

Differential diagnosis between glomus tumor and carcinoid of the stomach

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RESUMO | Apresentamos um caso raro de tumor glômico gástrico com diagnóstico pré-operatório de tumor carcinóide num paciente masculino de 57 anos. O painel imunofenotípico revelou expressão de actina de músculo liso e vimentina nas células tumorais, marcação pericelular do colágeno tipo IV e ausência de expressão de marcadores neuroendócrinos. Recentes avanços no diagnóstico e compreensão do comportamento do tumor glômico gástrico são revistos. O presente caso enfatiza a intersecção de achados entre tumor glômico e carcinóide gástricos, o que sugere que a imuno-histoquímica deve ser sempre aplicada para este diagnóstico diferencial.

Palavras-chave: Tumor glômico; Tumor carcinóide; Estômago.

SUMMARY | We report a rare case of gastric glomus tumor with pre-operative diagnosis of carcinoid tumor in a 57-year-old man. Immunophenotyping panel revealed expression of smooth muscle actin and vimentin by tumor cells with pericellular collagen IV and absence of expression of neuroendocrine makers. Recent advances on diagnosis of gastric glomus tumor and understanding of its biological behavior is reviewed. This case highlights the overlapping features of gastric glomus tumor and carcinoid suggesting that immunohistochemistry should be considered for this differential diagnosis in all cases.

Keywords: Glomus tumor; Carcinoid tumor; Stomach.

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INTRODUCTION

Glomus tumor is a mesenchymal neoplasm composed of cells that resemble modified smooth muscle cells of the normal glomus body, a dermal arteriovenous shunt involved in skin thermoregulation. It is a rare tumor (2% of all soft tissue neoplasms) and is usually located on distal extremities. It presents usually as small (< 1cm) red-blue nodule. Malignant variants are exceedingly rare and about 20 reports are available in the literature ⁽¹⁾.

Glomus tumors are rare outside the skin, and the most common extra-cutaneous organ affected is the stomach ⁽²⁾. Only recently the immunophenotypical features were reported in the literature and used in establishing a differential diagnosis with other gastric lesions ⁽³⁻⁷⁾. The typical morphologic picture of solid growth of round cells with varying number of pericytoma-like vascular channels is easily recognized by the pathologist. However, small fragments with predominance of solid growth of epithelioid cells may show considerable overlapping with other gastric neoplasms. Gastric glomus tumors are commonly ulcerative and cause upper gastrointestinal bleeding. About 130 cases have been reported to date and only one case of unequivocal malignant behavior is available ⁽³⁾.

CASE REPORT

A 57-year-old man present-

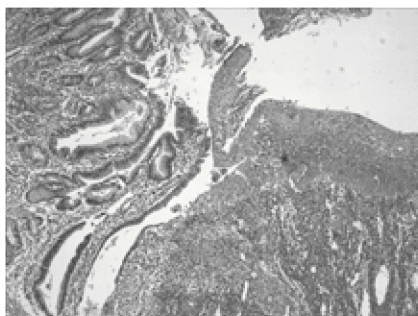


FIGURA 1 | Antral mucosa and ulceration area by glomus tumor with fibrin exsudate (H & E, 10x).

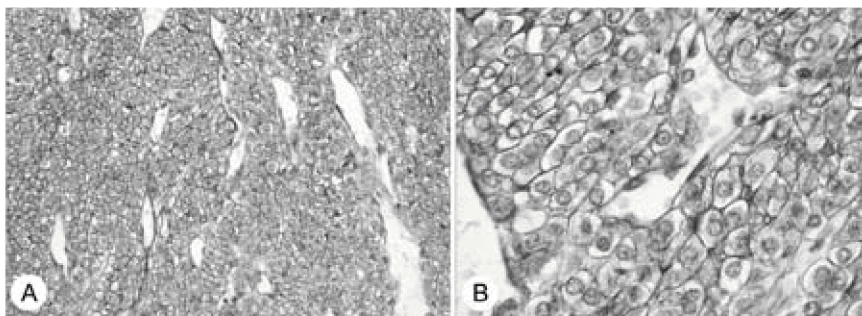


FIGURA 3 | Pericytoma-like vascular channels and round cells exhibiting pericellular expression of collagen IV (immunohistochemistry, peroxidase method: A, 10x and B, 40x).

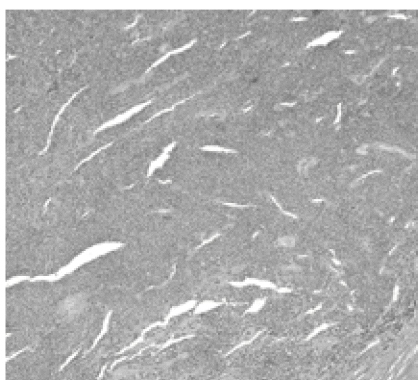


FIGURA 2 | Typical appearance of glomus tumor: Round/ovoid cells arranged as solid areas of proliferation around small blood vessels (H & E, 10x).

ted to the emergency department with severe epigastric pain. The patient reported past episodes of hematemesis and a persistent abdominal pain for several months. The endoscopy revealed a polypoid mass of 2.5 cm. Following an incisional biopsy, areas of carcinoid tumor were diagnosed. This first diagnosis was solely based on morphology. After one month of persistent epigastric pain, the patient underwent a subtotal gastrectomy with Roux-en-Y reconstruction. The surgical specimen revealed a 2.5-2.0-cm nodule (expansive mass) in the posterior wall of the gastric body. The gross specimen exhibited 1-cm ulceration, and the cut surface

revealed a white heterogeneous tumor predominantly involving the submucosal layer extending to the inner muscular layer. Microscopically, the tumor exhibited round/ovoid cells with regular/normochromic nuclei arranged as solid areas of proliferation around small blood vessels (Figures 1 and 2). No vascular invasion was observed. Mitotic count was less than 1 per 50 under high power magnification. Immunophenotyping of tumor cells detected the expression of smooth muscle actin (IA4) and vimentin with a basal pericellular distribution of collagen IV (Figure 3). Neither pan-cytokeratin (AE1,AE3), synaptophysin, chromogranin, neuron-specific enolase, desmin or CD34 were expressed by the tumor cells. The final diagnosis of both morphologic examination of the surgical specimen and the supplementary immunohistochemical evaluation was gastric glomus tumor.

The patient has been followed for 20 months with no signs of disease recurrence.

DISCUSSION

Gastric glomus tumors are rare neoplasms affecting the stomach. Approximately 130 cases have been reported to date [5]. In AFIP consultation files the frequency of gastrointestinal glomus tumor is one for each 100 cases of GISTs [3]. Our

case differs from some typical features of gastrointestinal glomus tumors reported in the literature. In the two largest recent series, a remarkable female predominance was reported: 22/9 on a study from the Armed Forces Institute of Pathology (AFIP), Washington DC, USA [3], and 9/3 in a study from Hallym University, Korea [5]. This difference is not observed in skin glomus tumors [1] and was not suggested in the largest review of the gastric counterpart in which female to male ratio was 27/25 [8]; however, the latter predates the use of immunohistochemistry for differential diagnosis. Without the immunohistochemical assays, we cannot predict how many cases could be classified as gastrointestinal stromal tumors (GISTs) or carcinoids. The median age in the three large gastric series/reviews of gastric glomus tumors ranged from 53 to 56 years [3,5,8] which is very close to the age of our patient.

Overall, the clinical presentation of our patient is in agreement with the two recent reported series: gastrointestinal bleeding was reported in 31-35% [5,3] of all cases and ulceration was observed in 45-46% [3,5]. The tumor size in the present report is also very close to the mean size reported of 2.5 [5] and 2.8 cm [3].

Microscopic appearance of glomus tu-

mors may require a careful differential diagnosis between GIST and carcinoid. Typical immunohistochemical features are smooth muscle actin and calponin positivity, detection of pericellular laminin and collagen type IV, and absence of desmin, S-100 protein, chromogranin and synaptophysin expression ⁽³⁾. In regard to the differential diagnosis with carcinoid, it should be highlighted that 3/17 (18%) of the AFIP series of gastric glomus tumors exhibited focal positive staining for synaptophysin, a neuroendocrine marker, and this may cause further confusion in distinguishing both neoplasms. The evaluation of 18 tumors revealed absence of oncogene KIT expression in all cases while analysis of GIST-specific c-Kit gene mutations in five specimens was also negative. These findings clearly support that those tumors are similar to peripheral glomus tumors and are a distinct entity from GISTs ⁽³⁾.


The hematopoietic/endothelial marker CD34 may exhibit focal positivity in some cases and may be used in the immunophenotyping panel ⁽⁶⁾. Its usefulness for the diagnosis of gastric glomus tumors is limited although focal positivity may occur in 20% of gastric glomus tumors in comparison with diffuse pattern in 53% of peripheral glomus tumors and 69% of epithelioid GISTs ⁽³⁾.

Some features of aggressive behavior in peripheral glomus tumors can be detected in their gastrointestinal counterpart: vascular invasion (11/32), focal atypia (13/32) and low mitotic index of 1-4 mitoses per 50 high power fields (HPFs) ⁽³⁾. Their relevance as predictors of malignant behavior in gastric lesions is not clear. One case of multiple glomus tumors of the stomach associated with extensive intravascular growth has been reported ⁽⁹⁾ but unequivocal malignant behavior is

restricted to one case of lethal metastatic disease. In that case, the tumor measured 6.5-cm at diagnosis and had low mitotic count (1 per 50 HPFs), mild atypia, vascular invasion and spindle cell foci ⁽³⁾. There are at least three other cases of malignant behavior in the Russian language literature ⁽¹⁰⁾. On the other hand, one case of a massive 30-cm gastric glomus tumor has been reported with a follow up of 20 years and necropsy with no evidence of recurrence or metastasis ⁽¹¹⁾. In the present case, we did not identify any feature that could predict malignant potential.

Previous reports mirror our case presentation of a preoperative diagnosis of carcinoid tumor. In one case, cytological evaluation revealed a 2.0-cm ulcerated submucosal mass suggesting a neuroendocrine differentiation ⁽⁴⁾. In addition, 6 preoperative diagnoses of carcinoid tumor and 5 differential diagnoses between glomus and carcinoid tumor were reported in the recent AFIP series of 32 gastric glomus tumor ⁽³⁾.

CONCLUSION

The present case emphasizes the considerable overlapping endoscopic and microscopic features of gastric glomus and carcinoid tumors. Immunohistochemistry should be considered in all cases of gastric neoplasia presenting a solid pattern, round / epithelioid cells for differential diagnosis between glomus tumor, carcinoid and epithelioid variants of GIST. 

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