4), local excision or wedge resection (n=3), or biopsy (n=1). The excision type was not specified in 4 cases. At follow-up, 10 patients were alive without recurrences for 1 to 4 years (median, 2.8 years). One patient died of nonneoplastic disease.

The maximum tumor diameters ranged from 1.0 to 5.4 cm (mean, 3.5 cm; median 3.8 cm). Tumors were described as ovoid or round mural masses with gross mucosal ulceration and hemorrhage present on 1 and 2 occasions, respectively. No areas of cystic change or gross necrosis were reported in any of the cases. Nine tumors were well circumscribed with a capsule-like boundary was noted in 6 cases. The tumors varied from fibrotic to rubbery, fleshy, or gritty. On sectioning, the cut surface of the tumors were white, yellow, yellow-white, yellow-pink, or yellow-gray with glistening or shiny with whorled, bosselated, or variegated pattern. Three cases were described as sessile growth into the stomach.

Of the 10 cases including the gastric mucosa, an ulcer was appreciated either grossly or histologically in 5 cases. A lymphocytic peritumoral cuff was present in all (100%) cases with germinal center was identified in 8 cases (67%) (Figure 1A). Diffuse intratumoral lymphoid infiltration was seen in all cases, with plasma cells present in 6 cases (50%) (Figure 1B). Nine tumors were infiltrating the muscularis propria. No definite true capsules were histologically detected. All tumors were composed of spindle cells, with 2 cases showing focal epithelioid morphology. A microtrabecular pattern was present in 8 cases (Figure 1C). Cellularity was moderate in the great majority of the cases. Nuclear palisading was vague in the majority of the cases. Well-developed nuclear palisading

Figure 1. Histologic features of gastric schwannoma. A: Peripheral lymphoid cuff with occasional germinal centers. B: Lymphoid infiltration entrapped smooth muscle elements within the tumor. C: Showing microtrabecular pattern. D: Moderate nuclear atypia was often focally present.
Schwannoma of stomach

Figure 2. Immunohistochemically typical features include positivity for (A) S100 protein and (B) SOX10. Tumor cells are usually negative or only focally positive for (C) CD34 and are consistently negative for (D) DOG1.

was seen in only 2 cases, and nuclear palisading was completely absent in 2 cases. Well-developed Verocay bodies were observed in only 2 cases. Mitotic activity was low (median, 1/50 high power field). All but 2 cases exhibited some degree of nuclear atypia (Figure 1D). The matrix was at least minimally collagenized, with the majority of the cases showing a moderate degree of collagen deposition. Five cases had areas of myxoid change. Xanthoma cells and vascular hyalinization without luminal dilatation were observed occasionally.

Immunohistochemically, all 12 cases showed strong S100 (Figure 2A) and SOX10 (Figure 2B) positivity. Nine cases showed variable positivity for GFAP ranging from 15% to 90% of the tumor cells. Most cases were negative for CD34. Three cases showed focal CD34 positivity (Figure 2C). All cases were negative for cytokeratin AE1/AE3, SMA, desmin, KIT, DOG1 (Figure 2D), NF, synaptophysin, and HMB-45.

Genetically, KIT exons 9, 11, 13, and 17 and PDGFRA exons 12, 14, and 18 were evaluated in 8 tumors. No mutations were detected in these regions known to be KIT and PDGFRA mutation “hot spots” for GISTs.

Discussion

Primary peripheral nerve sheath tumors of the GIT are extremely rare. The most common location in the GIT is stomach. The tumors are characterized by strong positivity for S-100, SOX10, and negative staining for c-Kit and DOG1 [1-4]. Although they share many clinical, morphological, and even some immunohistochemical features with GIST, it is important to make this distinction because roughly 50% of GISTs recur or metastasize. In contrast, malignant transformation of a solitary gastric schwannoma is a rare occurrence, with recurrences only being observed after incomplete resection [5].

Schwannomas in the GIT present either as a solitary tumor or multifocally in the context of von Recklinghausen’s disease [6]. Gastrointestinal tract schwannomas mostly occur in the stomach along the lesser curvature. They have also been observed in the colon and esophagus. Schwannomas of the stomach are extremely rare, representing only 0.2% of all gastric tumors [7]. They are more common in women between the ages of 50 to 60 years. In a recent study, gastric schwannomas accounted for 6.3% of 191 GIT mesenchymal tumors [8]. Gastric schwannomas are thought to arise from the sheath of Auerbach’s plexus or, less commonly from Meissner’s plexus. They are slow growing tumors that displace nerves to the periphery of the lesion and thus, neural function in the vicinity of the tumor is preserved. Malignancy transformation is extremely rare. Upon review of the literature, only 8 cases of malignant gastric schwannoma have been reported. Of these, 7 cases were associated with neurofibromatosis [9]. Between 3% and 29% of patients with von Recklinghausen’s disease develop some types of malignant schwannomas. The prognosis for such patients is poor, being characterized by a rapid clinical course and poor response to chemotherapy. Most patients died within 2 years, with an average 5-year survival of 23%.

Gastric schwannomas grossly appear as solid tumors measuring between 2 and 10.5 cm [3]. They are generally well-demarcated, without invasion. Most are found in the body, where they vary from small, dome-shaped mucosal...
necrosis, or cystic change. Histologically, gastric schwannomas show moderate cellularity, vague to focally distinct nuclear palisading, hyalinized vessels, and uniform bipolar spindle cells with tapered ends. Mitotic activity is generally very low. Characteristically, a prominent cuff of lymphoid follicles is seen surrounding the tumor. This feature has been described as highly distinctive for gastric schwannoma but is not always present.

A large number of morphologic variants of schwannoma have been described outside of the GIT, including cellular, plexiform, and melanotic schwannoma. Schwannomas can also display marked cellular pleomorphism (so-called ancient schwannoma) or be composed of predominantly epithelioid cells (epithelioid peripheral nerve sheath tumor) [1-8]. Occasionally, the stromal mucin can be substantial in these tumors mimicking other types of myxoid soft tissue neoplasms [10].

Gastrointestinal tract variants of clear cell sarcoma are another S100 positive neoplasm that can involve the stomach, although they are more common in the small intestine [11]. These tumors typically show mural involvement, often with a nested pattern. By their higher cellularity and significant general nuclear atypia, they are usually easily distinguished from gastric schwannomas. Metastatic malignant melanoma has sometimes been the submitted diagnosis for gastric schwannoma. To some degree, the microtrabecular to microfascicular pattern of gastric schwannoma resembles that of desmoplastic or spindle cell melanoma. However, metastatic melanoma usually manifests as a mucosa-based button-like lesion, showing greater degree of atypia and mitotic activity, very rarely forming a solid intramural mass. Gastrointestinal stromal tumors can have a similar clinical and gross presentation, involve the same demographic group of older adults, and have certain overlapping histologic features with GIT schwannomas [12]. Because GISTs are much more common than gastric schwannomas, it is not surprising that most reports on gastric schwannomas before modern immunohistochemistry in fact described as GISTs. Among these cases, gastric spindle cell GISTs of the palisaded-vacuolated type are perhaps the most common distinctive histology variant of gastric GISTs. Grossly, GISTs differ from schwannomas by their predominantly tan-pink or hemorrhagic appearance, as opposed to yellow to yellow-white color typically seen in gastric schwannomas. Histologically, some gastric GISTs, especially those of the palisaded-vacuolated subtype, have more prominent nuclear palisading than most gastric schwannomas but the perinuclear vacuolization is not seen in gastric schwannoma. Immunohistochemical studies separate GIST from schwannoma by the presence of KIT and DOG1 only in the former and S100, SOX10, and often GFAP only in the latter. Furthermore, CD34 is usually demonstrable in spindle cell GISTs and generally absent in gastric schwannomas.

In conclusion, we have reported 12 cases of gastric schwannomas. This tumor is much less common than gastric GIST and has a predilection for older adults with a female predominance. The clinical course is benign, and neither our study nor our review of the literature identified a malignant course. Gastric schwannoma should be distinguished from GIST and malignant S100-positive tumors, especially GIT clear cell sarcoma and metastatic melanoma.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Yong-Yong Lu, The First Affiliated Hospital of Wenzhou Medical University, Nanbaixiang, Ouhai District, Wenzhou 325003, Zhejiang Province, China. E-mail: lyy2100@126.com

References

Schwannoma of stomach


