

A Case of Pheochromocytoma with Recurrent Hypotensive Attacks

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ABSTRACT

Introduction: Most of the pheochromocytomas are presented with hypertension although sometimes hypotension could be seen. Because intra operative mortality of pheochromocytomas is high, preoperative preparation with alfa- and beta blockers is required. But there is not enough knowledge about preoperative preparation of pheochromocytomas with hypotension. We aim to mention about preoperative preparation of a case of pheochromocytoma with hypotension.

Case presentation: Sixty-one years-old woman first approved to the cardiology outpatient clinic 4 years ago. She was diagnosed arrhythmia so prescribed midodrine 2.5 mg/day and flekainid 100 mg/day. It is suspected that she has pheochromocytoma because of flushing and hypotension. Her blood pressure was 70/40 mm/Hg. Her pulse was 85/min. Metanephrine level was 1889.54 µg/24 hours urine. Then, abdominal computed tomography was performed. There was a left adrenal tumor sized 34x35 mm with a central hypodense area whose peripheral region was isodense. Its absolute washout was 26.5% and relative washout was 12.5%, pre-contrast density was below 10 Hounsfield Units (HU). Plasma aldosteron, Dehydroepiandrosterone Sulfate (DHEA-S), total testosterone levels were normal range. Serum cortisol level was suppressed (0.576 µg/dL) after 1 mg overnight dexamethasone suppression test. Chromogranin A was higher than normal range (189.2 ng/ml). Preoperatively midodrine was stopped, 3 g oral salt and 1000 cc % 0.9 NaCl were given and she continued to take flekainid. Doxazocin (4 mg/day) was given daily for 14 days under close follow up blood pressure. The beta blocker or phentolamine weren't required during operation.

Conclusion: Preoperative preparation of pheochromocytoma with hypotension is different from hypertensive patients.

INTRODUCTION

Pheochromocytomas are catecholamine-secreting tumors that usually originate in the adrenal medulla. The cardinal signs of pheochromocytoma are episodic or permanent hypertension, palpitations, headaches and sweating due to catecholamine release. Because intra-operative mortality of hypertension causing end-organ dysfunction in pheochromocytomas is high, preoperative preparation with alfa- and beta blockers is required generally. It is well-known that surgical extirpation of adrenal mass is curative, but intra operative hemodynamic instability, rapid and severe blood pressure fluctuations may develop in patients during both of pre and intra operative

preparation. Postoperative support requirements usually should be given for improved severe hypotension [1].

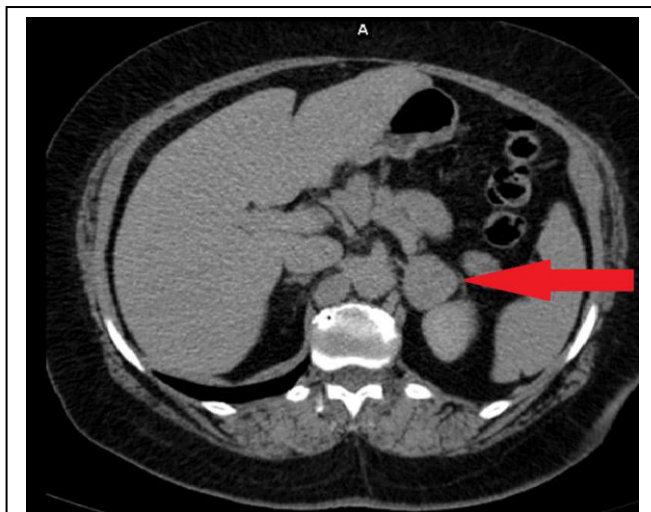


Figure 1: Left adrenal mass in abdominal computed tomography.

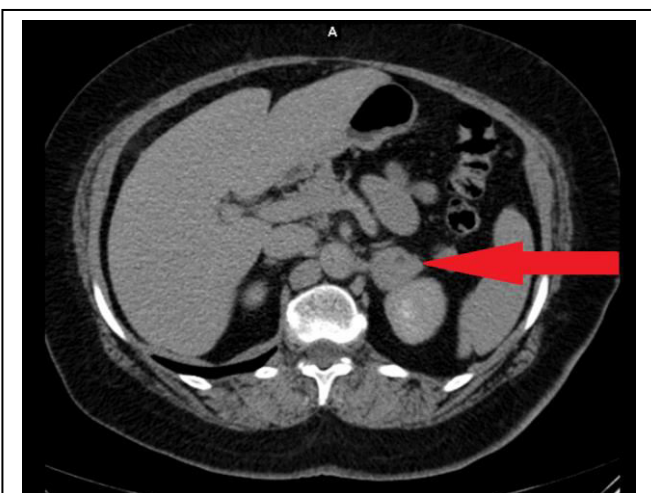


Figure 2: Left adrenal mass in abdominal computed tomography.

Hypotension could be seen in particular due to dehydration or Takotsubo syndrome although most of the pheochromocytomas are presented with hypertension [2]. There is not enough knowledge about preoperative preparation of pheochromocytomas presented with hypotension in existing literatures. Generally, alpha and beta-adrenergic blockade, calcium channel blockers, volume expansion and sometimes metyrosine have been used for appropriate preoperative preparation to avoid hypertensive attack [3]. It is recommended that preoperative adrenergic blockade at least

10-14 day prior to surgery by using alpha-adrenergic receptor blockers with or without beta-adrenergic blocking agents to prevent cardiovascular complications. However, the optimal adrenergic blockade strategy is still debated. Moreover, it is possible that postoperative hypotensive episodes may also appear in selectively blocked patients [4]. We aim to present an interesting case of preoperative preparation of pheochromocytoma with recurrent attacks of hypotension.

CASE PRESENTATION

Sixty-one years-old woman first approved to the cardiology outpatient clinic 4 years ago. She was diagnosed arrhythmia so prescribed midodrine 2.5 mg/day and flecainide 100 mg/day. It was suspected that she has pheochromocytoma because of flushing and hypotension attacks (70/30 mmHg). She referred our endocrinology department.

In our physical examination, her blood pressure was 140/80 mm/Hg and standing blood pressure was 70/40 mm/Hg. Orthostatic hypotension was considered. Her pulse was 85/min. Her weight was 110 kg, body height was 165 cm and body mass index was 40.4 kg/m². Other systemic examination was normal. Her electrocardiography was sinus tachycardia. Ejection fraction was normal (60%), mild mitral insufficiency and grade 1 diastolic dysfunction was found in echocardiography. Laboratory analysis was found as below:

Plasma metanephrine level was 1,57 nmol/L (normal range 0,08-0,51), urinary metanephrine level was 1889.54 µg/24 hours. Plasma aldosterone: 53 pg/ml (normal range 29,4-161,5), cortisol: 8,84 µg/dl (normal range 6,2-19,4), Adrenocorticotrophic Hormone (ACTH):23,99 pg/mg (normal range 7,2-63,3), Dehydroepiandrosterone Sulfate (DHEAS): 84,06 µg/dl (normal range 0-205), totally testosterone: 0,25 ng/ml (normal range 0,06-0,82). Serum cortisol level was 0.576 µg/dL (supressed) after 1 mg dexametasone supression test. Chromogranine A was 189.2 ng/ml higher than normal range (0-100ng/ml). Her other pituitary hormones and Parathyroid Hormone (PTH) were within normal range. Her thyroid examination was normal. Multiple endocrine neoplasia syndrome (type2a-b) was excluded. In abdominal computed tomography, an adrenal tumor was found 34x35 mm sized with a central hypodense area, whose peripheral region was isodense. Its absolute washout was 26.5%and relative washout

was 12.5%, pre-contrast density was below 10 HU. Preoperatively midodrine was stopped, 3 g oral NaCl and 1000 cc isotonic were given daily and she continued to take flecainide therapy. Doxazocin (2 mg/day) was given for 14 days under close follow up her blood pressure and it was titrated (maximum 4 mg/day) based on measured blood pressure and developed orthostatic hypotension because of loss of the baroreceptor reflex and achievement of alpha-adrenergic complete blockade. The beta blocker, phentolamine or vasopressor support was not required during her operation. According to the adrenal gland scaled score of the Pheochromocytoma, the postoperative pathology result was reported as benign.

A result of removal of left adrenal gland the size of tumor was 3,5 x 3,2 x 2,8 cm. There was no vascular invasion and no necrosis. The tumor had no atypical mitosis. The pleomorphism was not observed in tumor. Immunohistochemical examination revealed positive staining with chromogranin, synaptophysin and S-100 negative staining with pancytokeratin, EMA, inhibin and calretinin. Focal areas of the tumor had spindle and nuclear hyperchromasia. There was an increase in cellularity in the tumor.

DISCUSSION

The most common presentation of pheochromocytoma is hypertension causing serious and potentially lethal cardiovascular complications due to the effects of secreted catecholamines from the adrenal medulla [3]. A tumor predominantly secreting epinephrine is usually associated with paroxysmal hypertension, while the norepinephrine-secreting variant is associated with sustained hypertension. Symptoms such as light headedness, presyncope or syncope of orthostatic hypotension may be dominant during presentation, especially in patient with epinephrine-predominant and dopamine-predominant tumors or with secreted adrenomedullin. Pheochromocytoma presented with hypotension. Our patient was considered to have pheochromocytoma due to flushing and hypotension, which are not typical manifestation of pheochromocytoma.

Bergl and et al. reported that an incidence of hypotension in totally 539 cases of pheochromocytoma was approximately 2% during initial presentation. It was previously reported a women with pheochromocytoma to developed recurrent

episodes of chest and abdominal pain, dyspnea, palpitations, diaphoresis and recurrent episodes of severe hypertension (her systolic BP: 300 mmHg) and hypotension (her systolic BP: 50 mmHg) after treated with nitroglycerin and metoprolol [5]. But her preoperative preparation could not be performed since their patient has refused surgery.

There are possible mechanisms for causes of preoperative recurrent hypotension in our patient. Firstly, hypotension may be associated with adrenocortical insufficiency due to mass effect. But her serum cortisol and ACTH levels were normal range. Secondly, we considered that the excess epinephrine secretion may cause desensitization of baroreflex or volume depletion. Prolonged period of high catecholamine levels lead to down regulation of beta-adrenergic receptors due to decreases cardiac contractility [6]. The absence of hypertension can be explained by the desensitization of the cardiovascular system due to high catecholamine levels and hypotension disappear after the excision of tumor [7]. Thirdly, severe pheochromocytoma B type crisis as defined sustained hypotension, shock and multi-organ dysfunction might be possible develop in our patient. But there was not any organ dysfunction or shock status in her clinic presentation and laboratory findings [3]. Fourthly, Takotsubo cardiomyopathy may be possible occurred, because she complained for arrhythmia, chest pain, flushing and hypotension attacks in cardiology outpatient clinic 4 years ago. Takotsubo cardiomyopathy is a transient cardiac syndrome as left ventricular apical akinesis, hypotension, chest pain mimicking acute coronary syndrome, ST segment elevation on ECG. The possible mechanism of Takotsubo cardiomyopathy is stress induced catecholamine release. However, we did not determine any changes of ECG or any echocardiographic sign related to Takotsubo cardiomyopathy in our patient [8]. Similarly, Muhammed S.A. et al., [9] reported a case with cystic pheochromocytoma causing recurrent hypotension (68/34 mmHg), shock, non-cardiogenic pulmonary edema, and she had been stabilized with dopamine and norepinephrine infusion treatments. But we could not take any information for use the treatment of preoperative preparation in their case report. The other possible mechanism may be due to the abrupt cessation of catecholamine secretion. Abrupt cessation of catecholamine secretion due to hemorrhagic necrosis in the tumor, could be the

result of with initial severe hypertension followed by shock and hypotension [10]. It follows that the cyclic crisis could be self-limiting. Of note, the recorded peripheral hypotension could be falsely low secondary to severe vasoconstriction with concomitant severe central hypertension [11]. Wei-Ber L. et al., [12] previously reported that hypotension in patients with intratumoral necrosis of pheochromocytoma occurs due to an abrupt cessation of catecholamine secretion in the setting of constricted circulatory volume. However, we did not determined low cardiac output or hemorrhagic necrosis in the adrenal mass in our case.

Preoperative strategy of hypotensive pheochromocytoma management is still the most important problem. Because preoperative management of recurrent hypotension in patients with pheochromocytoma is not clear in both of the medical literature and the latest pheochromocytoma management guideline. According to conflicting data, the utility of fluid resuscitation and alpha-blockade were suggested in hypotensive patients with pheochromocytoma before the operation. There was no universal acceptance of the benefits of this preoperative treatment approach [13]. Our patient was initially treated with normal saline infusion and low dose selective alpha-blocker as Doxazocin (2 mg/day). She did not develop any hypo- and hypertensive attack during titration period of Doxazocin therapy. The beta blocker, phentolamine or vasopressor support was not required during her operation. Although phenoxybenzamine was first line drug for pre-operative preparation in our preoperative prepare, we use the smallest dose doxazosin (maximum 4 mg/day) due to absence of this drug in our country. Nowadays, some centers use the non-selective alpha-blocker phenoxybenzamine, while others use the selective alpha-blocker doxazosin. Moreover, [14] previously reported that side effects occurred less often in the doxazosin group. The other side-effects of phenoxybenzamine such as orthostatic hypotension, tachycardia, dizziness, and syncope are also more morbid and more profound than that seen in patients on selective alpha-1 receptor antagonists. Similar with our patient, Van Vliet et al., [10]. Reported a case with pheochromocytoma presenting as recurrent syncope due to hypotension. Treatment of their case for stabilized the blood pressure had used propranolol and large volume of infusion.

On the conclusion, pheochromocytoma may presented with recurrent hypotensive attacks. Preoperative preparation of pheochromocytoma with hypotension is different from hypertensive patients with pheochromocytoma such as low dose selective alpha-blockage.

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