

Case Report

EXTRA-ADRENAL GIANT PARAGANGLIOMA: CASE REPORT

PARAGANGLIOMA GIGANTE EXTRAADRENAL: REPORTE DE UN CASO

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Abstract

Masses that arise from extra-adrenal sympathetic and parasympathetic paraganglia are classified as extra-adrenal paraganglioma. The tumours can produce a hypersecretion of catecholamines that generate a variety of symptoms, which can be lethal if left undiagnosed. Adequate chemical/hormonal testing should be done and a selection of image studies performed to localize and categorize these lesions.

The classic triad of symptoms composed of headaches, palpitations and profuse sweating combined with elevated metanephrine or catecholamines levels and identification of an adrenal or retroperitoneal mass is needed for a correct diagnosis.

The cornerstone treatment for pheochromocytoma or paraganglioma is the surgical resection and preoperative imaging is essential for defining laparoscopic vs open approach as well as localizing tumour vascular supply.

Resumen

Introducción:

Las masas que surgen de ganglios simpáticos y parasimpáticos extraadrenales se clasifican como paragangliomas extraadrenales. Los tumores pueden producir hipersecreción de catecolaminas que generan una variedad de síntomas, que pueden ser letales si no se diagnostican. Se deben realizar pruebas bioquímicas / hormonales adecuadas y realizar una selección de estudios de imagen para localizar y categorizar estas lesiones.

La clásica tríada de síntomas compuesta por dolor de cabeza, palpitaciones y sudoración profusa combinada con niveles elevados de metanefrina o catecolaminas y la identificación de una masa adrenal o retroperitoneal es necesaria para un diagnóstico correcto.

El tratamiento fundamental para la feocromocitoma o paraganglioma es la resección quirúrgica y las imágenes preoperatorias son esenciales para definir el abordaje laparoscópico frente al abierto, así como para localizar el suministro vascular del tumor.

Keywords: Extra-Adrenal Paraganglioma; Extra-adrenal pheochromocytoma; Familial paraganglioma; Retroperitoneal; Catecholamines.

Introduction

Masses that arise from extra-adrenal sympathetic and parasympathetic paraganglia are classified as extra-adrenal paragangliomas (1). The tumours can produce a hypersecretion of catecholamines that generate a variety of symptoms, which can be lethal if left undiagnosed. Besides adequate chemical/hormonal testing, a selection of image studies should be performed to localize and categorize these lesions (2). The objective of this article is to present the case of a giant paraganglioma and review the literature available about this disease.

The incidence of pheochromocytoma and paraganglioma is about 0.6 cases per 100,000 person-years (2) and the classic triad of symptoms is composed of headaches, palpitations or tachycardia and profuse sweating. These typical symptoms combined with elevated metanephrine or catecholamines levels with identification of an adrenal or retroperitoneal mass is the triad needed for a correct diagnosis.

Moreover, the cornerstone treatment for pheochromocytoma or paraganglioma is the complete surgical resection, provided the correct preoperative preparation as well as preoperative imaging. The latter is essential for defining laparoscopic vs open approach as well as localizing tumour vascular supply.

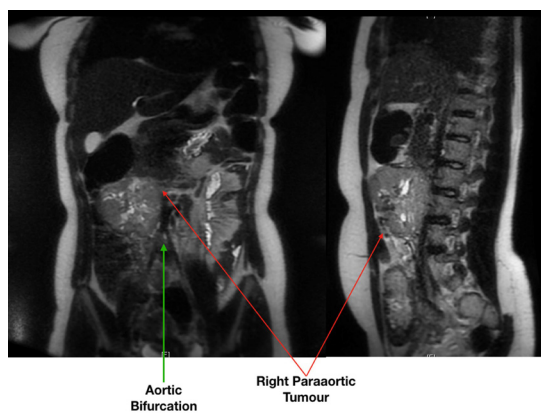


Figure 1. Mass extending from inferior uncinated process of the pancreas and second duodenal portion towards the aorta bifurcation

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Study was completed with an abdominal magnetic resonance (MRI) in which a 6.8 x 10.9 x 8.3 cm mass was seen, with defined borders at supraumbilical right paraaortic localization. Mass extended from the level of the second duodenal portion towards the aorta bifurcation (Figure 1).

This tumour was of a heterogeneous consistency, with multiple necrotic loci with mass effect compressing the inferior vena cava and displacement of small bowel.

Moreover, an arterial abdominal tomography (CT Scan) was made in order to delimitate vascular structures around the tumour as well as its vascular supply. This test reported a vascular network that depended on proximal portion of the superior mesenteric artery. On the other hand, an arterial branch was visualized, parallel to the right renal artery with two smaller ascending tortuous spiral arteries from the pelvis depending on a branch of the uterine right artery. The venous drainage depended mainly on the left renal vein (Figure 2).

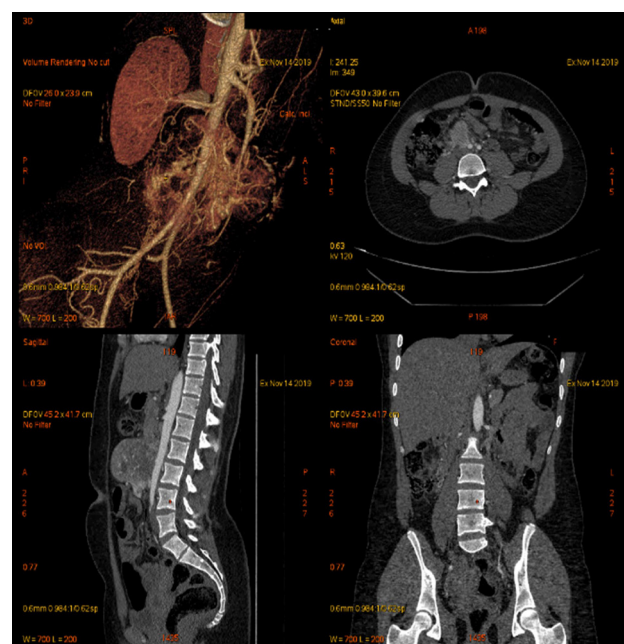


Figure 2. Arterial reconstruction

With the presumptuous diagnosis of a vasoactive amines-producing tumour (Pheochromocytoma vs Extra-adrenal paraganglioma), α -blocking was initiated with Phenoxybenzamine and posterior β -blocking for reflex tachycardia, during two weeks in which a midline supra-infra umbilical exploratory laparotomy was performed.

During surgery, a paraaortic 10-cm tumour was found, with an important vascular supply described above. A complete resection was performed; complementing the intervention with a peritumoral, inter aorto-cava and infra-renal lymphadenectomies.

Patient presented hemodynamic instability during surgery requiring intraoperative β -blocking and posterior introduction of noradrenaline (NA) after resection of the tumour.

Patient stayed in intensive care unit (ICU) during 4 days, requiring NA in descending doses considering it as a grade I complication according to Clavien-Dindo classification. Finally, she was discharged of the 7th post-operative day with adequate oral intake and without any complications.

During the initial 30-day follow-up, patient did not present any of the fore mentioned symptoms with normalization of the biochemical analysis.

The pathology report confirmed the suspicion of a poorly differentiated paraganglioma with metastasis in 1 of 3 lymph nodes around the lesion with the rest of the lymphadenectomy negative for metastasis (7/7). On the other hand, succinate dehydrogenase subunit B (SDHB) mutation was found.

Nevertheless, patient was re-admitted to the emergency department after the 30-day follow up for abdominal pain (Post-operative Day 40). CT scan was made observing a mild dilation of the right ureter with suspicion of entrapment- For this reason, a PET-CT scan and MRI were made that showed haemangioma around right ureter without any tumour relapse. No new therapeutic

gesture was needed. During 6 and 9 months follow-up, patient did not present elevation of metanephrines as well as a new MRI without any relapse.

Discussion

Masses that arise from extra-adrenal sympathetic and parasympathetic paraganglia are classified as extra-adrenal paragangliomas (1). These tumours can produce a hyper-secretion of catecholamines that generate a variety of symptoms, which can be lethal if left undiagnosed. Besides adequate chemical/hormonal testing, a selection of image studies should be performed to localize and categorize these lesions (2).

The incidence of pheochromocytoma and paraganglioma is about 0.6 cases per 100,000 person-years (2). The classic triad of symptoms made our patient seek medical attention. These symptoms are common to many other diseases and makes difficult identifying cases of pheochromocytoma or paraganglioma.

On the other hand, asymptomatic cases are increasingly diagnosed due to widespread use of CT scans for other purposes, identifying adrenal or extra-adrenal masses (2). In order to make a correct diagnosis of this pathology, a proof of excessive release of catecholamines and anatomical identification of the lesion are required. Typical symptoms combined with elevated metanephrine or catecholamines levels with identification of an adrenal or retroperitoneal mass is the triad needed for a correct diagnosis. Furthermore, after tumour extirpation, genetic testing can be done to find germline mutation in a susceptibility gene (2).

The cornerstone treatment for pheochromocytoma or paraganglioma is the surgical resection. As the diagnosis is confirmed with biochemical markers and CT scan or MRI, a new difficulty awakens; timing for surgery as well as surgical approach. The

use of combined α and β adrenergic blockers is the initial standard treatment for the adequate blood pressure control and to prevent intraoperative hypertensive crisis, that can lead to other complications (2). Successful adrenergic blocking can be accomplished with non-selective or selective α adrenergic receptor antagonist (e.g. Phenoxybenzamine), as the one used in our patient. Moreover, β -adrenergic antagonist (e.g. Metoprolol) can be used to prevent or treat reflex tachycardia secondary to α -block and targeting an average heart rate of 80 beats per minute. However, as seen in our patient, postoperative hypotension can be a complication of preoperative adrenergic blocking (2). Thus, requiring noradrenaline in the immediate post-operative period.

On the other hand, during surgical intervention, a few factors should be taken into account. Firstly, the selection of a laparoscopic vs open approach should be addressed. There are concerns about minimally invasive surgery, based on increased risk of cardiovascular complications due to hormone release secondary to mass mobilization with a consequent intraoperative hypertensive crisis. Nevertheless, this has been evaluated in several studies and laparoscopic excision is well established, although the main factor influencing the failure of laparoscopic approach is the tumour size and high recurrence rates (3). Paragangliomas can present difficulties in laparoscopic resection as they appear in unusual and surgically difficult access locations, which can result in incomplete tumour resection or tumour spillage. While laparoscopic approach is supported for the excision of small tumours (< 2.5 cm), there is little evidence reporting the outcome of minimally invasive surgery for giant sized lesions (> 8 cm) (3). For this reason, we selected an open laparotomy approach to achieve adequate complete tumour resection with clear margins.

On the other hand, laparoscopic and retroperitoneal approaches have been used for these type of lesions (4). Although there is some evidence that the retroperitoneal approach is

preferable in patients with prior surgical interventions as intraperitoneal adhesions can be avoided. Moreover, the posterior approach is also favored for bilateral adrenalectomy. The contraindications for retroperitoneal approach include morbid obesity and caudally located tumors near the renal hilum as in the case of our patient (5)(4).

Secondly, there is a fear of massive intraoperative catecholamine release, which can lead to uncontrollable hypertensive crisis (1). Therefore, a successful tumour extirpation should use minimal dissection as well as ligation of all arterial and venous drainage prior, if possible, to mobilization. This is the reason why pre-operative arterial CT scan becomes of great importance. These radiographic tests can dictate where the main tumour blood supply is located in order to facilitate its prompt ligation. Once devascularization is completed, tumour mobilization can be done freely because catecholamine release is already blocked (1).

Selection between either CT Scan or MRI is reasonable as a first test. Both detect a great percentage of all sporadic symptomatic tumors as most of them have more than 3 cm in diameter. So choosing between this two test depends more upon cost and availability of MRI (4).

Moreover, in this case lymph nodes seemed enlarged during surgical intervention. Although there is no evidence of lymphadenectomy in cases of paraganglioma, due to localization of this lesion and accessible lymph nodes, lymphadenectomy was performed.

Furthermore, there are studies describing the use of percutaneous ablation for the treatment of lesions of various organs, including adrenal glands. However, there is no evidence comparing percutaneous ablation with surgical intervention in extra-adrenal retroperitoneal tumours. In the case of catecholamine-secreting tumours, some cases of percutaneous ablation have been reported (6), but no percutaneous ablative

treatment of a primary paraganglioma has been described.

On the other hand, the genetic study may reveal succinate dehydrogenase subunit (SDH) mutation. This includes five syndromes of familial paraganglioma which are caused by pathogenic variants in the succinate dehydrogenase subunit genes (SDHB, SDHC, SDHD, SDHAF2, SDHA) (7). SDHA, SDHB, SDHC, and SDHD are four nuclear genes that encode the four subunits (A, B, C, D) of the SDH mitochondrial enzyme. These are known as the SDHx genes, and they are believed to work as tumour suppressor genes. The five hereditary SDHx paraganglioma syndromes have been described with different mutations in each type (8) (9). All these four genes can be involved in the development of Pheocromocytomas and Paragangliomas. In the case of our patient, she presented a mutation in the gene for the subunit B of SDH (SDHB). This type of mutations have a more noradrenergic or dopaminergic profile. Typically, SDHB-related paragangliomas appear in extra-adrenal locations (abdomen, organ of Zuckerkandl, thorax—mediastinum and pelvis) (8). SDHB gene mutations have been implicated as the most common cause in the pathogenesis of malignant Pheocromocytomas/Paragangliomas, in both, children and adults. Moreover, SDHB-associated tumours have been observed to be malignant in 43 % of cases (10). This implies stricter post-operative surveillance, thorough evaluation of the anatomic piece searching for malignant behaviour as well as completing the study for the rest of the family. The patient we reported is the index case, which implied screening of the gene mutation on the rest of the family. Furthermore, SDH mutations are a rare cause of paraganglioma/pheocromocytomas during childhood, but their screening is fundamental in all patients with this diagnosis, especially if there is a family history.

Radiation therapy has some evidence in the cases where malignant pheocromocytoma/paraganglioma are confirmed. Although these lesions were considered radio-resis-

tant, an external beam radiation therapy (EBRT) at doses > 40 Gy can provide local tumour control and relief of symptoms, as well as painful bone metastases. It is important, that this therapy is considered for malignant irresectable lesions, more readily studied in skull base and neck paragangliomas. Moreover, they can produce RT-induced inflammation of the tumour thus generative massive catecholamine secretion with hypertensive crisis (11).

Conclusions

Paragangliomas and Pheocromocytomas are rare, but their diagnosis is rising due to image studies for other purposes. When suspected, biochemical testing should be made and appropriate medical history and anamnesis developed to precise the diagnosis. Once the biochemical diagnosis is made, tumour size, localization and blood supply should be evaluated by imaging to define surgical approach and, surgery timing. If they are functional, preoperative alpha and beta blocking must be performed. Post-operative follow-up should focus in hormonal and clinical normalization as well as periodic CT/MRI to rule out relapse, especially in familial paragangliomas/pheocromocytomas and malignant lesions.

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