

## Gastric paraganglioma: case report and review of the literature

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**SUMMARY: Gastric paraganglioma: case report and review of the literature.**

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*Very few cases of gastric paragangliomas have been reported in the literature to date. We report a rare case of parietal gastric paraganglioma fortuitously detected during intraoperative exploration.*

*A 82-years-old woman presented to our emergency room for abdominal pain. On physical examination abdomen was painful on palpation and Blumberg's sign was present. The laboratory exams showed a*

*neutrophilia in absence of leukocytosis. Acute appendicitis was suspected and a laparoscopy was performed. At exploration, the vermiform appendix was normal while a lumpy, hard-fibrous and white-pinkish extraluminal lesion of the anterior wall of the gastric body near the greater curvature of about 2 cm in diameter was present. Laparoscopic resection of the gastric lesion was performed. The patient was discharged in good condition in the fourth postoperative day. Pathologic examination revealed a gangliocytic paraganglioma. The patient is alive and well without evidence of relapse 6 months after surgery.*

*Gastric paraganglioma is a very rare tumor and its diagnosis is very difficult. Surgical excision is the treatment of choice which can be performed successfully with laparoscopy.*

KEY WORDS: Stomach - Paraganglioma - Immunohistochemistry.

### Introduction

Paragangliomas are rare neuroendocrine tumors arising from the embryonic neural crest (1-3). They may be located from the upper cervical region to the pelvis, related to the autonomic nervous system. Paragangliomas are more often sporadic but there are forms associated with genetic syndromes. There are two types of paragangliomas: sympathetic (arising from the sympathetic paraganglia located along the paravertebral and paraaortic axis) and parasympathetic (arising from the paraganglia located in the head and neck proximal to the vascular structures that give rise to the carotid body, aorticopulmonary septum, intravagal and jugulotympanic tumors, as well as those arising from the wall of some organs such as the urinary bladder). Nearly 5 to 10% occur in extraadrenal sites, from the upper cervical region

to the pelvis, related to the autonomic nervous system (2). Visceral paraganglioma is an uncommon tumor but examples have been described in the bladder, liver, gall bladder, larynx and inter-atrial septum of the heart (4).

The clinical presentation depends on secretion of catecholamines, malignancy or mass effect; paragangliomas may also be discovered incidentally and they are called "incidentalomas" (3, 5, 6).

Although paragangliomas of the small bowel, particularly the duodenum, do occur and have been described in many publications (7), to our knowledge very few cases of gastric or paragastric paragangliomas have been reported (2-4, 7-11). Nine single cases of gastric paraganglioma have been identified in the literature (3, 4, 7-13) to date.

We report a rare case of parietal gastric paraganglioma fortuitously detected during intraoperative exploration.

### Case report

A 82-years-old woman presented to our Emergency Room for the sudden appearance of an abdominal pain localized in the right iliac fossa not associated with chan-

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ge in bowel habits, or nausea, or hyperpyrexia. The personal medical history was silent for endocrine and cardiovascular diseases. In the past she was submitted to a surgical intervention for the correction of hallux valgus bilaterally; the patient was taking therapy with vitamin D and was allergic to penicillin.

On admission the patient was in good general condition and the vital parameters were normal. On physical examination the abdomen was painful on palpation in the right iliac fossa and right flank; Blumberg's sign was present, while Rovsing's sign negative. The peristalsis was present.

The laboratory exams showed neutrophilia in absence of leukocytosis (white blood cells: 7.900/mmc, neutrophils: 77%) and a high PCR (PCR: 32.8 mg/l). The hemoglobin and the red blood cells were normal.

Abdominal ultrasound was substantially normal, bilateral renal cysts and a hepatic angioma have been reported.

Based on these symptoms and signs, an acute appendicitis was suspected. The patient underwent antibiotic therapy. The following day, being unchanged the clinical presentation, it was decided to perform a laparoscopy.

After performing the pneumoperitoneum with a Veress needle, a trocar was introduced to umbilical level, and then the camera; another trocar was inserted in the left iliac fossa. The peritoneal cavity was explored and the vermiform appendix was normal; no peritoneal fluid was present, nor a Meckel's diverticulum; also uterus and an-

nexes were normal.

Exploration of the upper abdomen showed a lumpy, hard-fibrous and white-pinkish extraluminal lesion of the anterior wall of the body of the stomach near the greater curvature of about 2 cm in diameter. Another operator trocar was introduced on the left flank and a wedge resection was performed with scissors opening the serum-muscular gastric wall which was sutured in single layer with self-locking point (V-lock).

The postoperative course was complicated by the appearance of atrial fibrillation in the second post-operative day spontaneously resolved. In the fourth day she was discharged in good condition with normal bowel function.

Pathologic examination revealed a gangliocytic paraganglioma (Figures 1, 2, and 3). Regarding immunohistochemistry, the tumor was positive for neuron specific enolase (NSE) (Figure 4) and S-100 protein (Figure 5) and negative for glial fibrillary acidic protein (GFAP), cytokeratins (CKAE1/AE3), smooth muscle actin and CD117.

The patient is alive and well without evidence of relapse 6 months after surgery.

## Discussion

Paragangliomas are neural crest-derived neuroendocrine tumors, originating from paraganglia, which are dispersed neuroendocrine organs characterized by cate-



**Figure 1 - Low magnification shows a well circumscribed lesion.**

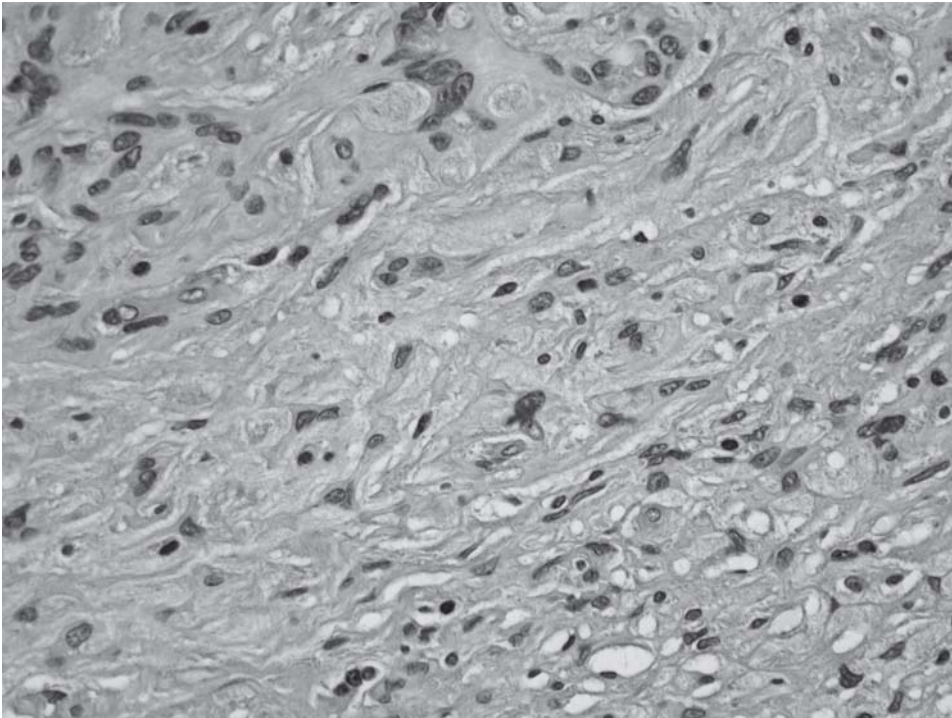


Figure 2 - The lesion is composed of epithelioid cells, ganglion cells or ganglion-like cells, and spindle-shaped cells; the components are unevenly distributed.

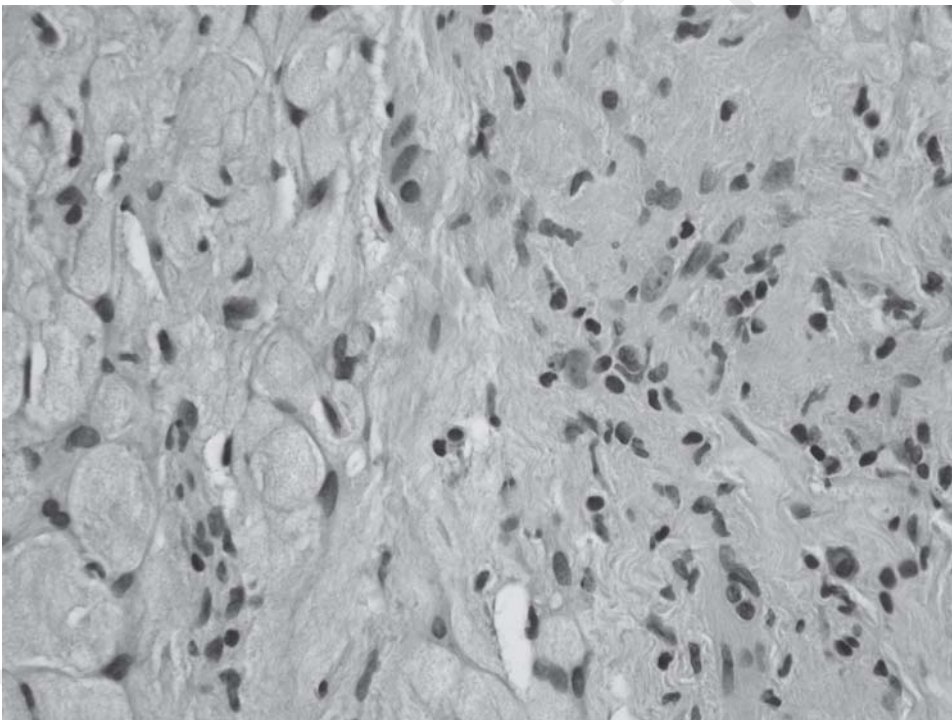


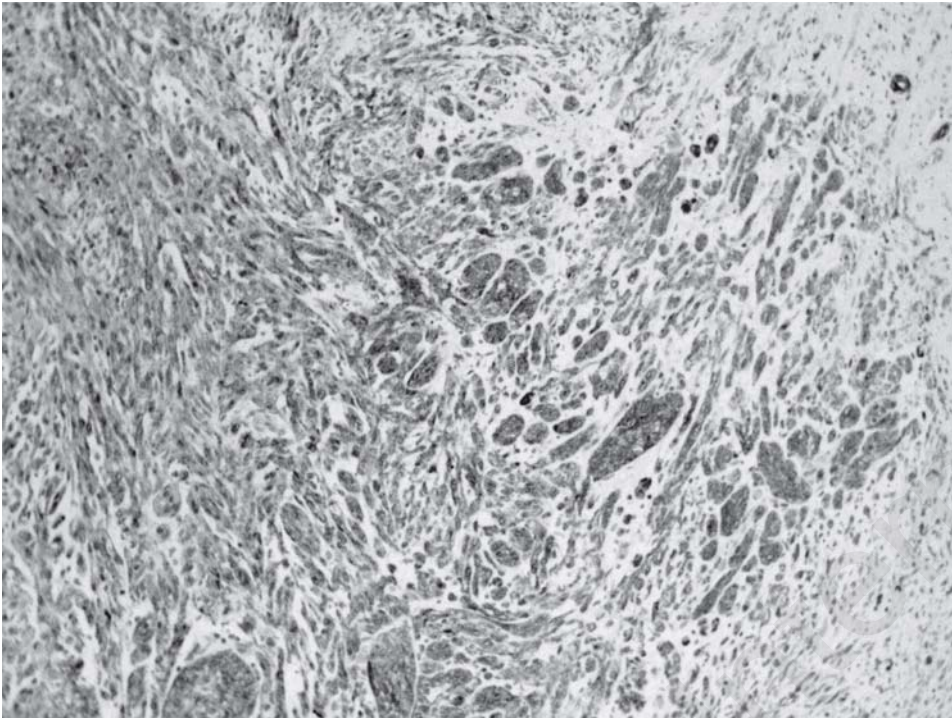
Figure 3 - The same lesion at higher magnification.

choline and peptide-producing cells. Paraganglioma represents 10% of catecholamine secreting tumors with an annual incidence estimated at 1/100,000 (3, 5). Males are affected slightly more commonly than females (1 to 1.8/1) and it has been encountered over an age ran-

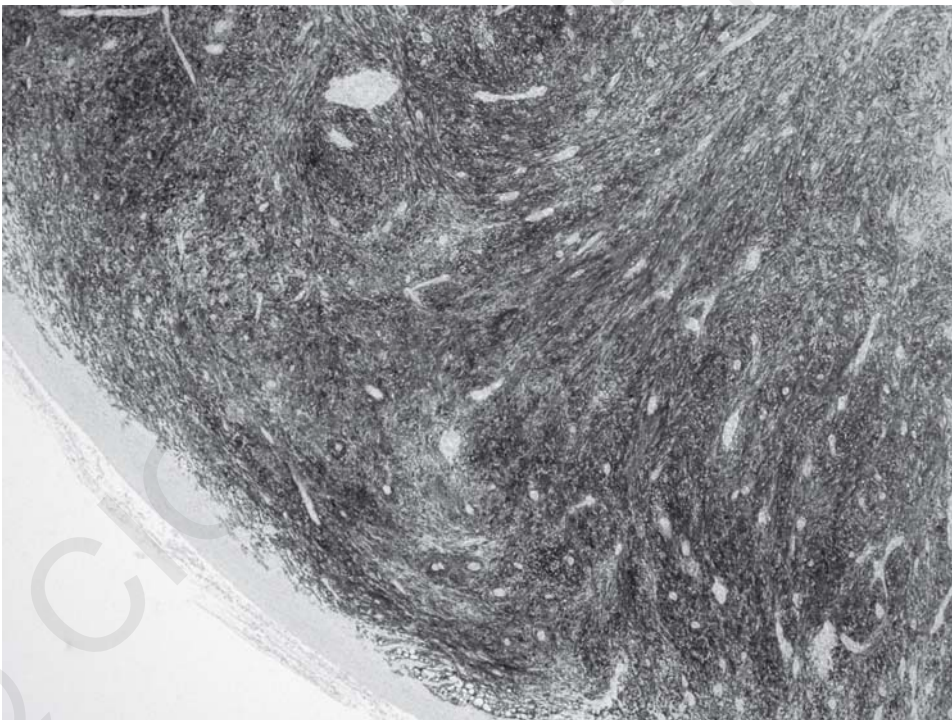
ge from 23 to 83 years although the fifties are preferred (3, 6).

Paragangliomas may be classified into two groups based on location into the autonomic nervous system: sympathetic and parasympathetic ones. The first ones arise





**Figure 4 -** The epithelioid cells, the ganglion cells and the spindle-shaped cells are stained by neuron-specific enolase (NSE).



**Figure 5 -** Strong immunohistochemical expression of S-100 protein.

from the sympathetic paraganglia located along the paravertebral and paraaortic axis relative to the cervical ganglia from the neck to the abdomen and pelvis; the second ones originate from paraganglia located in the head and neck proximal to the vascular structures that give rise to

carotid body, aorto-pulmonary septum, intravagal and jugulotympanic tumors, as well as those arising from the wall of some organs such as the urinary bladder (3).

Paragangliomas can rarely be found in visceral organs and, therefore, reports are restricted to single cases.

Although they occur relatively often in the small bowel, gastric localization, as in our case, is very rare, and in literature there are only isolated case reports (2-4, 7-11). To our knowledge, this is the tenth case reported.

Sympathetic paragangliomas usually secrete catecholamines and are located in the sympathetic paravertebral ganglia of thorax, abdomen, and pelvis. In contrast, the majority of parasympathetic paragangliomas are non functional, as was our case, and located preferably along the glossopharyngeal and vagal nerves in the neck and at the base of skull (3). So our case is particularly unusual.

In paragangliomas secreting norepinephrine the clinical presentation is characterized by arterial hypertension, headache, sweating and palpitations. In the tumors not secreting catecholamines the symptoms can be vague: psychiatric disorders, anxiety, facial pallor, weight loss, polyuria/polydipsia, hyperglycemia, secondary erythrocytosis, stroke and cardiomyopathy (3). Abdominal pain was the clinical presentation in 3 cases reported in the literature (2, 9, 11), as well as in our patient. Patients with paraganglioma can be asymptomatic and the diagnosis is fortuitous during testing for other clinical conditions; the tumors so discovered are called "incidentalomas" (3).

Computed tomography (CT) and magnetic resonance imaging are useful to determine features of tumor as the site, the number (single or multiple), the malignancy, the association with other neoplasms in context of hereditary syndrome (3).

The hallmark of this tumor is the presence of PAS-D intracytoplasmic granules and crystalline rods, readily identifiable upon ultrastructural examination, and the specific translocation t(X;17) (p11.2;q25) that correlates with nuclear location of the TFE3 protein by immunohistochemistry (2). Furthermore, measurements of the serum levels of Chromogranin A are useful in the diagnosis and in assessing tumor's response to therapy (2).

The distinction between benign and malignant paraganglioma is not possible on cytologic grounds (2). Cell pleomorphism is not a reliable criterion to predict malignancy, whereas mitotic activity and vascular invasion should be considered as signs of potential malignity. Sometimes the typical "zellballen" nested cells are pleomorphic and lack the structural organization typical of paraganglioma (7). The most characteristic are the groups of uniform cells that are surrounded by spindle cells known as "Zellballen". However, other patterns such as spindle cells, admixtures of large and small cells, and prominent cytologic atypia may be observed (2).

The presence of NSE and chromogranin is characteristic for neuroendocrine tumours, including paragangliomas, whereas leu-enkephalin is more specific for paragangliomas (7). In our patient, the lesion was

composed of epithelioid cells, ganglion cells or ganglion-like cells, and spindle-shaped cells; the components were unevenly distributed; the epithelioid cells, the ganglion cells and the spindle-shaped cells were positive for NSE and there was a strong immunohistochemical expression of S100 protein.

There is still significant debate regarding the biological behavior of paragangliomas (2). The malignant potential of a nonchromaffin paraganglioma is difficult to predict on histological grounds (11). It has been said that the only criterion for malignancy is the presence of metastases to sites where chromaffin tissue is not usually found. (2). According to the World Health Organization classification of tumors of the endocrine system, the presence of metastasis or tumor spread in size of normally devoid of chromaffin tissue define paragangliomas as malignant (2). Nonchromaffin paragangliomas are very vascular and this vascularity accounts for the propensity of gastrointestinal lesion to bleed. Growth is slow even in malignant lesions. Metastases are primarily to the lungs, bones, liver, and lymph nodes (11). About 30-40% of paragangliomas are malignant and the overall 5-year survival is around 50%. Currently, the only validated risk factor for malignancy and poor prognosis is the evidence of a germline mutation in the succinate dehydrogenase subunit B (SDHB) gene (3). Recently, the size and the weight of the tumor, the presence of tumor necrosis, Ki-67 index > 4% and the absence of pS100 are considered as high risk factors for malignancy and recurrence (3).

The therapeutic modalities of paragangliomas include open or minimally invasive surgery, nuclear medicine, chemotherapy, radiotherapy and biological targeted agents. The choice of the type of treatment depends on various factors: location, size, extension, symptoms, malignancy, and status of somatostatin receptors (3). The first line treatment for resectable tumors is complete surgical resection, that can be performed with open surgery or laparoscopic technique. In most cases of gastric paragangliomas reported in the literature a total or subtotal gastrectomy was performed (3); limited surgical excision is a feasible and safe treatment and appears in the present case to have been curative (4). According to the studies regarding the laparoscopic treatment of extra-adrenal intra-abdominal paragangliomas available in the literature, all tumors were less than 4 cm (3) as in our case. The choice between open or laparoscopic surgery depends on the experience of surgeon and findings, location and extension of the tumor (3). In our case, the intervention has began as to carry out a laparoscopic appendectomy but the intraoperative finding of a gastric lesion has led the operator to change the initial positioning plan of the trocars thus making easier the access to the stomach. A third trocar was positioned on the right flank of the patient, along the transverse um-

bilical line, rather than in hypogastrium as it would have been in case of confirmation of an appendicitis, to facilitate dissection maneuvers of the lesion, until then unrecognized. The initial exploration of the peritoneal cavity has enabled a correct approach to this case, and it has made possible to change the positioning of the trocars so as to be able to lead to successful completion of the surgery by laparoscopy. Surgical therapy is also indicated to palliative intent when a complete eradication

of disease is not achievable for metastatic status of malignancies (3).

## Conclusion

Gastric paraganglioma is a very rare tumor and its diagnosis is very difficult. Surgical excision is the treatment of choice which can be performed successfully by laparoscopy.

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