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Stomach Glomus Tumor

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Abstract: A glomus tumor is a benign mesenchymal tumor developing either from the neuromuscular glomus cells or from the glomus bodies of the smooth muscle cells. While the gastrointestinal system is rarely the location for glomus tumors, extracutaneous glomus tumors are often encountered in the stomach. This study presents a 36-year-old male patient who applied to the hospital with complaints of nausea and vomiting accompanied by a stomach pain that gradually increased over two days and the endoscopic inspections have revealed a subepithelial lesion, which was removed with partial gastrectomy. Histopathological evaluations have shown that the tumor is based on the submucosal layer and had infiltrated into the muscular mucosa. Histopathologic evaluations and immunohistochemical staining had revealed the tumor as a glomus tumor.

Keywords: Stomach Mesenchymal Tumors, Glomus Tumor, Pathology.

1. Introduction

A glomus tumor (GT) is a benign mesenchymal tumor developing either from the neuromyoarterial glomus cells located in the arteriovenous intersection points or from the glomus bodies of the smooth muscle cells (1-3). GT's represent approximately 1.5% of all soft tissue tumors (4). There are two different forms for GT's, namely the sporadic form in which the lesions are solitary and the familial form which is often encountered in children and in which the lesions are multifocal. GT sporadic form is predominantly encountered in women between the ages 50 and 60 (5-7).

GT's are generally located in the skin or subcutaneous tissues. In young adults, GT's are often encountered in soft tissues and distal extremity nail folds and occur as painful lesions (4, 6, 8-10). While the stomach is rarely the target location for them, extracutaneous GT's are still most commonly encountered in the stomach and represent approximately 2% of all benign stomach tumors. Gastric glomus tumors (GGT) often localize into the submucosa of the antrum and are solitary, round-shaped lesions. These tumors are either asymptomatic or are accompanied by bleeding and epigastric pain when they cause ulcerations (8, 11-13). Tumor sizes vary between 1 and 7 cm, and their mitotic activities are usually low. Malignant behaviors are unexpected for GGT's (14). GGT's are commonly mistaken for gastrointestinal stromal tumors (GIST), leiomyomas, and carcinoid tumors (15). The definitive diagnosis for GGT is based on the pathological and immunohistochemical evaluations of the resected material (5, 16, 17).

2. Material and Methods

2.1. Case

The case in the present study is a 36-year-old male patient who applied with complaints of increasing stomach pain for two days accompanied by nausea and vomiting. Physical inspection revealed sensitivity in the epigastric region and upper gastrointestinal endoscopy has shown the presence of a sub-epithelial lesion of 3-4 cm size, located in the large curvature of

the antrum and covered with normal epithelial tissue. There is no Computer Tomography (CT) information regarding the stomach or any stomach mass for the case.

The patient was surgically operated and the lesion located in the large curvature of the antrum was palpated first and then was removed with stomach wedge resection.

A tumoral lesion was observed during the inspection of the partial gastrectomy material, which was 1.8x1.5x0.6 cm in size and started from the submucosa and infiltrated into the muscular mucosa. The section surface of the tumor was grey-white and the tumor was solid in structure with point-like focal bleeding spots. The distance of the tumor to the surgical border was 0.4 cm.

The inspection of HE sections has shown that the tumoral lesion starts from the lamina propria and infiltrates through the muscular mucosa. The tumor consists of monotonous cells that form large nodules separated from each other with thick bands and with eosinophilic cytoplasms that sometimes contain 1-2 nucleoles with dispersed chromatins. Inside the tumor nodules, vascular gaps surrounded with glomus cells with round-shaped nucleus were observed along with neural bundles and perineural invasion was present. Lymphovascular invasion was also present, while no atypical mitosis or necrosis was observed. Similarly, there was no serosal infiltration.

The mucosa at the tumor surface is intact and no tumor tissue was observed along the surgical border (Figure 1A-F). Neuroendocrine tumors, small round blue cell tumors and GIST's were considered for the differential diagnosis. AE1/AE3, CD45, Chromogranin A, Synaptophysin, CD56, Ki67, CD117, CD34, SMA and Caldesmon stainings were applied as part of immunohistochemical evaluations and the tumor cells represented strong SMA and Caldesmon positivities, along with pale Synaptophysin positivity. AE1/AE3, CD117, CD56, S100, CD34 and Chromogranin A were all negative. Ki67 proliferation index was around 2-3% (Figure G-K). The fact that CD117 was negative reduced GIST potential. Considering all of these findings, the case was evaluated as a glomus tumor case.

3. Discussion

In histomorphological terms, benign GT's are localized in dilated vein walls and have a uniform nucleus and they consist of small, uniform, round glomus cells. These cells are localized around the vein walls in the form of nests.

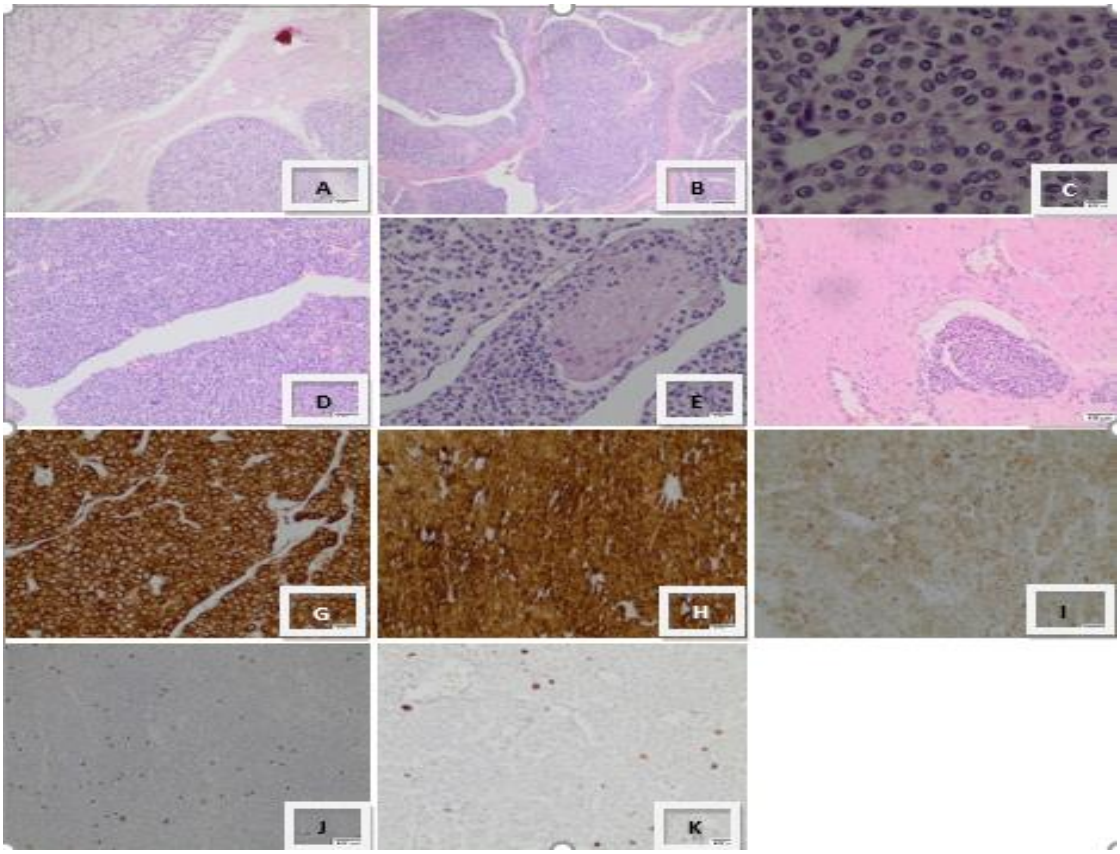

Figure 1: A. Tumor-mucosa relation, B. Nodular structure, C. Tumor cells, D. Vascular structures, E. Perineural invasion, F. Lymphovascular invasion, G. S100 positive, H. Caldesmon positive, I. Weak synaptophysin positive, J. CD117 negative, K. Ki67 (2-3%).

GT's can be separated into two groups as glomangioma and glomangiomyoma tumors based on the glomus cells, the vascular structures and the smooth muscle intensity involved. The most frequent variant is the solid glomus tumor which displays glomus cell islets surrounded by capillary veins and hyalinised stroma or stroma with myxoid changes. In glomangioma, a vein proliferation surrounded by with glomus cell nests with irregular borders can be observed, similar to that of cavernous hemangioma. Glomangiomyoma, on the other hand, is characterized by elongated glomus cells that are similar to mature smooth muscle cells (14-18). GT's have been defined by French researchers Barre and Manson in 1924 and by Russian researchers Markelov in 1934 and Liveschin in 1936. Histopathological findings of the tumor have been defined by Murray in 1942 (19). The first identification of GT in the stomach was performed by Key et al. in 1951 (20). GT's are often localized in the antrum or prepyloric region, are solitary and usually display submucosal nodule formations accompanied by gastrointestinal bleeding. Disturbances in the epigastric region, nausea and vomiting can also accompany these findings (3, 13). In the case of this study, an increasing sense of stomach pain and accompanying nausea and vomiting were present.

Gastric submucosal tumors (GMT) are neoplasms localized in the submucosa of the stomach wall or to the muscularis propria and are usually benign, but sometimes can become malignant. The most frequent malignant GMT is the GIST which 100 times more frequent than the GGT's. Unlike GIST's, GGT's are benign tumors that are c-Kit negative (6).

GT's are often seen as sub-epithelial masses during the endoscopic inspections, making endoscopic biopsy somewhat less effective in diagnosis (12, 17). The endoscopy performed in the present case has shown a submucosal mass of 3-4 cm size covered with regular mucosa and a mass of 2 cm size was found during the surgery. This is also indicative that endoscopic biopsy is not very accurate for the diagnosis and determination of lesion size.

It is thereby necessary to perform differential diagnosis on GT's to separate them from GIST's and other mesenchymal tumors. The pre-surgery diagnosis of GGT is relatively challenging. Endoscopic biopsies are unable to provide ample amounts of sample to represent the whole lesion in cases where the lesion is located deep in or is submucosal (11). Studies performed with barium usually reveal submucosal masses with either smooth mucosal surfaces or with ulcerations located in the large quarter of the antrum. Endoscopic USG and CT's are important for the diagnosis of gastric submucosal tumors, where findings of heterogenous hypoechoic round-shaped masses support the GT diagnosis.

In CT, GT's show up as submucosal masses of homogenous density with regular and smooth borders. In contrast viewing, the arterial phase shows strong enhancement, while the portal venous phase shows persistent enhancements. These viewing techniques can differentiate GT's from other stromal or mesenchymal tumors and can provide information regarding the tissue the tumor is based upon (17, 21-23). In the case of the present study the endoscopic biopsy failed to provide a definitive diagnosis and only revealed the presence of a submucosal mass. In CT, no information was provided for the stomach or any masses within it. The diagnosis of the detected mass could only be provided with the histopathological inspection of the surgery material. These events show that radiological scanning methods can fail to accurately diagnose GT's, and the resection and histopathological evaluation of the tissue are essential for a correct diagnosis.

From the histopathological perspective, GGT's consist of monotonous small round cell layers and vascular gaps (24, 25). While stomach GT's are often benign, they can nevertheless be malignant in rare cases. Felope et al. have defined certain criteria for malignant glomus tumors and have stated that a size larger than 2 cm, a deep localization (subfascial or organ), atypical mitosis, atypical nuclei and the presence of more than 5 mitoses' in 50 BBA's are findings that support malignity (3, 13, 18, 25). In the case of the present study, the only malignancy criteria is the fact that the lesion is located in an organ and none of the other criteria are met.

In differential diagnosis, leiomyomas, carcinoid tumors and paragangliomas should be considered.

Immunohistochemical staining is important for the differential diagnosis of the tumor. The tumor cells are SMA, calponin, vimentin, collagen type-IV and synaptophysin (dot-like) positive, while they are desmin, cytokeratin (AE1/AE3b), EMA, creatinine kinase, chromogranin A, p53, NSE, DOG1, s100, c-Kit negative. Gastrointestinal endocrine tumors are actin negative, but half of the GIST's are positive for it. The fact that GIST's lack dilated capillaries and are c-Kit and DOG-1 positive help differentiate them from GT's (13, 24). Leiomyomas and leiomyosarcomas are differentiated from GIST's with their desmin and SMA positivities and c-Kit and CD34 negativities (23).

While morphologically GT's can be confused with grade-1 neuroendocrine tumors, the presence of nest structures surrounded by thin veins and trabecular pattern in the neuroendocrine tumors, along with synaptophysin, chromogranin, cytokeratin, CD56 and NSE positivity and SMA and CD34 negativity, helps with their differentiation (26). GT differentiation with paraganglioma, on the other hand, is performed considering the chromogranin A and S-100 positivities and SMA negativity, along with histopathological findings of thin-wall organoid pattern that is rich in vein structures, presence of Zellballen pattern, nucleomegaly, hyperchromasia and wide eosinophilic cytoplasma (24,26).

GGT's are rarely encountered benign tumors and the results show that endoscopic biopsy has limited value in their diagnosis. Endoscopic USG and CT are important for accurate diagnosis, but the definitive

diagnosis requires resection of the mass and the histopathological evaluation of the sample.

Conflict of interest statement
No conflict of interest.

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