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Olgu Sunumu/*Case Report*

Anesthetic Management in Anterior Mediastinal Pheochromocytoma Case

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Anterior Mediasten Feokromasitoma Olgusunda Anestezi Yönetimi

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ABSTRACT

Paraganglioma can be found in different parts of the body. In this case report, a rare case of anterior mediastinal paraganlioma was examined. Pheochromocytoma can pose problems in intraoperative anesthesia management. A 17-year-old male patient with an anterior mediastinal mass was first scheduled for thoracoscopic tumor resection, and then proceeded with open thoracotomy. The patient, who was diagnosed with preoperative pheochromocytoma, had a history of dual antihypertensive drug use. The patient, who showed an intraoperative labile course, had episodes of hypertension (270/140 mmHg) and tachycardia (200 bpm). Esmolol and nitroglycerin infusion was applied and intervened. Diagnosis of paraganglioma-related pheochromocytoma can be challenging. Risks can be minimized by making appropriate decisions and interventions before and during the operation.

Keywords: *pheochromocytoma, paraganglioma, mediastinal mass, anesthesia, thoracotomy*

ÖZ

Paraganglioma, vücudun değişik bölgelerinde bulunabilir. Bu olgu sunumunda ender görülen anterior mediastinal paraganlioma olgusu incelenmiştir. Feokromasitoma, ameliyat içinde anestezi yönetiminde sorunlar oluşturabilir. On yedi yaşında anterior mediastinal kitlesi olan erkek hastaya ilk olarak torakoskopik tümör rezeksiyonu planlandı ardından açık torakotomiye geçildi. Preoperatif feokromasitoma tanısı olan hastaya 2'li antihipertansif ilaç kullanım öyküsü mevcuttu. İntraoperatif labil bir seyir gösteren hastanın hipertansiyon (270/140 mmHg) ve taşikardi (200 atım/dk) atakları oldu. Esmelol ve nitrogliserine infüzyonu uygulanarak müdahale edildi. Paragangliomaya bağlı feokromasitomanın teşhisi zor bir durum olabilir. Ameliyat öncesinde ve içinde alınacak kararlar ve uygun yaklaşımlar ile riskler en aza indirilebilir.

Anahtar kelimeler: *feokromasitoma, paraganglioma, mediastinal kitle, anestezi, torakotomi*

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INTRODUCTION

Pheochromocytoma and paraganglioma are rare variations of neuroendocrine tumors arising from the sympathetic chain focus of the adreneal medulla and non-adrenal medulla [1,2]. Paraganglioma can be seen in a wide variety of locations including abdomen (80-85%), pelvis, neck and head (5%) and chest cavity (5%). The mediastinal location of the paraganglioma is extremely rare (1%) and accounts for less than 0.3% of all mediastinal tumors. Anterior mediastinal insertion is rare. When they are found in rare settlements, they cause errors in diagnosis and treatment [3,4]. If the tumor is in the adrenal gland, it is called pheochromocytoma. If the tumor is outside of the adrenal gland, it is called paraganglioma.

Pheochromocytoma occurs at a rate of 2-8 per million per year [3]. Although the end product of the chromaffin cells outside of the adrenal glands is norepinephrine, the end product in the adrenal gland is epinephrine. The tumor is 80% unilateral and solitary, 10% bilateral and 10% extra adrenal. The primary diagnostic method is to detect hormones and other metabolites in blood and urine. Detection of catecholamine metabolites shows high sensitivity in detecting paragangliomas. In addition to tests, clinical findings, imaging tools (CT, MR, PA chest radiography, scintigraphy) aid in both diagnosis and treatment. Surgical approach yields positive results in 90% of these patients [4]. In the anterior mediastinal location, large vessels close to the heart may cause surgical difficulties leading up to application of cardiopulmonary bypass. There is a 7-18% incidence of airway obstruction under general anesthesia in patients with mediastinal masses [5]. In patients with prolonged and high levels of hypertension, permanent damage may be seen in distant organs, especially in the heart, kidney, eye and central nervous system [6].

In this case report, I aimed to share anesthesia management in a paraganglioma case with hypertensive and tachycardic attacks occurring during thoracic surgery.

CASE REPORT

Written informed consent was obtained from the patient for the study. An operation was planned for a 17-year-old male patient with a pre-diagnosis of paraganglioma. The patient had complaints of sweating, headache, weakness and tremors accompanied by hypertension for 3 years, but diagnosis of pheochromocytoma was not made. Blood pressure values remained stable with the ACE inhibitor and calcium channel blocker used. A mass was observed in the left anterior mediastinal upper region in the chest radiography, thorax CT and scintigraphy of the patient, who was admitted to the emergency department of the hospital one month ago with nasal bleeding (Figures 1, 2, and 3). Scintigraphy showed a "54×35 mm diameter heterogeneous lesion with apical location in the left hemithorax paramediastinal area". Thoracic surgery was scheduled for the patient. Before the operation, the departments of cardiology, internal medicine and psychiatry evaluated the patient. Ejection fraction (EF) was 67% on echocardiography (ECHO), and electrocardiography

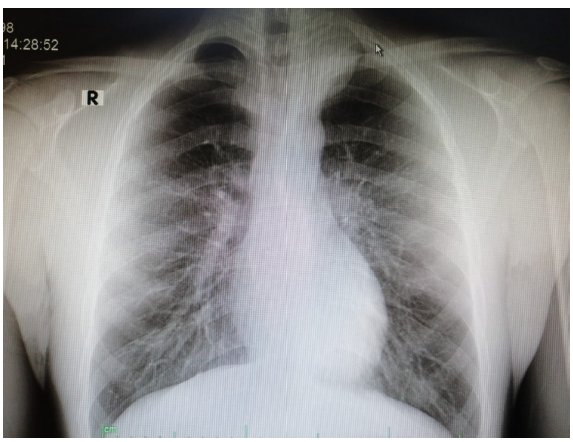

Figure 1. Chest x-ray of the patient. Mass indicated by arrow.

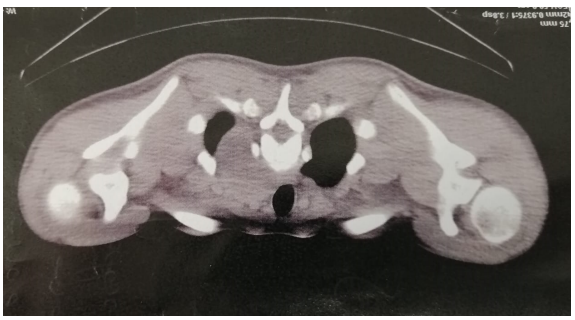

Figure 2. Scintigraphy of the patient. Mass indicated by arrow.

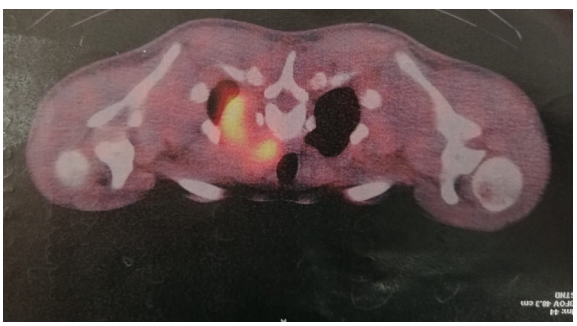

Figure 3. Scintigraphy of the patient. Mass indicated by arrow.

(ECG) demonstrated normal sinus rhythm. Exercise capacity was within normal limits. The internal medicine department did not start any additional treatment for the patient whose blood pressure was stable. The Physical Health Score of the American Society of Anesthesiologists (ASA) was rated as "2"; the Mallampati airway classification score was "1". Results of laboratory tests, routine liver and kidney tests, tumor markers and blood gas analysis were within normal limits. The patient stated that she was using antihypertensive medication (amlodipine 10 mg and enalapril 10 mg) since the age of 14. The patient was 175 cm tall, and weighed 65 kg. Sufficient erythrocyte suspension was prepared. In order to avoid hypotension after induction of anesthesia, preoperatively 500 cc crystalline infusion was administered intravenously (iv) within 2 hours. The patient was carefully transferred to the operating table to prevent any attack that could cause catecholamine release. The first measured blood pressure of the patient was 130/70 mmHg, and heart rate (HR) was 80 bpm. Midazolam 2 mg iv was administered as premedication. Intraoperatively, heart rate, invasive and noninvasive blood pressure (BP), body temperature, peripheral oxygen saturation (SPO_2) and urine output of the patient were monitored. A large lumen vascular access was established on the dorsum of the hand. Right subclavian vein catheterization was performed. Inotropic agents (dopamine hydrochloride, norepinephrine bitartarate) were prepared to manage hypotension that may occur after removing the mass. Initial central venous pressure (CVP) value was +2 mmHg. Preoperative blood pressure was 130/80 mmHg, heart rate 78 bpm and peripheral oxygen saturation was 99%. Glyceryl trinitrate, esmolol hydrochloride infusions were prepared. For the induction of anesthesia, 40 mg lidocaine, 2 µg/kg fentanyl, 2 mg/kg propofol and 0.6 mg/kg rocuronium were administered. The patient was intubated with a 35 Fr right double lumen tube without any problem. Intravenous and inhalation anesthesia were combined for anesthesia maintenance; 1-2 MAC sevoflurane, 50% oxygen, 50% air and 0.25-0.5 µg/kg/min remifentanil infusion were administered. The patient was turned to the left lateral position. With the start of the operation, the patient's blood pressure and pulse rate started to increase (200 bpm, 270/140 mmHg). Then 1.5 mg/kg lidocaine, 200 µg glyceryl trinitrate, 2+3 mg metoprolol were administered via intravenous route and anesthesia was deepened. The patient was hypertensive and tachycardic throughout the operation. Excessive increases in tachycardia and hypertension values were observed especially during the irritation of the tumor capsule. Esmelol hydrochloride infusion for tachycardia (0.5 mg/kg loading, 50-100 µg/kg/min infusion) and glyceryl trinitrate infusion (5-50 µg/kg/min) for hypertension maintained until the end of the operation. As a surgical approach, the patient was firstly treated with VATS (Video Assisted Thoracic Surgery), but the intervention did not provide sufficient visual field and thoracotomy was started. The operation lasted 7 hours. Blood sugars varied between 120-180 mg/dL. Glyceryl trinitrate and esmelol hydrochloride infusion continued in the patient who intraoperatively had hypertension and tachycardia. Mean blood pressure was 170/80 mmHg and pulse rate was 90 bpm. Then 3 ml/kg/hour crystalloid iv was given to the patient, 200 cc bleeding and 500 cc urine output were observed. Last CVP value of +6 mmHg was observed. He did not need a blood transfusion. At the end of the operation, while under profound anesthesia, he was extubated and taken to the recovery unit. He was followed up in intensive care for 24 hours without any problem. Hemodynamic instability was not observed and sedation was not required. Pain treatment was provided with tramadol hydrochloride and paracetomol. Later, the patient was taken to the service and was discharged home after 7 days of follow-up. Pathology result was compatible with paraganglioma.

DISCUSSION

Paraganglioma is a rare neuroendocrine tumor causing episodes of hypertension, tachycardia, sweating, palpitations, headache, and anxiety (Table 1). In general, catastrophic release of catecholamines and

Table 1. Common pheochromocytoma/paraganglioma signs and symptoms.

- Hypertension
- Palpitation
- Headache
- Excessive sweating
- Anxiety / irritability
- Tachycardia /reflex bradycardia
- Hyperglycemia
- Weakness and fatique
- Weight loss
- Epistaxis
- Nausea
- Postural hypotension

cardiovascular instability are seen in cases during induction of anesthesia, surgical manipulations, pain and position changes [7]. Sudden increases in catecholamine release are called "attacks". This situation increases especially during tumor resection. The amount of catecholamine that passes into the blood in stimulation of any tumor tissue can reach 1000 times the normal serum level or more [6]. Catecholamine release occurs in 80-85% of patients with paraganglioma and causes severe clinical symptoms [2]. In contrast, only 40% of patients experience paroxysmal hypertension. Paragangliomas are the cause of hypertension seen in 0.2-0.6% of the patients [8]. However, these cases are usually silent and do not cause clinical symptoms.

Detection of plasma and urinary catecholamines and their end products and imaging methods (CT, MRI, scintigraphy) are used in the diagnosis of paraganglioma [7,9,10]. In our case, well-circumscribed nodular lesions were observed in the anterior mediastinum on PA chest radiography, thorax CT and scintigraphy. Radioactive iodine labeled methiodobenzylguanidene scintigraphy is a very reliable approach in the diagnosis of paraganglioma [1,6]. In the biochemical study conducted 1 month ago, high urinary metanephrine and normetanephrine levels were observed.

Gold standard in preoperative preparation for paraganglioma; is to control the patient's blood pressure, heart rate and fluid replacement [7,7,11,12]. The main

Table 2. Roizen criteria.

1. No in-hospital blood pressure > 160/90 mmHg for 24h prior to surgery
2. No orthostatic hypotension with blood pressure <80/45 mmHg
3. No ST or T wave changes for 1-week prior to surgery
4. No more than 5 premature ventricular contractions per minute

route to follow in symptomatotic patients is preparation and optimization for hypertension and vascular enlargement. In the perioperative period, complications such as severe hypertensive attacks and dysrhythmia may occur. Blood pressure in our patient reached 270/140 mmHg. To prevent these complications, antihypertensive agents such as α and β blockers, calcium channel blockers, and magnesium sulfate can be used in combination or singly [6]. When we evaluated our patient for preoperative α-adrenergic block according to Roizen criteria 7, we encountered normal results (Table 2). In the light of items 3 and 4 of these criteria, there were no ST-T changes and premature ventricular beats in the ECG; for the other two items, blood pressure values were met under the following conditions (TA: 130/80 mmHg, HR: 68 bpm). Roizen Criteria should be met to reduce perioperative mortality and morbidity. Our patient had been using enalapril and amlodipine for blood pressure control for 3 years. The internal medicine department did not recommend preoperative α-adrenergic blockade or additional medical treatment.

Preoperative evaluation of paraganglioma patients should be done carefully. Our patient was evaluated 7 days previously in the anesthesia clinic. Evaluation of these patients 1-2 weeks before is important in terms of both blood pressure control and determination of accompanying diseases. In these cases, multiple endocrine neoplasms, neurofibramatosis type 1, von Hippel-Lindau syndrome, Sturge-Weber syndrome can be seen. In our case, no other clinical finding was found except hypertension. The com-

monly used treatments in combination for paraganglioma are α-adrenergic receptor blockers,-adrenergic receptor antagonists, angiotensin receptor blockers (ACE inhibitors) and calcium channel blockers [1,3,7]. ACE inhibitor (enalapril) and calcium channel blocker (amlodipine) were used in our case. Phenoxybenzamine is frequently used for blood pressure control in the perioperative period. It irreversibly blocks α1 and α2 receptors [9]. Side effects such as orthostatic hypertension, reflex tachycardia, nasal congestion and syncope often occur during preoperative use. It has been discontinued in some countries due to its pronounced side effects [13,14]. Selective α1 antagonists (prozacin, terazosin, and doxazosin) are short-acting alternative drugs to phenoxybenzamine [7,9]. The most important side effect of prozacin, which is the most preferred drug in this group, is orthostatic hypotension. There are studies showing that phenoxybenzamine is effective in perioperative blood pressure control in some studies, and some studies did not find evidence to support this result [15,16]. Some studies argue that α-adrenoreceptor blockade may not be necessary. Calcium channel blockers prevent hypertension and tachycardia, hypotension or orthostatic hypotension in the normative period. Some medical institutions prefer calcium channel blockers as the primary drug for preoperative treatment in normotensive pheochromocytoma patients [17]. The use of calcium channel blockers continues to be a good choice in low-risk patients. In patients who receive only α-adrenergic receptor blockers, a β adrenergic blocker can be added to the treatment in the presence of tachycardia. Concomitant use of α and β blockers (labetolol) may cause hypertensive crisis as a result of paradoxical hypertension [18].

Anesthesia management can create very troublesome situations in patients with pheochromocytoma. The main expected complication is hemodynamic instability. Applied anesthetic drugs, tumor size and location, plasma catecholamine level, type of surgical technique and genetic syndrome affect intraoperative stabilization [19,20]. It is important to be prepared for the sympathetic crisis that may occur due to induction, intubation and surgery before anesthesia. Complications related to high blood pressure values are cerebrovascular hemorrhage, heart failure, arrhythmias, hemorrhage and myocardial infarction [21]. Because of the high frequency of hyperglycemia in these cases, blood glucose was monitored at frequent intervals. Bleeding can be seen in paraganglioma surgeries. In our case, despite switching to VATS and then open thoracotomy, 200 cc bleeding was observed, and 100 cc came out from the thorax drain in the intensive care follow-up. Erythrocyte suspension was prepared in the preoperative period against the possibility of intraoperative bleeding. Appropriate fluid therapy is important in these patients because in some cases severe hypotension may occur after tumor tissue is removed. The initial CVP value of our patient was +2 mmHg and the initial value was +6 mmHg. If too much fluid is given, symptoms of pulmonary edema and heart failure can be seen. During the recovery unit and intensive care follow-up, invasive arterial monitoring was continued, hypotension and bradycardia were not observed. CVP and invasive arterial monitoring were continued during the ICU follow-up. Necessary preparations were made against development of hypertension and hypotension.

The gold standard in paraganglioma surgeries is close blood pressure monitoring, in other words invasive arterial monitoring. Urinary catheterization is a routine follow-up procedure in these patients. In a study conducted in two health institutions, the CVP monitorization had been applied in 30% and 60% of the cases. Measuring cardiac output (CO) with a pulmonary artery catheter (PAC) may be an alternative method because CVP follow-up may give false results in conditions that reduce left ventricular compliance, such as patient's position and extreme hypertensive conditions [7]. In a study comparing two major health institutions, PAC application in pheochromocytoma surgery had been performed in 8% and 24% of the cases. Measurement of pulmonary capillary wedge pressure may be required to assess cardiac filling pressure and cardiac function in the presence of cardiomyopathy [22]. Transesophageal echocardiog-

raphy (TEE) can aid real-time diagnosis of intravascular volume status, myocardial wall abnormality, and myocardial ischemia. In addition to its benefits, it may not be beneficial due to the need for sedation for patient comfort in the postoperative period, the risk of aspiration, and the need for continuous expert evaluation [7].

In paraganglioma, regional or general anesthesia is successfully used as a method of anesthesia [3,23,24]. In general anesthesia, sevoflurane can be safely used in inhalation anesthesia, propofol as an intravenous agent, remifentanil as a muscle relaxant in addition to dormicum, vecuronium, rocuronium and cisatrocurium. Drugs that increase histamine release (morphine hydrochloride), induce catecholamine release (ketamine, ephedrine and pethidine) and exert vagolytic effect (pancuronium) should be avoided [3,7].

In a study of 258 patients in pheochromocytoma and paraganglioma surgery, acute renal failure, respiratory failure, fluid overload, and thromboembolic events were listed as potential complications [25]. Hypotension in the postoperative period in 20-70% of patients due to the use of a preoperative alpha-receptor antagonist and intraoperative antihypertensive agent. There were no postoperative complications in our case, and blood pressure and heart rate remained within normal limits.

CONCLUSION

In this article, we discussed the anesthetic management of a rare case of paraganglioma in the anterior mediastinal wall. According to our experience, as important points in the preparation of these cases for the operation; coordination of units such as anesthesia, cardiology, endocrinology also starts days in advance and the patient is followed up completely. In our case, the internal medicine and cardiology departments did not add alpha-adrenergic blocker and beta blocker drugs to the treatment because the hemodynamic data of the patient remained stable with the treatment, but intraoperatively severe hypertensive attack was encountered. It is clear that these cases should be evaluated more carefully and their treatment should be planned. Following adequate preparation, careful intraoperative monitoring and medical approach will improve further anesthesia management.

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