

# Paraganglioma: A Case Report

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Paragangliomas are very rare tumors that must be excluded in the patients with hypertension associated with abdominal incidentaloma and/ or unexpected drug-induced blood pressure changes. We report a 36-year-old woman with abdominal mass who had had a history of hypertensive attacks and a life-threatening hypotension after some drugs were being administered. Diagnostic procedures including measurement of urinary catecholamine metabolites, Computed tomography scan, [<sup>131</sup>I] Metaiodobenzylguanidine scintigraphy, and histological examination of excised mass revealed the diagnosis of paraganglioma.

**Key words:** Paraganglioma, pheochromocytoma, hypertension

## Introduction

Pheochromocytoma accounts for 0.1% of hypertensive patients. Most of them (90%) arise from the adrenal medulla, whereas 10% are extra-adrenal. Extra-adrenal pheochromocytomas are called paragangliomas and may arise anywhere but are mostly located in the retroperitoneum arising from the sympathetic chain or from the organ of Zuckerkandl (1). Patients with such tumors typically present with symptoms resulting from excess production of catecholamines (2).

## Case Report

A 36-year-old female patient was referred to our department because of an upper left side mass of the abdomen on ultrasound examination. The medical

history included occasional palpitation with flushing and sweating for two years and hypertensive attacks for two months. Two months before admission she was seen in another hospital because of nausea, abdominal pain, and a hypertensive episode (220/110 mmHg). At that time she was being given metoclopramide 2 mg, hyoscine-N-butyl bromide 20 mg, and ranitidine 50 mg intravenously. Her blood pressure had dropped (70/30 mmHg) and respiratory failure had developed immediately after injections. She was admitted to our intensive care unit because of hypotension and acute respiratory failure. One week later she felt good and an ultrasound examination demonstrated a mass in the upper left side of the abdomen.

She did not drink alcohol, or use drugs. But she was a smoker (6 packets/year). There was also a history of headache and weakness. The patient's mother had primary hypertension.

The temperature was 36°C, the respirations were 16/min, and the pulse-rate was 88/min. While the patient was supine, the blood pressure was 120/70

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mm Hg in the right arm and 130/70 mm Hg in the left arm; while he was standing, the blood pressure was 110/60 mm Hg. She was otherwise unremarkable.

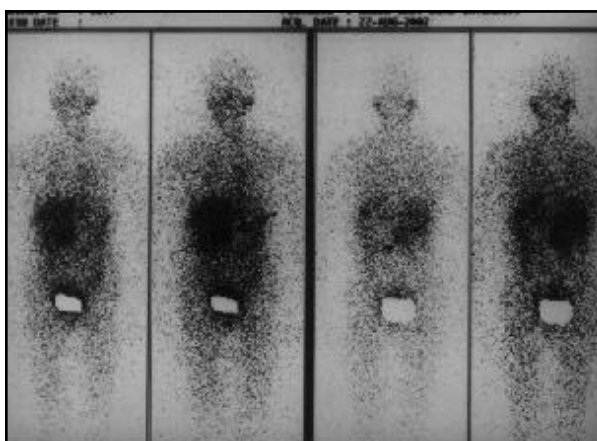
During the hospital stay, the patient experienced several attacks of palpitation, mild sweats, which lasted from a few hours to several hours and which were accompanied by hypertensive attacks of maximal level of 180/110 mm Hg. Hematologic laboratory values, blood chemical levels including calcium were normal. Serum parathormone (PTH IRMA, intact) and 24- hours urinary calcium levels were normal. Fundoscopic examination of the eyes was also normal. During attacks urinary specimens were collected for assay 24-hours urine metabolites of catecholamines. Results of 24-hour urinary studies were as follows: vanillylmandelic acid, 14.4 mg/24 h and 11.6 mg/24 h (normal range: 1.9-9.8 mg/24 h); normetanephrine, 7344  $\mu$ g/24 h (normal range: 88-444  $\mu$ g/24 h); metanephrine, 78  $\mu$ g/24 h (normal range: 52-341  $\mu$ g/24 h). A computed tomography (CT) scan demonstrated a lesion at the site of pars horizontalis of duodenum which was inhomogeneous, and an intravenous bolus of contrast material made the central, low -density region and the surroundings, hyper-density region of the tumor (Figure 1). [ $^{131}$ I] metaiodobenzylguanidine scintigraphy (MIBG) revealed pathological storage at the same region and no metastatic activity was reported (Figure 2). Antihypertensive medication (doxazosin 2 mg/d and thereafter atenolol 1x25 mg/d) was started two week prior to the operation, and the patient felt better with this treatment. Under general anesthesia, laparotomy revealed a well-demarcated, 6x8 cm, soft, mobile tumor near the duodenum.



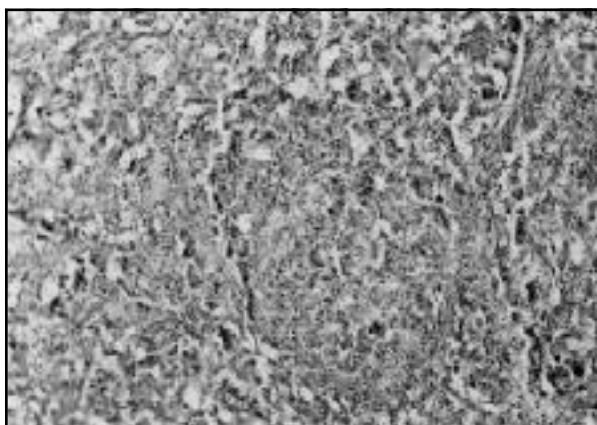
**Figure 1.** In the CT image of the abdomen, a well-demarcated tumor measuring approximately 8x6 cm was localized near the duodenum.

After resection of the tumor her blood pressure dropped to 90/60 mm Hg. Bolus saline infusion was started immediately and the blood pressure was stabilized. On pathologic examination, the biopsy specimen was compatible with paraganglioma. Tumor cells were positive for chromogranin, neuron specific enolase and vimentin. Sustentacular cells were positive for S-100 protein (Figure 3).

The postoperative course was uncomplicated. Antihypertensive medication was stopped, and the patient was discharged 9 days after operation without any of the former symptoms.



**Figure 2.** Result of iodine 131- MIBG scintiscan showing pathological storage in the abdomen.



**Figure 3.** Large cells groups were separated by vascular stroma with prominent bleeding areas (H.E.x100).

## Discussion

Paraganglioma is a rare tumor and may occur in any area of the body where paraganglionic tissue is present, including chemoreceptors, retroperitoneal ganglia, and adrenal medulla, where it is called

pheochromocytoma (3). Most of paragangliomas are located within the abdomen in association with the celiac, superior mesenteric, and inferior mesenteric ganglia. Approximately 1 % are in the thorax (4,5), 1 % within the urinary bladder (3), less than 1 % in the neck (6), and rarely in the gallbladder (7).

Most pheochromocytomas secrete both norepinephrine and epinephrine, with norepinephrine being the predominant catecholamine secreted. Most extra-adrenal pheochromocytomas secrete norepinephrine exclusively. The other rarely secreted products are dopamine, chromogranin A, adrenomedullin, endothelin, parathyroid hormone-related protein, and neuropeptide Y. These peptides may contribute to the clinical manifestations (8).

The most common clinical findings are sustained or paroxysmal hypertension, headache, palpitation, and sweating. Symptomatic episodes can occur as often as 30 times a day or as infrequently as once every few months. Triggers include abdominal pressure, which may increase catecholamine secretion by the tumor, and a sudden drop in blood pressure, such as may occur during the induction of general anesthesia. Drugs can also precipitate a hypertensive crisis, including drugs that lower blood pressure, thereby stimulating catecholamine secretion by the tumor; those that block neuronal uptake of catecholamines, such as tricyclic antidepressants; and other substances thought to alter catecholamine secretion by the tumor, such as glucagon, opiates, and metoclopramide. In our case, there was a history of life-threatening hypotension after some drugs (metoclopramide, hyoscine-N-butyl bromide, and ranitidine) which were given intravenously. We believe that metoclopramide may play a role on this outcome. Hypertensive crisis induced by massive catecholamine release from tumor necrosis followed by depletion of the catecholamine store may result in shock, as has been confirmed in animal models. Coronary vasospasm has also been reported as an important cause of shock in pheochromocytoma (9).

The diagnosis of pheochromocytoma and paraganglioma are initially established by demonstrating elevated urinary or plasma catecholamines or catecholamine metabolites, typically in urine samples but also sometimes in plasma samples (8). Diagnostic accuracy is improved by measuring at least two of three substances. The sensitivity is increased if the

urine is collected during or soon after a hypertensive crisis, when the levels of catecholamines and their metabolites are typically at least three times as high as normal (5). CT has good sensitivity (93% to 100%) for detecting adrenal pheochromocytoma.

Sensitivity decreases to approximately 90% for extra-adrenal pheochromocytomas. In contrast, magnetic resonance imaging has lower or equal sensitivity for detecting adrenal pheochromocytomas but is superior for detecting extra-adrenal tumors. Both imaging methods have poor specificity, as low as 50% in some studies. MIBG scanning offers superior specificity (95% to 100%) and is helpful in diagnosing extra-adrenal tumors. However, it is not sensitive enough (77% to 90%) to exclude pheochromocytoma (10).

The definitive treatment for pheochromocytoma and paraganglioma is surgical excision of the tumor. Surgery for pheochromocytoma entails several considerations. Induction of anesthesia before surgery, manipulation of the tumor, or other stimulation can cause massive outpouring of catecholamines from the tumor, resulting in hypertensive crisis, stroke, arrhythmias, or myocardial infarction. To prevent these problems, patients must undergo pharmacologic blockade of catecholamine synthesis or effects before surgery (10). For acute treatment of severe hypertensive episode either  $\alpha$ -blockade with phentolamine or sodium nitroprusside infusion is indicated, followed by  $\beta$ -adrenergic blockade once  $\alpha$ -blockage is accomplished (8).

Alpha-Methyl-para-tyrosine competitively inhibits tyrosine hydroxylase and decreases catecholamine formation. The combination of metyrosine, phenoxybenzamine, a  $\alpha$ -blocker, and liberal salt intake starting 10 to 14 days before surgery leads to better control of blood pressure and decreases surgical risks. Aggressive fluid replacement to manage intra- and postoperative hypotension is very important (8). Residual nonparoxysmal hypertension is found in 27% to 38% of patients after tumor removal (10).

Ten to 15% of the pheochromocytomas are malignant with metastatic spread. The malignancy rate is 29 to 40% with extra-adrenal localization, compared with 2-11% in adrenal localization (11). Although there was no invasion or distant metastasis, it is reasonable to provide lifelong follow-up for this patient.

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Even though paraganglioma is rare, it should be considered in the differential diagnosis of hypertension associated with incidentaloma and/or with unexpected drug-induced blood pressure changes.

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