Challenges in the surgical treatment of undiagnosed functional paragangliomas
A case report

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Abstract

Introduction: Paragangliomas (PGs) or extra-adrenal pheochromocytomas are rare neuroendocrine neoplasms of ubiquitous distribution. Those that produce excess catecholamine are categorized as functional, and those that do not are categorized as nonfunctional. Although modern medical technology is becoming more widespread, there are still substantial risks of misdiagnosis or missed diagnosis of PGs.

Case presentation: A 38-year-old woman who lived in an autonomous region of inner Mongolia presented complaining of having experienced coughing for approximately the past month. Chest computed tomography (CT) and magnetic resonance imaging (MRI) revealed a lesion on the right side of thoracic vertebra 5–8 of approximately 66 mm × 54 mm, and it was deemed to be a mediastinal tumor that required surgical treatment. The patient exhibited severe hemodynamic instability during the operation, resulting in substantial challenges and risks with regard to anesthesia management.

Conclusion: When a patient is suspected having PG, whether the surgery should be continued or not depends on their overall condition and whether hemodynamic fluctuation can be controlled to within the normal range. Both are factors that should be considered during intraoperative management. Communication between the surgeon and anesthesiologist is necessary, in order to accurately assess the risks associated with the operation. The combination of central venous pressure and the Flotrac/Vigileo system may provide precise guidance for complementary liquid therapy and reduce cardiopulmonary complications. After the operation, hemodynamic changes should be monitored continuously in the intensive care unit, and vasoactive drugs are required to avoid postoperative hypotension. Dramatic hemodynamic changes are certainly a challenge for patients and anesthesiologists, regardless of their origin, and sufficient attention should be paid to avoid serious consequences.

Abbreviations: BP = blood pressure, bpm = beats per minute, CT = computed tomography, ECG = electrocardiography, HR = heart rate, IBP = invasive blood pressure, ICU = intensive care unit, MIBG = metaiodobenzylguanidine, MRI = magnetic resonance imaging, PG = paraganglioma.

Keywords: flotrac/vigileo, general anesthesia, invasive hemodynamic monitoring, paragangliomas, posterior mediastinum

1. Introduction

Paragangliomas (PGs) or extra-adrenal pheochromocytomas are rare neuroendocrine neoplasms of ubiquitous distribution. They arise from the aorticosympathetic paraganglia,[1] which are rare neuroendocrine neoplasms of ubiquitous distribution. They

mediastinal tumors,[4,5] Those that produce excess catecholamine are categorized as functional, and those that do not are categorized as nonfunctional. Although modern medical technology is becoming more widespread, there are still substantial risks of misdiagnosis or missed diagnosis of PGs. In the case reported herein, a diagnosis of PG was missed before an operation in a patient harboring a tumor with sympathetic neuroendocrine activity. The patient exhibited severe hemodynamic instability during the operation, resulting in substantial challenges and risks with regard to anesthesia management.

2. Case presentation

The ethics committee of the Aerospace Center Hospital in the city of Beijing has reviewed this case report and approved its publication. A 38-year-old woman who lived in an autonomous region of inner Mongolia presented complaining of having experienced coughing for approximately the past month and was admitted to the hospital’s Department of Thoracic Surgery. Physical examination did not reveal any abnormalities. She had an 8-year history of hypertension accompanied by intermittent dizziness, headache, and sweating, but no heart palpitations or other symptoms. She had been diagnosed with cerebral hemorrhage 2 months prior, without sequelae. Her blood pressure (BP) was controlled to within the normal range by nifedipine and angiotensin-converting enzyme inhibitor.
The patient weighed 56 kg and was 161 cm tall. Cardiopulmonary examination results were normal. BP was stable at approximately 130/70 mm Hg for 3 consecutive days during hospitalization, and there were no observations of hypertension or hypotension. Her American Society of Anesthesiologists physical status was 2, and her Mallampati airway classification was 2. Chest computed tomography (CT) and magnetic resonance imaging (MRI) revealed a lesion on the right side of thoracic vertebra 5–8 of approximately 66 mm × 54 mm, and it was deemed to be a mediastinal tumor that required surgical treatment (Fig. 1). In routine laboratory blood tests, biochemical and coagulation functions were normal, but the gastrin-releasing peptide concentration was 85 pg/mL (normal range 0–50 pg/mL).

Electrocardiography (ECG) revealed sinus rhythm and nonspecific ST and T wave changes. Head CT revealed left lateral capsulation, and right frontal lobe softening. Cardiac ultrasound revealed reduced left ventricular diastolic function, and a left heart ejection fraction of 68%.

ECG monitoring and oxygen inhalation were initiated upon admission to the operating room, and the patient was prepared for general anesthesia. Invasive BP (IBP) monitoring was performed in the left radial artery before the induction of anesthesia. IBP was 160/100 mm Hg, and heart rate (HR) was 80 beats per minute (bpm). Despite the successive administration of etomidate, sufentanil, and cisatracurium besylate, hemodynamic instability occurred. When the first hypertensive peak occurred, the highest IBP recorded was 260/150 mm Hg, and HR increased to 107 bpm. Phenolamine and esmolol were administered to control BP and HR. It became evident that the tumor was located in the posterior mediastinum and was accompanied by sympathetic ganglion and vein. After consulting the anesthesiologist, the surgeon decided to cut off the sympathetic nerves first, then gradually remove the tumor. Hemodynamic stability was maintained with alpha blockers and beta blockers during the excision, and the plasma was administered, which was particularly important to ensure adequate blood volume before the tumor was removed.

Intraoperative pathological biopsy confirmed that the mediastinal tumor was PG. Before tumor resection, 3.5 L of crystal and colloid at a ratio of 2:1 was utilized, and the amount of bleeding was approximately 200 mL. Immediately after the tumor was removed, BP dropped to 67/39 mm Hg due to hemorrhage of tumor-associated veins and decreased catecholamines, and HR was 85 bpm. Dopamine, norepinephrine, and epinephrine were administered to maintain hemodynamic stability. Pumped dopamine was administered continuously at 3 to 6 μg/kg/min, while pumped norepinephrine was administered at 0.05 and 0.08 μg/kg/min to maintain systolic BP fluctuation between 90 and 120 mm Hg. After complete excision of the tumor, approximately 2 L of blood had been lost. A total of 5 L of crystals and colloidal fluids (2:1 ratio) and 2 units of concentrated red blood cells were administered to maintain effective circulating blood volume. The intubated patient was transferred to the intensive care unit (ICU) after the operation, and she was extubated the next day in the ICU. Two days after the surgery, the patient was transferred to the general ward with stable hemodynamics, and she was discharged on the sixth day after the operation.

3. Discussion
PGs are uncommon neuroendocrine tumors originating from chromaffin cells located in extra-adrenal sympathetic ganglia, which are groups of cells associated with the autonomic nervous system.
Most PGs arise from the adrenal medulla as pheochromocytomas, which are also known as intra-adrenal PGs, while the remainder are derived from aortic-sympathetic extra-adrenal paraganglia along the paravertebral axis as extra-adrenal sympathetic PGs. PGs account for 15% to 20% of pheochromocytomas, and are associated with a high incidence of malignancy (13–26%). Patients with sympathetic endocrine tumors often exhibit hypertension, headache, palpitation, sweating, tremor, pallor, or flushing. Complications associated with extremely high BP include cerebrovascular hemorrhage, heart failure, arrhythmias, and myocardial infarction. Notably, 50% to 80% of patients with PGs are asymptomatic and the diagnosis is usually incidental or related to wider effects caused by the tumor. Although the current patient had symptoms of hypertension and cerebral hemorrhage, the possible involvement of a mediastinal tumor had not been considered during preoperative diagnosis or treatment. In patients with combined hypertension, dynamic blood pressure should be monitored for 24 hours before surgery, to determine potential tumor involvement. Cardiac ultrasound and fundus examination can help determine whether there are other relevant organ complications.

Because PGs with neuroendocrine activity may exhibit characteristics that are similar to those of pheochromocytoma, the anesthetic management of any patient with a tumor affecting sympathetic neuroendocrine function who is undergoing surgery is challenging, particularly if the tumor has not been diagnosed. A proportion of patients are diagnosed incidentally at the time of surgery, when the induction of anesthesia may precipitate a hypertensive crisis. In such situations, the rate of mortality is reportedly approximately 80%.

A pertinent question is, when an emergent case of malignant hypertension that was strongly suspected to involve a sympathetic neuroendocrine tumor was first encountered intraoperatively, given the absence of sufficient preoperative preparation should we have proceeded with the surgery or delayed it?

In the present case, preoperative BP monitoring did not reveal any signs of malignant hypertension. However, BP was dramatically increased during anesthesia induction and at the beginning of the operation, which was suspected to be associated with a sympathetic neurogenic tumor. HR did not change significantly, but hemodynamic changes occurred dramatically. This may be because the neurotransmitter released by the tumor was primarily an alpha receptor agonist, which was confirmed during tumor excision. BP can be controlled to within normal range via the administration of phentolamine and esmolol. After consulting the anesthesiologist, the surgeon decided to change the procedure used for tumor excision, in an effort to reduce the risk of uncontrollable hemodynamic changes. In such cases, an appropriate amount of fluid should be administered before tumor resection, to prevent severe hypotension thereafter. Liquid therapy was performed under the guidance of central venous pressure and the Flotrac/Vigileo system, which proved to be safe and effective. As well as facilitating the restoration of adequate circulating capacity, it negated cardiopulmonary complications associated with excessive circulating volume.

Whether the operation should be delayed in the above-described circumstances should be decided based on the patient’s overall condition, because that will determine their ability to withstand the operation. Whether hemodynamic fluctuation can be controlled to within the normal range is an important factor that should be considered in the anesthetic management. In addition, the surgeon has an important and decisive role in the planning of the surgical procedure. During the operation, it is necessary to use multiple monitoring devices to monitor changes in hemodynamics and manage the patient’s condition in real time. However, if the risk of surgery is considered too high after a comprehensive assessment, the operation should be suspended until adequate preoperative preparation has been performed.

Complete resection of PGs is demanding due to their highly vascular nature and anatomical position, especially when they are close to major vessels or coronary arteries. Surgical resection is often complicated by excessive hemorrhage and reconstruction of the surrounding structures. It is important to replenish red blood cells and plasma when excessive hemorrhage occurs during surgery. Due to the decrease in catecholamine secretion in plasma and the relative shortage of circulating blood volume, continuous monitoring of hemodynamic changes is needed in the ICU, and vasoactive drugs are usually required to avoid postoperative hypotension.

It has been recommended that patients with pheochromocytoma be treated with liquid replacement before surgery, but the requirement for preoperative intravenous fluid has been questioned. Lentschener et al. observed no difference in mortality when intravenous fluids were given on an “as needed” basis only, as determined via arterial blood pressure, indicating that prophylactic administration of intravenous fluids may not improve outcomes in pheochromocytoma and PG surgery when appropriate anesthetic expertise is available. However, retrospective data suggest that fluid and salt replacement may limit postural hypotension and postoperative hypotension by optimizing intravascular status.

On the basis of the present case, despite its low incidence, a diagnostic work-up to rule out suspicious neuroendocrine tumor is necessary for lesions located in areas of sympathetic ganglion distribution—especially in the adrenal, mediastinum, neck, and retroperitoneal regions—before the patient is sent to surgery. Testing of serum biochemical markers (metanephrines, normetanephrines, and chromogranin A) is the preferred initial workup for lesions suspected of being pheochromocytomas or PGs. With regard to imaging techniques, MRI is associated with the lowest false-negative localization rate, and radioactive iodine-labeled metaiodobenzylguanidine (MIBG) scintigraphy is the least sensitive imaging modality. Although lacking in sensitivity, MIBG scintigraphy is highly specific and may yield the only positive imaging test result in some patients.

4. Conclusion

Undiagnosed functional PG has high morbidity and mortality rates, and is challenging with regard to anesthetic management. Therefore, it is important to determine all aspects of a patient’s medical history, and test serum biochemical markers if functional tumor is suspected before surgery. Imaging examinations such as CT or MRI are also valuable for identifying and diagnosing suspicious endocrine neoplasms. When a patient is suspected having PG, whether the surgery should be continued or not depends on their overall condition and whether hemodynamic fluctuation can be controlled to within the normal range. Both are factors that should be considered during intraoperative management. Communication between the surgeon and anesthesiologist is necessary, in order to accurately assess the risks associated with the operation. During the operation, the combination of central venous pressure and the Flotrac/Vigileo system may provide precise guidance for complementary liquid therapy and reduce cardiopulmonary complications. After the operation,
hemodynamic changes should be monitored continuously in the ICU, and vasoactive drugs are required to avoid postoperative hypotension. Dramatic hemodynamic changes are certainly a challenge for patients and anesthesiologists, regardless of their origin, and sufficient attention should be paid to avoid serious consequences.

Author contributions
L-Y Lu drafted the manuscript. L-Y Lu, Z-M Yang, and G-Y Zhang participated in the diagnosis and administration of the patient. All authors were involved in the discussion of the case and the revision of the manuscript. Z-M Yang confirmed the final manuscript.

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