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CASE REPORT

Granular cell tumor of stomach: A case report and review of literature

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Abstract

Granular cell tumor (GCT) was described for the first time by Abrikosoff in 1926. It is a relatively rare neoplasm that may occur at many sites, but most commonly in the skin or soft tissues. The occurrence of GCT in the gastrointestinal tract is rare, accounting approximately for 8% of all tumors, among which the most common site is the esophagus, whereas gastric localization is very rare. Gastric GCTs can be solitary or, more frequently, associated with other gastrointestinal localization. Although GCTs are usually clinically and histologically benign, some malignant cases have been reported. Histologically, these tumors consist of polygonal and fusiform cells disposed in compact "nests" and immunohistochemical staining for S-100 protein supports the proposed derivation from Schwann cells. A correct preoperative diagnosis of this tumor can only be made in 50% of all patients and it is always based on endoscopic biopsy. Laparoscopic or conventional wedge resection represents the treatment of choice. In this study, the authors reported a case of a 49-year-old woman with a solitary granular cell tumor of the stomach with infiltrative pattern, successfully treated with surgical resection. A review of literature is also presented with emphasis on diagnostic criteria concerning the malignant form.

Key words: Granular cell tumor; Stomach; Benign; Surgical resection

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INTRODUCTION

Granular cell tumors (GCT) were described for the first time by Abrikosoff in 1926. They are uncommon, usually benign, soft tissue tumors rarely seen in clinical practice. They may occur at many sites, although it affects most frequently skin or subcutaneous tissues of the chest and upper extremities, tongue, breast and female genital region. The onset of this type of tumor in the gastrointestinal (GI) tract is rare. Approximately 8% of all GCTs occur in the digestive tract[1] and among these the most common site is the esophagus, followed by the large intestine[2]. Gastric localization is seldom seen. Yasuda et al[3], reported a case of gastric GCT in 1995 and underlined that this lesion was previously found in the stomach only in 24 patients. Since 1996, five more cases have been described[4-9].

In this study, we report a case of a woman with a solitary GCT of the stomach, incidentally found upon GI endoscopy, which had an infiltrative growth pattern and was successfully treated by surgical resection.

CASE REPORT

A 49-year-old woman was admitted to our Unit for further evaluation of a gastric mass which had been incidentally in an abdominal ultrasound examination for her nonspecific dyspeptic symptoms (Figure 1). She had no remarkable past medical history, and no significant alcohol consumption or history of smoking or drugs. Upon hospitalization, physical examination, biochemical data and tumor markers (CEA, CA-19-9) were all within normal limits. Upper gastrointestinal endoscopy was performed and revealed a hemispherical mass of about 3 cm in diameter, located on the lesser curvature of the gastric antrum and overlaid by normal mucosa. Search for *H pylori* by biopsy urease (Pantorc® *Hp* Test, Byk Gulden Italia S.p.A.) was negative. The esophagus, duodenum and the remaining parts of stomach were normal. Multiple deep (jumbo) biopsies from the gastric mass and from the surrounding gastric mucosa were performed. Histopathological examination of mass biopsies showed a pattern compatible with GCT, whereas other mucosal biopsies were normal. A subsequent CT scan of the abdomen showed a solid mass, with a slight contrast enhancement, of about 3 cm in diameter with well-defined margins located near the gastric angulus, arising from a layer of the gastric wall. Neither further invasion beyond the gastric wall, nor visible metastatic lesions in the liver or enlarged lymph nodes were observed. During laparotomy a tumor mass was found on the anterior wall of the lesser

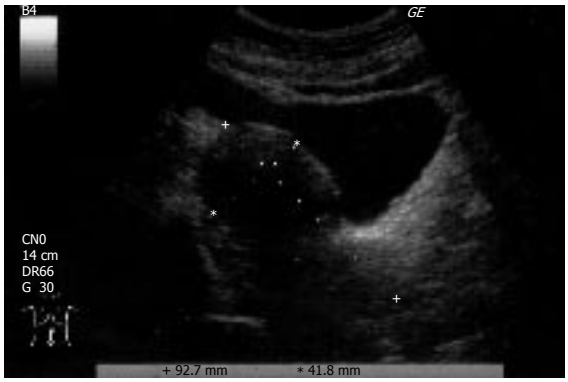

Figure 1 Echo tomography of gastric region. A solid hypoechogenic mass with a diameter of 2.7 cm × 2.2 cm protruding from beyond the anterior wall of the stomach.

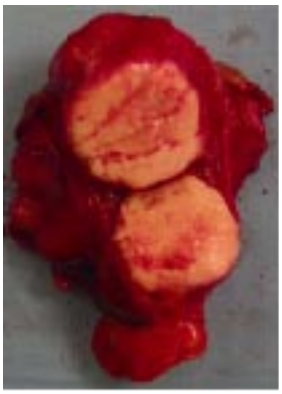

Figure 2 Macroscopic appearance of resected specimen: section of surgical specimen: a soft yellow mass of about 2 cm in diameter.

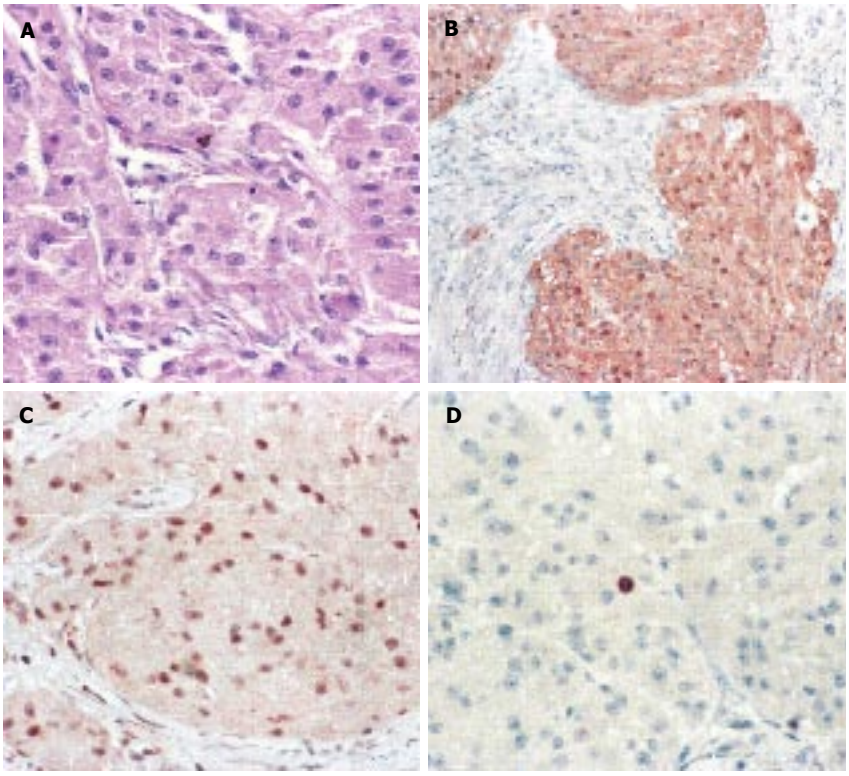

Figure 3 Histological findings of the resected specimen. **A:** hematoxylin–eosin staining. Sheet of large and polygonal cells with round to oval, eccentrically located nuclei and eosinophilic granular cytoplasm with lower mitotic activity; **B**: immunohistochemical staining for S-100 protein. Diffuse and strong expression of S-100 protein; **C**: immunohistochemical staining for p53. Some of the tumor cells are positive for p53; **D**: immunohistochemical staining for Ki-67. Some of the tumor cells are positive for Ki-67.

curvature of the stomach. There were no liver metastases or regional lymph node swelling. A wedge resection, with a gastric section performed at a distance of about 1.5 cm from the macroscopic margin of the tumor, was carried out, obtaining a total removal of the lesion.

In the resected specimen, the tumor measured 2 cm in diameter and appeared as a yellow mass (Figure 2). Microscopically, the tumor was located mainly in the muscle layer of the stomach. It formed solid nests of cells ranging from round to polygonal shape associated with few spindle cells. The nuclei were of different sizes with nucleoli at times evident and finely dispersed chromatin. The cytoplasm was abundant and finely granular. Mitotic activity was very low. The tumor focally infiltrated near muscular layer but did not affect mucosal surface (Figure 3A). Immunohistochemistry showed, S-100 protein present nearly in all cells within the tumor mass (Figure 3B), p53 in 40% of cells (Figure 3C) and Ki-67 in less than 9% of cells (Figure 3D). These histological findings met the criteria for a diagnosis of benign GCT[10].

The postoperative course was uneventful and the patient was discharged on postoperative fifth day. She remained asymptomatic and no recurrent disease was observed after a two year follow-up.

DISCUSSION

From an extensive review of literature about gastric GCT, no differences of tumor incidence was found as regard to gender, whereas fourth through sixth decades of life seem to be more affected. In term of ethnical issue of affected patients, the most reported cases were described in Japanese population. Moreover, in 50% of cases, gastric GCT proved to be associated with esophageal synchronous localization and was rarely associated with other benign or malignant gastric diseases. In only two reported patients,

Table 1 Characteristics of reported gastric granular cell tumors since 1998

Authors (yr)	Country	Age (yr)	Gender	Tumor size (cm)	Gastric site	Simultaneous occurrences of GCT	Simultaneous gastric lesions	Treatment
Sebastian (1998)	Spain	53	M	7	Upper	Esophagous	Ulcers	Surveillance
David (1999)	USA	45	F	2	Upper	Esophagous	No other lesions	Surgical
Eguchi (2002)	Japan	64	M	1.5	Body	No other occurrences	Cancer and lymphoma	Surgical
Maekawa (2003)	Japan	53	M	NR	Upper multiple	Esophagous	No other lesions	Surgical
Sailors (2005)	USA	65	F	1.5	n.r.	Tranverse colon	Cancer	Surgical

NR: non reported; GCT: granular cell tumor.

similarly to our case, gastric GCT did not show multiple localizations or was associated with other gastric lesions[3,11] (Table 1).

These gastric tumors are mostly confined macroscopically to submucosa. Their size may range from few millimeters to some centimeters, never surrounded by capsule. Histologically, gastric GCTs are composed by polygonal and fusiform cells arranged as compact "nests". Immunohistochemical staining for S-100 protein supports the proposed origin of the tumor from Schwann cells[12].

Although GCTs are usually benign clinically and histologically, some malignant cases have been reported. There are less than 30 reported cases of malignant GCTs in world literature[13] and the only documented case of a malignant GCT of the stomach was reported in 1996 by Matsumoto *et al*[9] (Table 1).

Features associated with malignancy include local recurrence, rapid growth to a size greater than 4 cm, cell necrosis, spindling of tumor cells, cytologic atypia and high mitotic activity, vescicular nuclei with large nucleoli, and a high nuclear-to-cytoplasm ratio[5,10]. It has also been reported that, on immunohistochemical staining, positivity rate of more than 50% for p53 and more than 10% for the Ki-67 index respectively, was significantly correlated with malignancy[7,10]. Extent of infiltration[5] or highly developed tumor microvessels[14] or focal pleomorphism[7] have never been considered as a criterion for diagnosis of malignancy. Altogether, these features are suggestive for malignant potential of the tumor. The tumor mass in our patient infiltrated only focally and marginally the muscular layer and did not display high expression of p53 and Ki-67. Furthermore, after the follow-up for two years, no evidence of recurrences was seen.

It is questionable whether these tumors always produce GI symptoms[15], even when they are of small size. It is quite likely that, if small, a change (pre-symptomatic) was found during upper GI endoscopy, X-ray or ultrasound examination performed for nonspecific dyspepsia. When large, gastric GCTs may instead present as gastric outlet obstruction[11], or massive upper GI hemorrhage[16].

A correct preoperative diagnosis of this tumor can be made by endoscopic biopsy. It is generally accepted that the best way to obtain an appropriate sampling of such tumors beneath the mucosa is either by boring or by performing a jumbo biopsy. A definitive diagnosis can only be established by endoscopic biopsy in 50% of the patients[17]. Endoscopic ultrasonography has recently been used more frequently for determining the depth of tumor invasion in the gastrointestinal wall, and may also be useful to evaluate GI tract submucosal tumors[2]. Endoscopic excision of GCT should be strongly considered[3]. If the tumor is attached to muscularis propria, an injection of saline can be useful to increase the distance, so that endoscopic removal can be performed more safely[3]. Therefore, since the gastric GCT is without capsule and focal areas of infiltration of the gastric wall can be present, laparoscopic or conventional wedge resection, including at least one centimeter of normal tissue, is the best therapeutic option. Laparoscopic approach could be difficult due to tumor localization beneath the posterior wall or lesser curvature, or mass size (very large or very small). Almost all gastric GCTs, observed from 1990 to date, were treated with conventional surgical approach.

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