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Case Report

Surgical intervention as a curative major for secondary hypertension

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ABSTRACT

Retroperitoneal functional paraganglioma is a rare type of neuroendocrine neoplasm which secrete excess catecholamines including epinephrine, norepinephrine, dopamine and their metabolites metanephrine, normetanephrine, 3-methoxytyramine respectively. Early diagnosis of functional paraganglioma is important because its removal is often curative. The extent of disease is evaluate using 2(18F)-fluoro-2 deoxy-D-glucose positron emission tomography (FDG-PET), where increased uptake of 18-FDG observed the mass. It is one of the rare curable causes of secondary hypertension. Here, we have presented the rare case of a young female who was recently diagnosed with hypertension and pain in abdomen, was later found to have functional paraganglioma.

Keywords: Functional paraganglioma, retroperitoneal paraganglioma, surgical management, Secondary hypertension, FDG-PET

INTRODUCTION

Functional retroperitoneal paragangliomas are rare tumours arising from paraganglia cells derived from neural crest which are catecholamine-producing tumours. Also known as extra-adrenal pheochromocytomas. The rule of thumb in pheochromocytoma is that approximately 10% of them are extra-adrenal (of which 10% are extra-abdominal), 10% are malignant, 10% are not associated with hypertension and 10% are hereditary.[1] The classical symptoms of functional paraganglioma, present in approximately half of all patients, are attacks of severe hypertension accompanied by headache, palpitation and sweating caused by intermittent release of catecholamines.[2] They are characterized by the classic triad of features composed of headache, diaphoresis and tachycardia (with or without palpitation). However, this presentation is not mandatory, occurring in only 24% of the cases.[3] The concomitant presentation of these three symptoms associated with arterial hypertension has a diagnostic specificity greater than 90%.[4] Despite the low prevalence of induced hypertension by paraganglioma in the general population, hypertension is the most frequent cardiovascular manifestation, present in about 90% of patients with these tumours and usually it is a persistent hypertension.[5] The annual incidence of pheochromocytomas is located between 500 to 1600 cases per year, with an equal sex distribution and peak in the fourth and fifth decades of life.[6] Paragangliomas affects approximately 0.1% of individuals with hypertension.[5] Most paragangliomas are benign, however a few of them are diagnosed with metastasis and in this case patient's five-year survival rate is between 40% and 77%, with a progression-free survival period that ranges from 4 to 36 months.[7] It is now well established that there are several factors correlated with an accelerated disease progression, including male sex, diagnosis at an old age, synchronous metastasis, bigger tumour size, increased dopamine level, and failure to remove primary tumor.[5] Diagnosis is made through a combination of laboratory and imaging tests. Paraganglioma is diagnosed through the analytical evidence of excessive production of catecholamines or their metabolites. Adrenaline and norepinephrine are

metabolised by catecholamine-O-methyl transferase into metanephrine and normetanephrine, respectively (inactive metabolite). Consistently metanephrine measurement in both plasma and urine is an excellent diagnostic method and is currently recommended as an initial method of diagnosis, according to the recommendations of clinical practice of the society of endocrinology (JCEM 2014).[8] Imaging methods are used for diagnostic confirmation in order to locate and evaluate the tumour mass anatomically and functionally, allowing subsequent planning of the therapeutic approach. We are presenting a case report of the patient with an extra-adrenal retroperitoneal paraganglioma at an unusual site located using PET CT scan, which is the reason for developing hypertension and can be cured with surgical intervention.

CASE REPORT

A 30-year-old female patient was admitted to the hospital for left sided abdominal pain. The patient gives history of painful attack at left side of abdomen in the past 2 years, previously 6 months back she had an attack of pain in abdomen, associated with headache, palpitation and excessive sweating with systolic BP of 180 mmHg and was hospitalised for 2 days (persistently BP was >160/100 mmHg) and was started on tablet Losar-H (losartan 40 mg+hydrochlorothiazide 12.5 mg) and metoprolol 25 mg. On present admission CT scan of abdomen and pelvis was done which showed 40×43 mm well defined heterogeneously enhancing isodense mass lesion involving the retroperitoneum on the left side inferiorly to the left ureter, inferior to the inferior pole of left kidney with mild peritoneal fat stranding and compressing the left proximal ureter. USG guided FNAC was done which shown clusters of rounds to polygonal cells (some plasmacytoid) with indistinct cell borders to abundant pale, finely granular to fibrillar cytoplasm with conspicuous reddish granules on Romanowsky stain in few cells with background composing of RBCs suggestive of benign round polygonal cell tumour probably of neural origin. Hence, diagnosis of retroperitoneal paraganglioma was done. Free plasma normetanephrine, 3-methoxytyramine and vanillyl-mandelic acid was done and was found to be elevated (Table 1) and thus, rare diagnosis of functional retroperitoneal paraganglioma was made.

Table 1: Laboratory investigation with report.

Investigation	Report	Lab reference
Plasma free metanephrine	13.8 ng/l	7.90 - 88.70
Plasma free nor-metanephrine	1910ng/dl	20.10 – 135.45
Plasma 3-Methoxytyramine	28.7mg/dl	<18.40
24hrs urine VMA	9.90 mg/dl	1.60 – 7.30

The extent of the disease was evaluated with Ga-68-Dotanoc pet scan. With the patient fasting for 3 hours, 3.5 mci of Ga-68-Dotanoc was injected intravenously and 3D PET CTscan was performed. Physiological concentration was seen in the adrenals, spleen, kidneys, liver, thyroid and bladder. Ga-68-Dotanoc accumulation was seen in the mass in peritoneum (suv: 16.4). A polypoidal somatostatin receptor avid mass in retroperitoneum displacing the left ureter posteriorly and abutting the D3/D4 segments of duodenum (Figure 1). All other haematological and biochemical profile were within the normal range. Based on the above result's surgery was planned and pre-operative optimisation of blood pressure (Table 2) was done for 1 week using tablet prazosin 5 mg and atenolol OD 25 mg. Excision surgery was performed.

During procedure, there was a spike of BP with maximum of 210/140 mmHg and was controlled with the use of injection esmolol 0.15 mg/kg body weight/min and nitroglycerine 20 mcg/min infusion; the patient was stable on post operation. The excised specimen (Figure 4) was sent for histopathology examination and it confirmed extra-adrenal paraganglioma.

Table 2: Pre-operative optimisation of blood pressure in patient with functional paraganglioma.

Time before operation	Morning BP		Evening BP		Medications
	Supine	Standing	Supine	Standing	
7 days before	160/100	160/90	160/90	150/80	Tab. Prazosin 5 mg 1-1-1-1 Tab. Atenolol 25mg 1-0-0
6 days before	154/100	150//90	150/94	150/80	Tab. Prazosin 5 mg 1-1-1-1 Tab. Atenolol 25mg 1-0-0
5 days before	154/90	150/90	150/90	140/90	Tab. Prazosin 5 mg 1-1-1-1 Tab. Atenolol 25mg 1-0-0
4 days before	134/80	140/90	120/90	122/80	Tab. Prazosin 5 mg 1-1-1-1 Tab. Atenolol 25mg 1-0-0
3 days before	130/94	136/84	120/90	122/80	Tab. Prazosin 5 mg 1-1-1-1 Tab. Atenolol 25mg 1-0-0
2 days before	124/90	128/84	130/90	134/80	Tab. Amlodipine 5mg 1-0-0
1 days before	130/90	130/80	120/80	120/76	Tab. Amlodipine 5mg 1-0-0

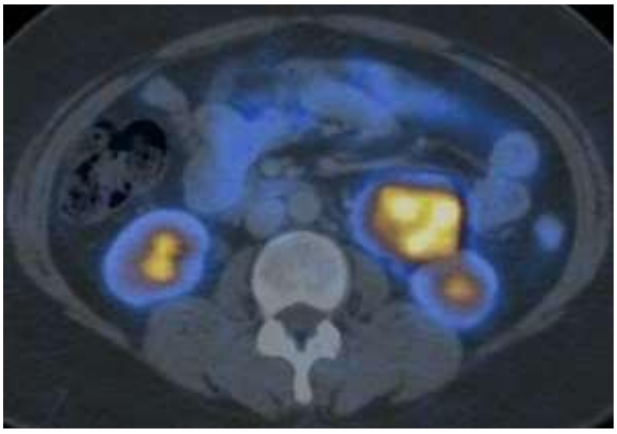

Figure 1: PE CT scan of patient.

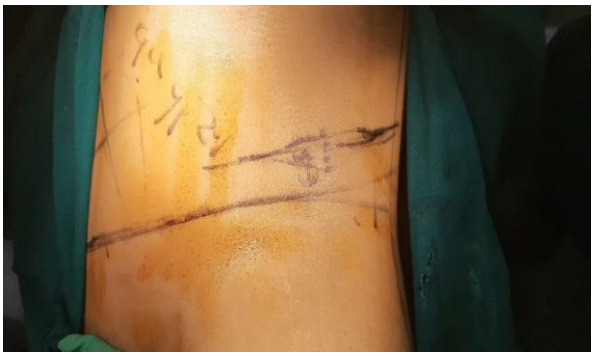

Figure 2: Left subcostal incision.

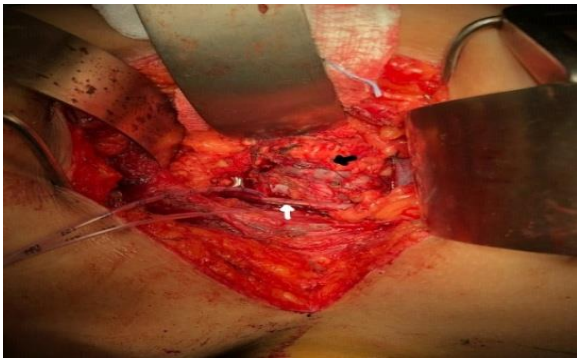

Figure 3: Intraoperative arrow indicate tumor.

DISCUSSION

Tumour resection is the gold standard treatment for disease related to paraganglioma and is the only surgically curative therapeutic modality.[9] Open surgery especially in case of invasive disease is preferred over laparoscopic approach to ensure complete tumour resection, to prevent rupture and to avoid local recurrence, constituting the preferred approach.[8] In non-metastatic paragangliomas, the five-year survival rate is higher than 95%.[9] In fourth edition of WHO's Classification 2017, it is admitted that paragangliomas have some metastatic potential.[10]

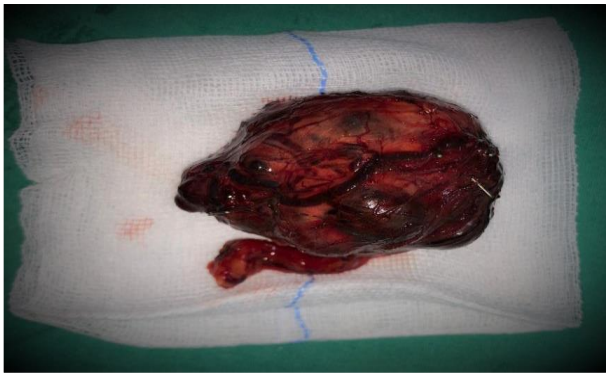

Figure 4: Specimen of 4x5 cm retroperitoneal tumor resected.

It is to be understood that paragangliomas have the potential to metastasize, sometime many years after diagnosis.[11] The mutation in the Succinate dehydrogenase gene subunit b gene is the one that poses the greatest risk of development of metastatic disease.[12] There are other risk factors for metastasis including tumour mass greater than 5 cm, advanced age at the time of diagnosis and tumours with a high dopamine production.[13] Histological evaluation and immunohistochemical study are not truly predictive of tumour behaviour in the long form, however in retrospective studies, some common characteristics were identified.[14] There are five main parameters: invasion (vascular or peritumoral soft tissue), architectural variations (diffuse, irregular, confluent growth), cytological variations, necrosis and activity proliferation (atypical mitosis, proliferative index) identified by the grading system for paragangliomas whose result allows the assessment of the risk of metastasis and possibility of survival.[15] After the development of metastatic disease, the survival rate five years after diagnosis varies between 34% and 60%; however, there are many cases with an extremely aggressive evolution awaited with two- to four- year survival period, as well as cases of patients with indolent evolutions that survive 20 years or more after diagnosis. In these cases, therapeutic approaches are limited and are mostly palliative. Clinical practice of society of endocrinology 2014 recommends follow-up with all patients with paragangliomas regardless of the risk of recurrence initially estimated.[8] Which must be annual, with biochemical profile control in order to ascertain the presence of persistent, recurrent or metastatic disease.[9]

CONCLUSION

There are variable and limited data available about clinical features and surgical management of extra-adrenal retroperitoneal functional non-malignant paragangliomas. In this case, patient had a rare case of paraganglioma in unusual site which was associated with functional causing secondary hypertension and a surgical intervention can be consider as a preferable measure to cure secondary hypertension.

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