Trakya Univ Tip Fak Derg 2007;24(2):141-145

Case Report / *Olgu Sunumu*

Glomus Tumor of the Stomach

Midenin Glomus Tümörü

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Submitted/ Başvuru tarihi: *12.09.2006* ***Accepted / Kabul tarihi:*** *03.10.2006*

A sixty-four-year old male patient presented to the emergency room with massive upper gastrointestinal tract bleeding. During distal gastrectomy, a submucosal, well demarcated mass with a diameter of 2.4 cm was palpable in the antral region of the lesser curvature. Histopathological examination of the mass revealed uniform tumor cells with clear cytoplasms and round nuclei, forming nests, strands and sheets between dense, irregularly branching, thin-walled vessels. Immunohistochemistry was positive for vimentin and SMA and negative for cytokeratin, CD34, synaptophysin, chromogranin A, NSE, CD117 (C-kit) and S-100 protein. Electron microscopy demonstrated tumor cells with clear cytoplasms and round nuclei with coarsely dispersed chromatin, forming groups around vascular structures. Clinical findings, gross appearance, tumor pattern, immunohistochemical findings and electronmicroscopic findings were all consistent with a glomus tumor.

Key Words: Glomus tumor/pathology; immunohistochemistry; stomach.

Altmış dört yaşında erkek hasta masif üst gastrointestinal sistem kanaması ile acil servise başvurdu. Distal gastrektomi uygulanan hastada ameliyat sırasında antral bölge küçük kurvaturda submukozal yerleşimli, 2.4 cm çapında, iyi sınırlı bir kitle palpe edildi. Kitlenin histopatolojik incelemesinde, düzensiz dallanan, ince duvarlı damarların arasında yuvalanmalar, kordonlar ve tabakalar oluşturan berrak sitoplazmalı uniform tümör hücreleri görüldü. İmmünohistokimyasal olarak vimentin ve SMA ile pozitif; sitokeratin, CD34, sinaptofizin, kromogranin A, NSE, CD117 (C-kit) ve S-100 protein ile negatif sonuç elde edildi. Elektron mikroskopik olarak berrak sitoplazmalı, kaba kromatinli yuvarlak nukleusa sahip hücrelerinin damar yapıları etrafında gruplar oluşturdukları görüldü. Klinik bulgular, makroskopik görünüm, tümör paterni, immünohistokimyasal ve elektron mikroskopik bulgular glomus tümörü ile uyumlu bulundu.

Anahtar Sözcükler: Glomus tümörü/patoloji; immunohistokimya; mide.

Glomus tumors are uncommon tumors of mesenchymal origin which generally arise from peripheral soft tissues, particularly in the distal parts of the extremities.[1,2] However, rare cases with visceral involvement are reported in the literature.[3] In the gut they are most commonly

Presented at the 18th National Symposium of Pathology, May 7-11 2006, Çeşme (18. Ulusal Patoloji Sempozyum'unda sunulmuştur. 7-11 Mayıs 2006, Çeşme).

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found in antrum of the stomach and typically they are single tumors.[4,5] We present a 64-year-old man with a glomus tumor in his stomach presenting with massive upper gastrointestinal tract bleeding, which led him to an urgent laparatomy and distal gastrectomy.

CASE REPORT

A 64-year-old man presented to the emergency department of our hospital, suffering from vomiting fresh blood for two hours. Because of massive hematemesis, the patient has undergone an urgent distal subtotal gastrectomy and Billroth II anastomosis after his initial examination and endoscopic evaluation. At exploration, a well demarcated mass was palpable in the wall of the antral region of the lesser curvature. The location of the tumor precluded a successful resection with safe surgical margins. The patient did not require any additional medical therapy except for a blood transfusion of 500 ml and intravenous fluid support for four days. The postoperative course of the patient was unremarkable and he was discharged from the hospital on postoperative day five tolerating a regular diet.

The macroscopic inspection of the dissected specimen revealed a 2.4 cm submucosal mass in the lesser curvature of the antrum. The hyperemic and hemorrhagic mucosa overlying the mass had an ulceration of 0.5 cm in diameter. The cut sections revealed a grossly well demarcated, solid, gray-colored, partly hemorrhagic mass located in the submucosa, extending to the subserosa of the stomach (Fig. 1).

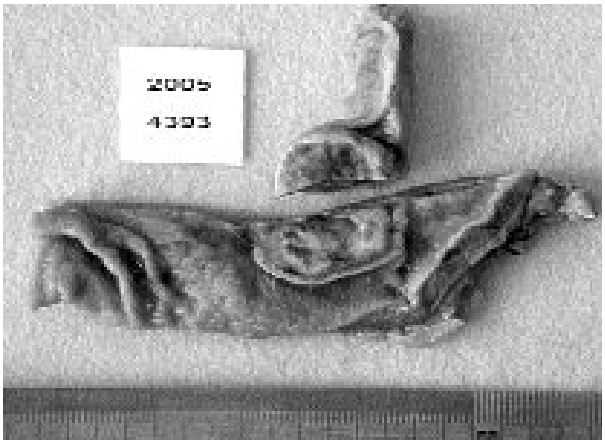

Fig. 1. *Gross appearance and the cut section of the tumor.*

The air dried and Giemsa-stained imprint cytology revealed individually scattered tumor cells throughout the slides. The tumor cells did not form any distinct, well formed groups. They had eccentrically located, uniform nuclei with an average diameter of two to three times of an ordinary mature lymphocyte. There was no nuclear atypia and mitotic figures were scanty. At first glance, the cytomorphologic features of the tumor suggested a carcinoid tumor (Fig. 2).

A sample of 0.5 cm in diameter was obtained from the fresh tumor tissue and fixed in gluteraldehyde for electronmicroscopic evaluation. The rest of the distal gastrectomy specimen was sampled after an overnight fixation in 10% formaldehyde at room temperature. The 5 mm-thick paraffin sections were stained with routine hematoxylin-eosin (H-E) stains. Sections from a selected tissue block were immunohistochemically stained for vimentin, cytokeratin, alpha smooth muscle Actin (SMA), CD34, synaptophysin, chromogranin A, NSE, CD117 (C-kit), S-100 protein and Ki-67. Reticulin silver stain was applied to a section of the tumor for histochemical evaluation.

The HE-stained slides revealed a tumorous mass beginning from the submucosa, extending to the subserosa of the stomach. The monotonous, uniform tumor cells with clear cytoplasms and round nuclei, formed nests, strands and sheets between dense, irregularly

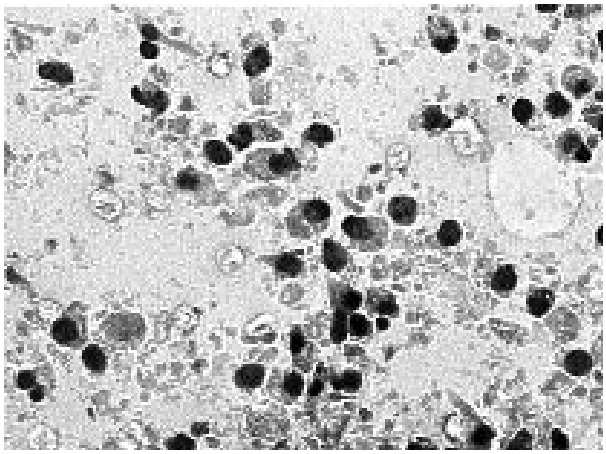

Fig. 2. *Tumor cells with broad cytoplasms and eccentrically located round nuclei. Some nuclei are bare and there are cytoplasmic fragments in the background (MGG x 400).*

branching, thin-walled vessels (Fig. 3a). The tumor cells revealed 2 mitosis/50 high power fields (HPFs). Neither cytological atypia nor necrosis was present. There was a ruptured vessel causing hemorrhage through the partly ulcerated mucosa, into the lumen of the stomach (Fig. 3b). The tumor showed local invasion to the adjacent tissues with scattered tumor islands. Immunohistochemistry was positive for vimentin and SMA and negative for cytokeratin, CD34, synaptophysin, chromogranin A, NSE, CD117 (C-kit) and S-100 protein. The Ki-67 proliferative index of the tumor was 30%, which may be considered high for a benign tumor. The reticulin stain revealed fine reticulin fibers encircling nests of two to four tumor cells (Fig. 3c). Electron microscopy revealed tumor cells with clear cytoplasms and round nuclei with coarsely dispersed chromatin, forming groups around vascular structures. Well-formed intercytoplasmic desmosomes were established between the tumor cells. There were excess amounts of mitochondria and some neurosecretory granules in the cytoplasms of the tumor cells (Fig. 4a, b).

The clinical findings, gross appearance, tumor pattern, immunohistochemical findings and electron microscopy results were all consistent with a glomus tumor.

DISCUSSION

Vascular tumors of the gastrointestinal tract (GIT) are extremely rare, accounting for <2% of all benign tumors of the GIT. The largest portion of these vascular tumors are glomus tumors.[3,5] Glomus body is a neuromyoarterial receptor that regulates blood flow within arteries and these tumors originate from the modified smooth muscle cells of the glomus body.[3,6]

Although gastrointestinal glomus tumors may present with a variety of symptoms, they typically present with gastrointestinal bleeding because of the ulceration of the overlying mucosa.[2,6] Other presenting symptoms include obstruction and non-specific ulcer symptoms, but still many may remain asymptomatic.[7] Our patient was asymptomatic until the massive upper gastrointestinal bleeding led him to an urgent surgical operation.

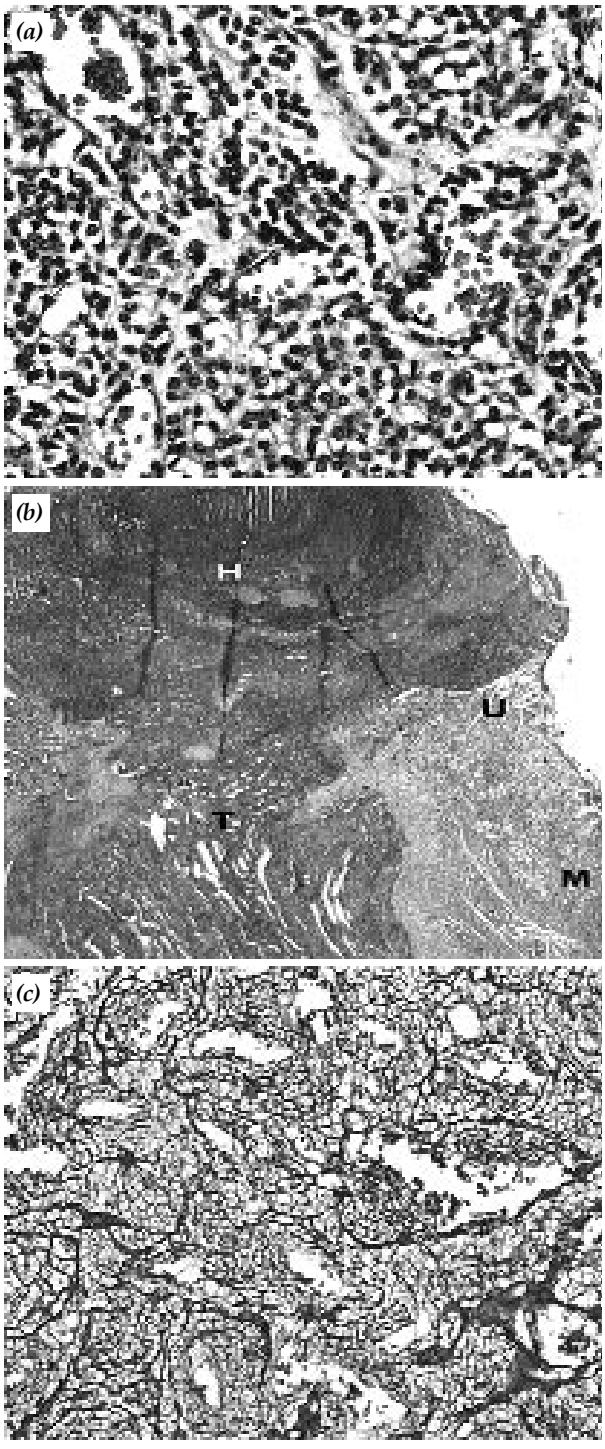

Fig. 3. ***(a)*** *The monotonous, uniform tumor cells with clear cytoplasms and finely dispersed chromatin, forming nests, strands and sheets between dense, irregularly branching, thin-walled vessels (H-E x 100)* ***(b)*** *Hemorrhage through the partly ulcerated mucosa, into the lumen of the stomach. (H-E x 50)* ***(c)*** *Fine reticulin fibers encircling nests of two to four glomus cells (Reticulin silver stain x 100).* *H: Hemorrhage; U: Ulcerated mucosa; M: Mucosa; T: Tumor.*

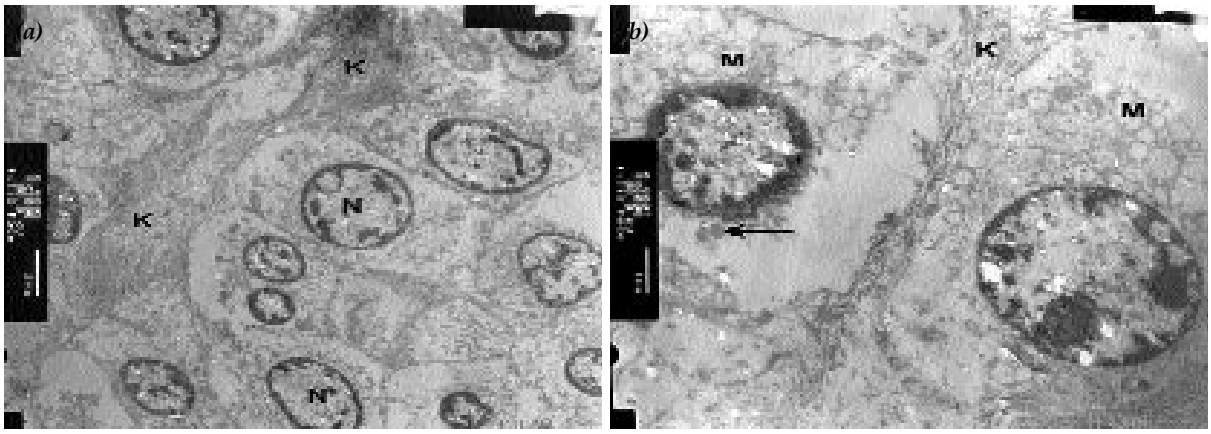

Fig. 4. ***(a)*** *Tumor cells with clear cytoplasms and round nuclei with coarsely dispersed chromatin; K: Collagen; N: Nucleus (x 3000)* ***(b)*** *Excess amount of mitochondria and a few neurosecrotory granules in the cytoplasms of the tumor cells; M: Mitochondria; K: Collagen; Arrow: Neuroendocrine granules (x 6000).*

The only large series of gastrointestinal glomus tumors belongs to The Armed Forces Institute of Pathology (AFIP) which comprises 31 gastric and one cecal glomus tumors collected over a 28-year period.[2] All other cases in the literature are individual case reports.[3] Most glomus tumors seem to be benign, well demarcated with distinct tumor borders. However, metastatic disease has rarely been reported in tumors greater than 5 cm in diameter. Among the cases with gastrointestinal glomus tumors in the series of the AFIP, only one case with metastasis to the liver has been reported. This patient died of metastatic disease at the 50th month of the follow-up period. This metastatic tumor revealed spindle cell foci, mild atypia, vascular invasion and one mitosis per 50 HPFs.[2] Thus, although these tumors may have a small, unpredictable potential for malignant behavior, overall they have a good prognosis.[2]

The prognostic criteria of gastrointestinal glomus tumors are not well established.[1] In a study by Folpe et al, 52 glomus tumors (one of them was gastric) were analyzed and it was suggested that, the term "malignant glomus tumor" should be reserved for lesions with a marked risk of metastases. Such lesions should fulfill at least one of the following criteria; deep location and size bigger than 2 cm, or the presence of atypical mitotic figures, or a combination of moderate to high nuclear grade and mitotic activity (Five mitosis/50 HPFs).[8]

The differential diagnosis of gastric glomus tumor includes carcinoid tumor, hemangiopericytoma and gastrointestinal stromal tumor (GIST). It has been postulated that the glomus tumor exists as an intermediate form between hemangiopericytomas and leoimoyomas in a broad spectrum of smooth muscle tumors and this may account for similarities between entities considered during differential diagnosis.[7] The examination of vascular spaces usually reveal ectatic thin-walled vessels in glomus tumors, whereas in carcinoid tumors vascularity and fibrosis is prominent.[4] The glomus cell nuclei are round and frequently have a perinuclear pale area or clear cytoplasms. Both hemangiopericytomas and epithelioid GISTs lack these features. The cells of glomus tumors usually lack both immunohistochemical and electronmicroscopic evidence of neuroendocrine granules, though some may present these features.[4] In our case there were a few neuroendocrine granules at ultrastructural level which were not supported by immunohistochemistry. Glomus tumors are almost always positive for SMA and vimentin and negative for cytokeratin and S100 protein, and are usually negative for CD34, CD117 and neuroendocrine markers such as chromogranin A, synaptophysin, NSE and neuroflament.[1,2,8] In the presented case, results of immunohistochemistry were all consistent with the findings of a suspected glomus tumor.

The diagnosis of glomus tumor is almost never made preoperatively and even intraoperatively, as frozen section and imprint cytology diagnosis is difficult and a large number of cases are misinterpreted as carcinoid tumors.[7,9] The imprint slides of the presented case also had the cytomorphologic features of a carcinoid tumor.

As mentioned above, glomus tumors are essentially benign in nature and local resection is curative.[7] Our patient still survives without any significant morbidity at 12 months after resection of the tumor. Nonetheless, long-term follow-up of this patient will be necessary, because of the unpredictable potential for malignant behavior of these tumors.

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