

An unusual presentation of Mesenteric Paraganglioma

Manuel Alexandre Viana Ferreira, Aires Martins, Álvaro Gonçalves, Alberto Midões, Rui Torres

ABSTRACT

Introduction: Paragangliomas are rare tumors derived from neural crest cells, which are mostly localized in the adrenal medulla. Only 5–10% occur in extra-adrenal localizations. Given the potential of the paraganglioma to secrete catecholamines, some patients present constitutional symptoms such as headaches, tremors and hypertension. However, most patients are asymptomatic. Preoperative diagnosis of paraganglioma in asymptomatic patients is difficult but should be included in the differential diagnosis of solid mesenteric tumors. The gold standard therapy is complete resection, with the need for a long-term follow-up after surgery. **Case Report:** Our case study takes a look at a 32-year-old nulliparous woman observed in the emergency room with a severe low abdominal pain. The ultrasonography and computerized tomography revealed a large pelvic tumor with apparent origin in the left ovary. During an exploratory laparotomy, an encapsulated, well vascularized mass was found in the mesentery of the ileum, behind the uterus, conditioning the twisting and consequent bottlenecks of 30 cm of the small intestine. An enterectomy was performed

and the final histopathology revealed a 6 cm paraganglioma. **Conclusion:** This case is unique due to its unusual location and clinical presentation. Only 20 cases of mesenteric paraganglioma are described and this is the first found in the context of an emergency.

Keywords: Chromaffin, Extra-adrenal, Paraganglioma, Paraganglia

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INTRODUCTION

Chromaffin cells develop from the embryonic neural crest and are commonly found in tissues such as the adrenal medulla, carotid and aortic bodies, organs of Zuckerkandl, paraganglia of sympathetic and parasympathetic plexus [1, 2].

Chromaffin cell Tumors can be divided in two groups; pheochromocytomas, located in the adrenal medulla, and paragangliomas which arise from extra-adrenal chromaffin cells [3]. Only 5–10% of chromaffin cell Tumors are extra-adrenal [1]. Thus, paragangliomas are rare Tumors, with an annual incidence of around 2–8 per million [4].

Paragangliomas can be further subclassified into two more groups according to their distribution. The first group arises from parasympathetic ganglia and is mainly located in the skull and neck. The most common extra-adrenal paragangliomas occur as carotid bodies

Manuel Alexandre Viana Ferreira¹, Aires Martins¹, Álvaro Gonçalves¹, Alberto Midões², Rui Torres³

Affiliations: ¹MD, Resident of General Surgery in the General Surgery Department of Hospital de Santa Lúzia, Viana do Castelo, Portugal; ²MD, Director of the General Surgery Service in the Hospital de Santa Lúzia, Viana do Castelo, Portugal; ³MD, Colorectal Surgeon of General Surgery in the Hospital de Santa Lúzia, Viana do Castelo, Portugal.

Corresponding Author: Manuel Alexandre Viana Ferreira, Rua António De Mariz, nº22, 4715-279 Braga, Portugal; Email: manuel.alexandre.ferreira@gmail.com

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[2]. The second group arises from sympathetic ganglia of the thorax, abdomen and pelvis, usually in the para-aortic area [3]. Of these, mesenteric paragangliomas are extremely rare [4], only a few cases have been studied and published.

Paragangliomas represent ten percent of catecholamine secreting Tumors [5]. Due to their catecholamine secreting properties, paragangliomas have the potential to present as a mass with paroxysmic symptoms such as diaphoresis, headaches and hypertension. However, the majority of extra-adrenal paraganglioma (75%) is non-functional, presented only as an abdominal mass usually discovered incidentally [5].

With 20 cases of mesenteric paraganglioma described (Table 1), this study describes a quite rare Tumor with a unique presentation and the first to be treated in an emergency context.

CASE REPORT

A 32-year-old woman, nulliparous, without pathological antecedents or relevant chronic medication, was observed by gynecology after complaints of left low abdominal pain.

Analytically, the patient had microscopic hematuria. A renal ultrasound was performed and showed a pelvic mass, slightly to the left of the midline, and the patient complained of pain when experiencing the ultrasound probe.

The examination proceeded with a transvaginal ultrasound and a CT scan which revealed a heterogeneous neof ormation in the apparent dependence of the left ovary, with a 6 cm diameter at its highest (Figure 1). The differential diagnosis included fibroid or an ovarian tumor.

Due to worsening of the symptoms, the patient underwent an exploratory laparotomy. During the procedure, a mass in the mesentery of the ileum was found. The mass found itself stuck behind the uterus which conditioned twist and subsequent ischemia on a loop of small intestine (Figure 2). The mass was resected along with 30 cm of ischemic ileum followed by a primary anastomosis. The post-operative course was uneventful.

Histological analysis revealed a well delimited nodule, encapsulated, located in the mesentery, not infiltrating the wall of the small bowel. The tumor described corresponded to a limited neoplasia, surrounded by a fibrous pseudocapsule and comprising nests and cords of small and intermediate size cells separated by thin abundant fibrovascular septae, giving the characteristic "zellballen" pattern (Figure 3). The cells had clarified cytoplasm and small nuclei, rounded and irregular chromatin. The mitotic count was low (< 2 mitoses / HPF) and Ki67 was found to be 2%.

Immunohistochemical analysis was positive for chromogranin A, CD56, synaptophysin, S100 + and NSE

(Figure 3). Based on histologic and immunohistochemical features, a diagnosis of paraganglioma was reached.

The study was completed with the research for plasma catecholamines, plasma free metanephrines, urinary catecholamines, urinary vanillylmandelic acid and urinary metanephrines which revealed no significant changes.

Imagiological exams (echography cervical, thoracic, abdominal and pelvic CT) revealed adenopathies located



Figure 1: (A) Coronal plane and (B) Axial plane of the CT scan showing a heterogeneous neof ormation in the apparent dependence of the left ovary, with a 6x6x5.3 cm

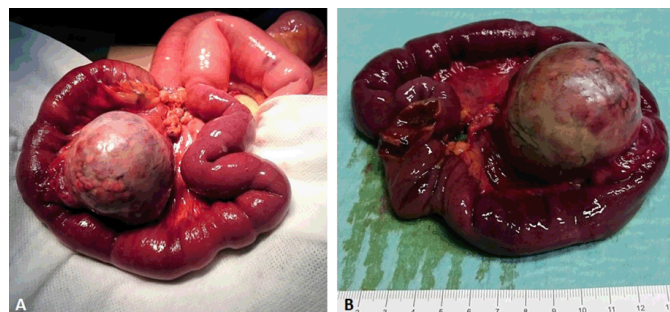


Figure 2: (A) Tumor present in the mesentery of the ileum. The tumor was stuck behind the uterus which conditioned the twist and subsequent ischemia on a loop of small bowel. (B) Resected specimen

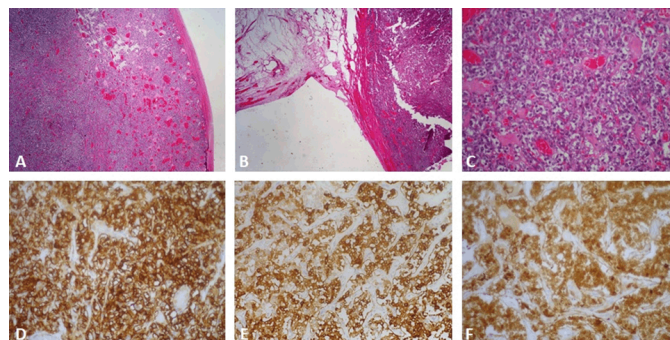


Figure 3: (A and B) The encapsulated Tumor, (HE stain x20); (C) Nests and cords of small and intermediate size cells separated by thin abundant fibrovascular septae giving the characteristic Zellballen pattern). The cells had clarified cytoplasm and small nuclei, rounded and irregular chromatin (HE stain, x200); (D) Immunohistochemistry of CD56 (x200); (E) Immunohistochemistry of Chromogranin A (x200); (F) Immunohistochemistry of S100 (x200), supporting the diagnosis of paraganglioma.

pre and latero-tracheal, below the level of the thyroid gland, all with less than 1 cm. Thyroid and adrenal glands were unchanged. Mesenteric ganglions were present with various diameters, apparently reactive. On the right adnexal region, a nodular image persisted, with solid features, possibly corresponding to a fibroid tumor. The examination was completed with PET-scan which revealed no contrast anchor zones.

The patient was oriented to gynecological, endocrinal and genetic consultation 24 months after surgery there is no evidence of recurrence.

DISCUSSION

Paragangliomas are rare tumors derived from neural crest cells that arises from the autonomic nervous system. These cells can migrate to almost anywhere along the paravertebral and para-aortic axis [1].

Although the most common location of paragangliomas is the adrenal gland, 5–10% of paragangliomas can occur in other locations, almost in all places where normal paraganglia exist [1]. 70–85% of extra-adrenal paraganglioma occur intra-abdominally, mostly adjacent to the aorta and in the area corresponding to organ of Zuckerkandl [1].

Mesenteric paragangliomas such as those discussed in this article, are extremely rare, with only 20 known cases (Table 1). It has been hypothesized that this kind of Tumor derives from the mesenteric paraganglia, resulted from the vertebral migration along the root of the superior mesenteric artery [6].

The paraganglioma pathogenesis is not completely understood. They can be sporadic or hereditary [1]. Hereditary paragangliomas occur in 10–50% and are more often multifocal and may be associated with other syndromes such neurofibromatosis, with multiple endocrine neoplasia type 2, von Hippel-Lindau disease, familial paraganglioma and Carney triad [7]. For this reason, these patients, like the one in this case study, should be oriented to genetic evaluation.

Mesentery paraganglioma seems to occur more often in women with a mean age of 53-year-old (Table 1). The retroperitoneal paragangliomas have a slight predilection for younger men with ages between 39 and 43 years [2].

Extra-adrenal paragangliomas could present with abdominal pain palpable abdominal mass [4]. Most patients undergo hypertension and the typical triad associated with pheochromocytoma: palpitations, headaches, and diaphoresis [1]. In the case described, the patient was a woman of young-age, with no previous symptoms known, showing acute abdominal pain, which is truly uncharacteristic for paraganglioma.

The diagnostic of paragangliomas is particularly challenging. These Tumors have the potential to secrete catecholamines, however, only 25% are functional [2]. When functional paraganglioma is suspected, plasma or urinary metanephrines should be analysed and precede any imaging study [5].

Image studies such as US, CT or MRI are effective in identifying abdominal masses, however the tissue characteristics and density overlaps those of other neoplasms including gastrointestinal stromal tumors, leiomyoma, malignant lymphoma and metastatic tumor [1].

Specific functional imaging with ^{131}I -metaiodobenzylguanidine (MIBG) is one of the best exams for diagnosis in functional neoplasms. PET imaging with 6 ^{18}F fluoro-DOPA offers even higher accuracy in detecting paragangliomas and helps identify and characterize the extent of the mass as well as the staging [8]. The final step of the diagnosis is the biopsy of the lesion.

In afore discussed case, none of the previous examinations were realized due the clinical presentation of the patient and the need to perform an urgent exploratory laparotomy. Once again, another pitfall, which helped the misdiagnosis, was the tumor's location, away from the para-aortic region. Although rare, paragangliomas should be considered as a differential diagnosis of solid mesenteric tumors.

There is a malignant potential associated to MP, with an incidence of 14–50% [9]. Only a few articles reported malignant paragangliomas (Table 1). A cervical lymph node was reported in a case of retroperitoneal paraganglioma [10], a local metastasis was found in one case of MP [5] and there is also a MP with lymphovascular invasion described (Table 1) [3]. In these reports, the diagnosis of malignancy was based on the histology findings. Mitotic count and the Ki-67 label are also considerable significant in grading the malignant potential of those tumors [11].

In the present case, the Ki-67 was low and mitoses were rare. The tumor presented as a solid well defined mass with no metastases, reason why it was ruled as a benign MP.

The treatment of choice for paraganglioma is surgical resection [1]. The majority of MP described in literature were excised with an enterectomy of the small bowel [12]. Chemotherapy and radiotherapy didn't show convincing results in patients with unresectable or metastatic disease [5]. Treatment with radiolabelled MIBG has been postulated due to its avidity for the chromaffin cell tumors and its involvement as an adjuvant to surgical therapy as well as the possibility of a synergistic effect with chemotherapy seem promising [13].

Since MP is a very rare entity with a limited number of cases reported, the knowledge of this entity is short, which makes long-term follow-up after surgical excision necessary.

The follow-up of MP consists in annual biochemical testing with plasma catecholamines, plasma free metanephrines, urinary catecholamines, urinary vanillylmandelic acid and urinary metanephrines. Image studies such as CT scans and/or MRI and MIBG scans, are essential in the assessment for metastatic disease and recurrence [4].

Table 1: Data from 20 previous cases of mesenteric paragangliomas

Author	Publish year	Gender	Age	Associated Symptoms	Pre-operative diagnosis	Tumor size	Methastasis
1 Areán et al. [14]	1956	Male	32	Nausea, vomiting, Diarrhea	Abdominal mass	10	None
2 Carmichael et al. [15]	1970	Female	62	Nausea, vomiting, pain	Abdominal mass	3.2	None
3 Tanaka et al. [16]	1991	Female	29	Nausea, vomiting	Abdominal mass	10x9x7	Liver
4 Ishikura et al. [17]	1996	Female	33	Abdominal pain	Ovarian tumor	15x15x15	Unknown
5 Onoue et al. [18]	1999	Female	38	None	Mesenteric tumor	4.5x3.2x3	None
6 Jaffer et al. [19]	2002	Female	76	Abdominal mass, vomiting	Abdominal mass	8.5x8x2	None
7 Muzaffar et al. [20]	2002	Female	76	Abdominal mass	Abdominal mass	20x15	None
8 Ponsky LE, Gill IS [21]	2002	Female	35	Abdominal mass, headache	Abdominal mass	5.5	Unknown
9 Canda et al. [22]	2004	Male	70	None	Mesenteric tumor	18	None
10 Nobeyama et al. [23]	2004	Male	53	Abdominal mass	Abdominal mass	15x10x7	Unknown
11 Kudoh et al. [24]	2005	Female	72	Abdominal mass, pain	Mesenteric tumor	10x10x9	None
12 Matsumoto et al. [25]	2006	Female	77	Abdominal mass	Mesenteric tumor	7x5.5	Unknown
13 Svajdler et al. [26]	2007	Male	65	Abdominal mass	Mesenteric tumor	12x9x8	None
14 Guo et al. [27]	2009	Female	22	Abdominal mass	Pelvic tumor	11.5x6x11.5	None
15 Jacob et al. [28]	2012	Female	63	Lethargy	Abdominal mass	10	Unknown
16 Chetrit et al. [5]	2012	Male	55	None	Abdominal mass	11.5x9.5x6.5	Lymph node
17 Fujita et al. [1]	2013	Female	78	None	Mesenteric tumor	3x1.5x1.5	None
18 Zeynep Ozkan et al. [2]	2014	Female	54	Abdominal mass, pain	Mesenteric tumor	6	None
19 Pedroso Célia et al. [4]	2015	Female	32	Abdominal mass	Ovarian mass	11.5x6.5x5.5	None
20 Mohd Afiq et al. [3]	2015	Female	69	Abdominal mass, pain	Ovarian mass	18x15x11.5	Lymphovascular
21 Current	2016	Female	32	Abdominal pain	Ovarian mass	6.5x6x5.3	None

CONCLUSION

MP is an extremely rare entity. Preoperative diagnosis of extra-adrenal paraganglioma in asymptomatic patients is difficult but should be included in the differential diagnosis of solid mesenteric tumors. This case highlights how paragangliomas may be mistaken for gynaecological Tumors and how they can present in variable ways. The surgical therapy is the treatment of choice and, even after a complete resection, these patients should be oriented for a long-term follow-up.

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Author Contributions

Manuel Alexandre Viana Ferreira – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Aires Martins – Substantial contributions to conception and design, Acquisition of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Álvaro Gonçalves – Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published

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Guarantor of Submission

The corresponding author is the guarantor of submission.

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Consent Statement

Written informed consent was obtained from the patient for publication of this case report.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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