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CASE REPORT

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Massive pheochromocytoma causing adrenal crisis during surgery: a case report and review of the literature

Jiyu Zeng[1*], Ting Yang[2], Yong Wang[3] and Li Wu[1]

Abstract

Background Pheochromocytoma is a rare adrenal medulla tumor that overproduces catecholamines, causing major cardiovascular issues. It is often found incidentally during imaging, but large tumors pose unique perioperative challenges. Patients are usually symptom-free until the tumor grows, risking an adrenergic crisis during surgery. This case underscores the complexities of managing large pheochromocytomas, highlighting the risks of unstable hemodynamics and the need for thorough preoperative planning and a multidisciplinary approach for successful surgery.

Case report We present a case of a 55-year-old Chinese man admitted for surgery after a routine exam revealed a 7.8 cm mass in his left adrenal gland. Initially asymptomatic, he was diagnosed with pheochromocytoma via blood tests and computed tomography scans. Pre-surgery, he received an α-receptor blocker. During the tumor removal, which was large and adhered to nearby vessels and tissues, he suffered an adrenergic crisis with unstable hemodynamics.We implemented emergency measures to stabilize the patient's vital signs in a rare case of large pheochromocytoma with adrenal crisis. With multidisciplinary team management, the patient recovered well post-surgery.

Conclusion This article discusses the disease's unique clinical features, reviews literature on the link between massive pheochromocytoma and adrenal crisis, and outlines perioperative management strategies as a reference.

Keywords Pheochromocytoma, Adrenal insufficiency, Perioperative management, Anesthesia, Case report

Background

Pheochromocytoma is an infrequent neuroendocrine neoplasm arising from the adrenal medulla, distinguished by the overproduction of catecholamines, such as epinephrine and norepinephrine. It has an incidence rate of approximately 2–8 per million individuals [1]. The clinical presentation of pheochromocytoma is intricate and varied, predominantly manifesting as hypertension, headache, and tachycardia, among other symptoms [2]. Notably, the majority of massive pheochromocytomas, defined as tumors exceeding 7 cm in diameter, are asymptomatic [3].

Adrenal crisis represents a critical, life-threatening condition and is a major contributor to mortality among individuals with adrenal insufficiency [4]. Pheochromocytoma serves as a significant precipitating factor for adrenal crisis, as it may induce acute cardiovascular decompensation, manifesting as severe hypertension, hypotension, and heart failure [5].

In our situation, an adrenal crisis happened during the operation, causing severe hemodynamic instability that required immediate resuscitation to stabilize blood pressure. Furthermore, we reviewed literature on the link

*Correspondence:
Jiyu Zeng
13629017775@163.com
[1] Department of Anesthesiology, West China Hospital of Sichuan University Ziyang Hospital, Zi Yang, Si Chuan, China
[2] Department of Medical Education, West China Hospital of Sichuan University Ziyang Hospital, Zi Yang, Si Chuan, China
[3] Department of Urology, West China Hospital of Sichuan University Ziyang Hospital, Zi Yang, Si Chuan, China

between large pheochromocytoma and adrenal crisis, along with perioperative management strategies.

Case presentation

A 55-year-old Chinese male patient presented to the outpatient clinic following the incidental discovery of a left retroperitoneal mass during a routine examination conducted 2 months earlier. The patient reported experiencing occasional discomfort in the lumbar region. His blood pressure was recorded at 145/98 mmHg, and the electrocardiogram demonstrated sinus tachycardia with a heart rate of 111 beats per minute. Abdominal ultrasonography identified a solid mass located superior to the left kidney, with dimensions of approximately 7.8 cm × 5.9 cm × 6.4 cm. Enhanced abdominal computed tomography (CT) revealed a mass of heterogeneous density in the left retroperitoneum, raising suspicion for a neoplastic lesion, potentially a left adrenal pheochromocytoma or a neurogenic tumor. Plasma catecholamine levels were elevated, with norepinephrine (NE) at 9.85 nmol/L (reference value < 3.55 nmol/L) and epinephrine (E) at 1.57 nmol/L (reference value < 0.68 nmol/L). The 24-hour urinary vanillylmandelic acid (VMA) level was 27.66 mg (reference range 0–12 mg/24 hours). Cardiac ultrasound, thyroid function tests, and blood glucose levels were all within normal limits.Considering the preoperative laboratory and examination findings, a diagnosis of left adrenal pheochromocytoma was considered.The patient was administered oral prazosin at a dosage of 2 mg three times daily for a period of 14 days preceding the surgical intervention. In the 3 days leading up to the operation, the patient received daily infusions of 1000 mL of crystalloid and 500 mL of colloid for the purpose of volume expansion, with blood pressure maintained within the range of 132–145/75–98 mmHg and heart rate stabilized around 90 beats per minute. On the day preceding the surgery, a comprehensive evaluation was conducted by a multidisciplinary team comprising specialists in intensive care, endocrinology, anesthesiology, cardiology, and radiology to assess potential risks. The assessment concluded that the left adrenal tumor was likely exerting pressure on both the splenic and renal veins and had close anatomical proximity to the left kidney, spleen, and pancreas (Fig. 1). Consequently, the surgical plan was formulated for an open resection of the left adrenal tumor.

Upon entering the operating room, the patient presented with a heart rate of 85 beats per minute, blood pressure of 120/70 mmHg, a respiratory rate of 18 breaths per minute, and oxygen saturation (SpO_2) of 99%. Anesthesia induction was achieved using 10 mg of pancuronium, 20 μg of sufentanil, 0.5 mg of etomidate, and 20 mg of lipid emulsion of propofol, followed by the oral insertion of a 6.5 F tracheal tube. Anesthesia maintenance involved the intravenous infusion of remifentanil at 0.1 μg/kg/minute and dexmedetomidine at 0.2 μg/kg/minute, in conjunction with the inhalation of sevoflurane at 1.5%, with dosages adjusted according to intraoperative vital signs. Following anesthesia induction, the left radial artery and right internal jugular vein were punctured and cannulated. During the surgical exposure of the left adrenal tumor, it was observed to be closely adhered to the spleen and splenic artery, complicating the separation process. After consultation with a hepatobiliary surgeon, a splenectomy was performed. Subsequent dissection of the adrenal tumor revealed significant adhesion to the renal artery and vein, resulting in bleeding from the renal vessels, which necessitated repair of the renal artery and vein.

During the surgical procedures involving the dissection of the adrenal tumor and the splenectomy, the patient experienced a marked elevation in both blood pressure and heart rate. To manage the hypertensive crisis, intravenous infusions and intermittent boluses of phentolamine and sodium nitroprusside were administered, with blood pressure reaching a peak of 250/110 mmHg. Subsequent to the resection of the adrenal tumor, the patient exhibited a precipitous decline in blood pressure. Efforts to stabilize the hypotension through intravenous administration and intermittent doses of norepinephrine proved ineffective, resulting in a critically low blood pressure of 50/30 mmHg. In response, aggressive fluid resuscitation was promptly initiated, accompanied by the intravenous administration of 80 mg of methylprednisolone. Concurrently, epinephrine was infused and intermittently bolused at a dose of 0.5 mg per administration, which gradually led to the stabilization of blood pressure at approximately 90/50 mmHg. Approximately 30 minutes prior to the conclusion of the surgical procedure, the administration of epinephrine was gradually tapered, leaving norepinephrine as the sole agent infused upon exiting the operating room. This approach effectively stabilized the patient's blood pressure within the range of 100–130/50–70 mmHg. The surgery had a total duration of 3 hours and 25 minutes, during which the estimated blood loss was approximately 800 mL. The patient exhibited a urine output of 350 mL and received a transfusion of 4 units of packed red blood cells, in addition to 1000 mL of colloid and 1450 mL of crystalloid solutions. On the first postoperative day, the intensive care unit (ICU) team successfully extubated the patient. However, continuous infusions of norepinephrine and vasopressin were maintained to support circulatory function until the third postoperative day, when these infusions were discontinued. Hydrocortisone was administered at a dosage of 50 mg daily as replacement therapy. The patient was

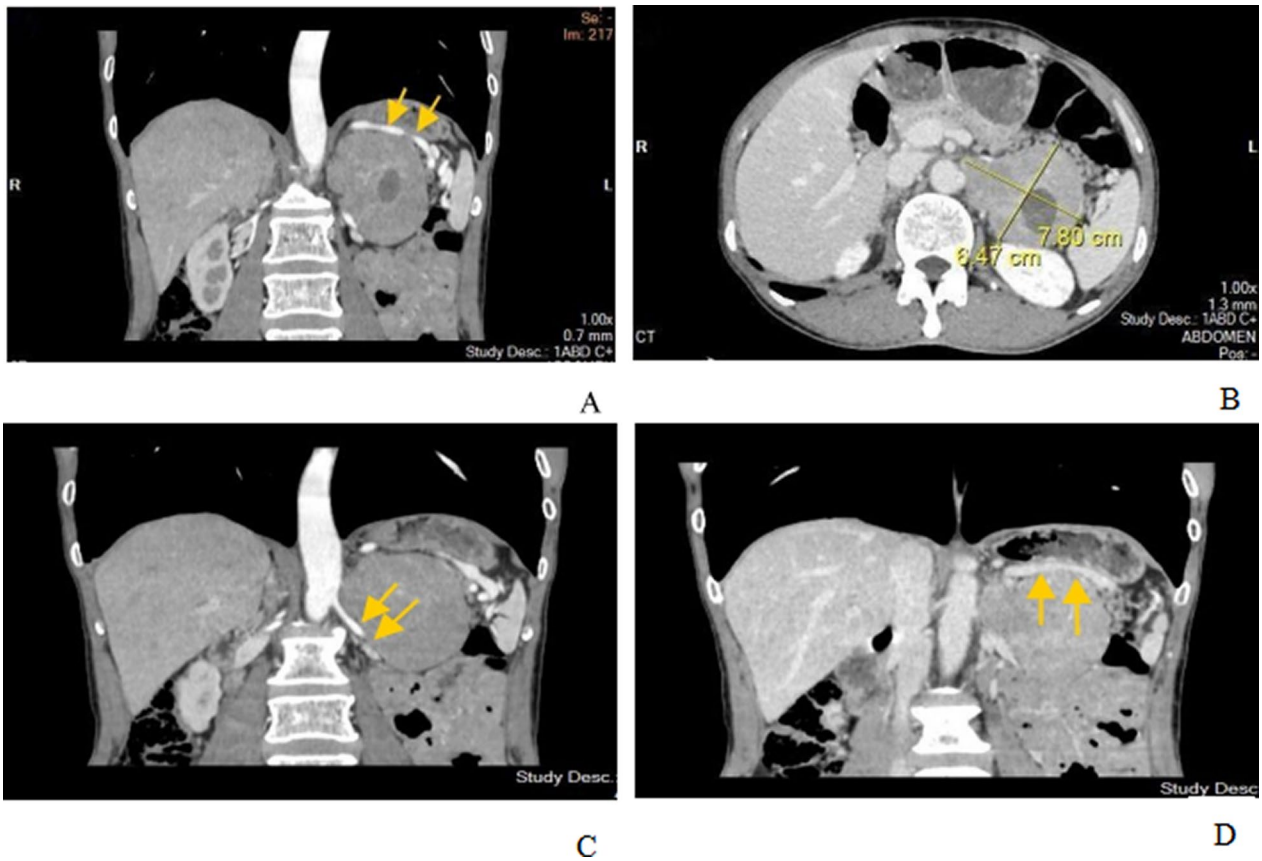

Fig. 1 Size of the adrenal tumor and its relationship with surrounding blood vessels. **A** The left adrenal tumor compressing the splenic artery (yellow arrows). **B** The size of the left adrenal tumor closely related to the left kidney, spleen, and pancreas (marked in yellow). **C** The left adrenal tumor closely related to the renal artery (yellow arrows). **D** The left adrenal tumor closely related to the renal vein (yellow arrows)

subsequently transferred back to the urology ward on the fourth postoperative day.On the fifth postoperative day, an attempt was made to discontinue hormone therapy; however, the patient developed symptoms of drowsiness, poor appetite, and altered mental status. Consequently, hydrocortisone therapy was maintained. The patient was discharged on the 15th postoperative day with a prescription for oral hydrocortisone at a dosage of 10 mg twice daily. A total of 7 days postdischarge, the hydrocortisone dosage was reduced to 5 mg twice daily and was ultimately discontinued on the 14th day following discharge. The serum adrenocorticotropic hormone (ACTH) levels measured on the second and sixth postoperative days were 6.83 pg/mL and 18.27 pg/mL, respectively, with the normal range being 7.0–65 pg/mL. Pathological examination confirmed a diagnosis of pheochromocytoma of the left adrenal gland. Immunohistochemical analysis revealed positive staining for chromogranin A (CgA), synaptophysin (Syn), CD56, GATA-3, S-100, and inhibin (Fig. 2).

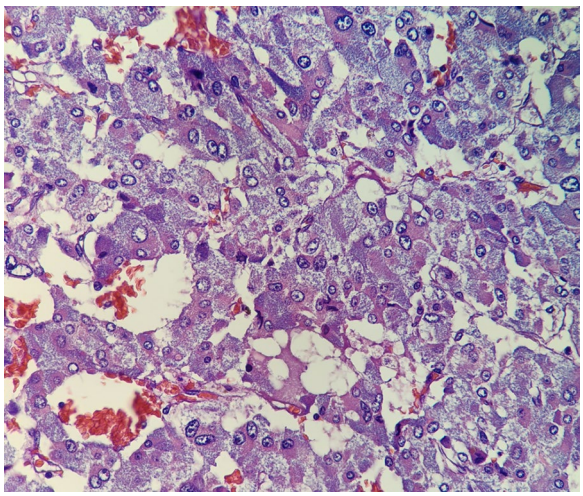

Fig. 2 Histopathological slide of the left adrenal tumor tissue

On the fourth day after surgery, tests showed norepinephrine at 0.92 nmol/L, epinephrine at 0.38 nmol/L, and dopamine at 0.10 nmol/L, all within normal ranges. CT scans at 2 and 5 months post-op revealed disorganized structures, blurred fat spaces, and slight effusion in the left adrenal gland (Fig. 3). The patient is recovering well, with no signs of pheochromocytoma recurrence or residue.

Discussion

Pheochromocytoma is predominantly characterized by episodic hypertension, diaphoresis, and cephalalgia, all of which are associated with catecholamine secretion [6]. The hypertension observed in these patients is notable for its considerable variability in blood pressure, with approximately 30–50% of individuals with pheochromocytoma experiencing elevated nocturnal blood pressure compared with diurnal levels. Furthermore, 20–30% of these patients may exhibit normotensive readings [7–9]. Adrenal crises are commonly precipitated by factors such as anesthesia, tumor manipulation, physical exertion, and various pharmacological agents, including opioids, metoclopramide, and glucagon [6]. The stability of hemodynamics during surgical procedures is intricately linked to tumor size. Massive pheochromocytomas frequently exhibit significant endocrine activity, which can precipitate severe hypertension during tumor resection. Additionally, larger tumors are often associated with reduced blood volume and abrupt decreases in catecholamine levels, potentially leading to pronounced hypotensive episodes following adrenal tumor removal [10]. The incidence of adrenal crises is modulated by various factors, including tumor size and location, the patient's underlying health status, and the presence of additional precipitating factors. The tumor size serves as a significant predictor of intraoperative hypertensive episodes, particularly in surgical procedures involving retroperitoneal pheochromocytomas. Patients with tumors exceeding 4.25 cm are at an elevated risk of experiencing intraoperative hypertension [11]. There exists a notable correlation between adrenal tumor size and intraoperative hemodynamic instability, especially in scenarios necessitating the use of vasoactive medications, which may subsequently increase the risk of postoperative complications [12].

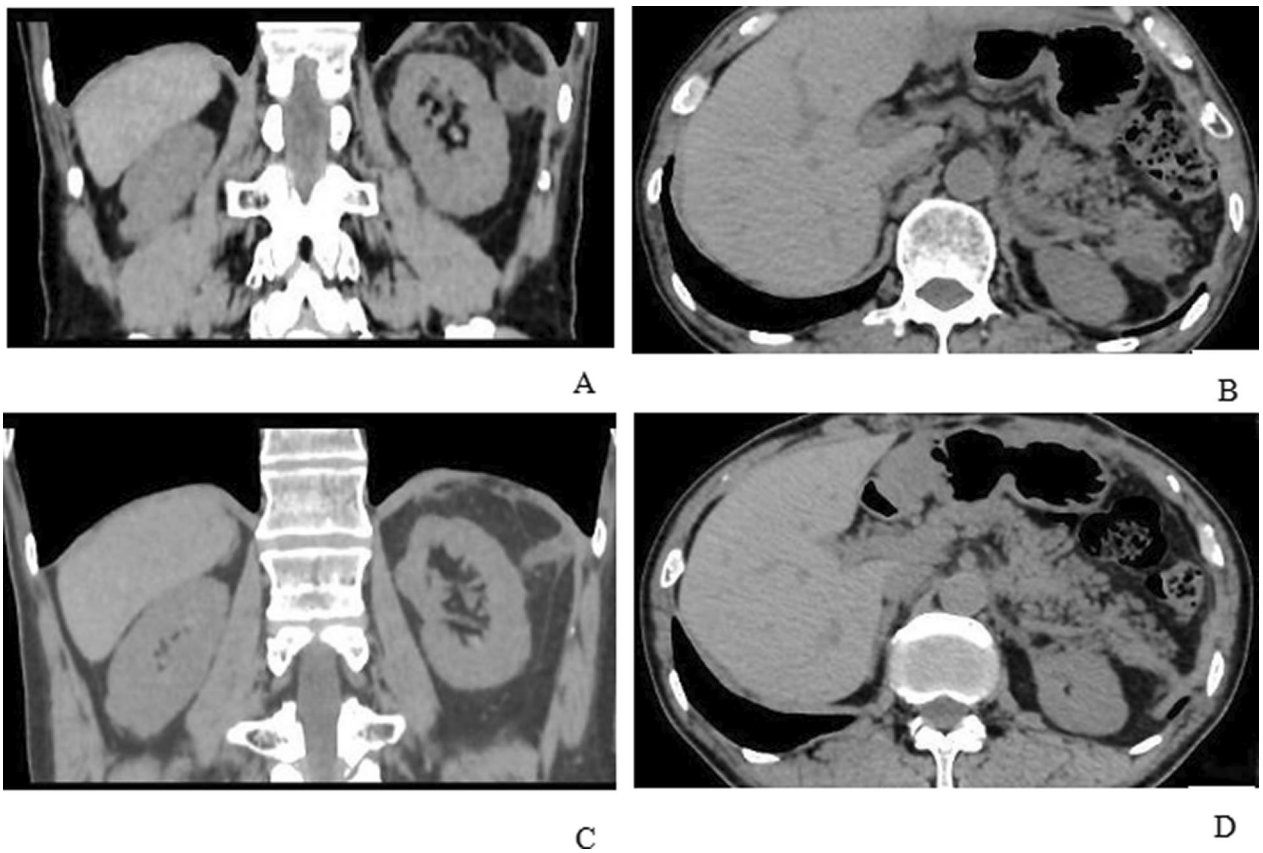

Fig. 3 CT scans 2 months and 5 months post-surgery. **A** Coronal view 2 months post-surgery **B** Axial view 2 months post-surgery **C** Coronal view 5 months post-surgery **D** Axial view 5 months post-surgery

One study investigated the relationship between catecholamine levels and tumor size in pheochromocytoma patients, revealing that larger tumors are often associated with elevated catecholamine levels, thereby potentially heightening the risk of adrenal crises [13]. Furthermore, another study underscored that spontaneous rupture of pheochromocytomas can precipitate acute catecholamine crises, characterized by severe blood pressure fluctuations and cardiovascular complications. Although this condition is relatively uncommon, its occurrence may be linked to the tumor's size and location [14]. For patients undergoing surgical resection, intraoperative hemodynamic instability constitutes a major risk, necessitating comprehensive preoperative preparation and vigilant monitoring throughout the procedure [15]. Consequently, the size of the tumor is a critical factor in the management of pheochromocytomas. It may necessitate the implementation of specialized management strategies, both preoperatively and intraoperatively, including multidisciplinary collaborative approaches, to minimize mortality and enhance the long-term prognosis of patients.

The diagnosis of pheochromocytoma is primarily based on the quantification of plasma or 24-hour urinary free norepinephrine and epinephrine, with diagnostic significance typically attributed to values exceeding twice the normal range [16]. These metabolites are considered highly reliable for diagnostic purposes due to the continuous release of catecholamines from storage vesicles within tumor cells [17]. To minimize the risk of false-positive results, patients are instructed to remain in a supine position for a minimum of 20 minutes prior to the measurement of plasma norepinephrine and epinephrine levels [18]. Anatomical imaging modalities such as CT and magnetic resonance imaging (MRI) demonstrate a sensitivity of 100% in localizing adrenal pheochromocytomas [19]. Furthermore, ultrasound has proven to be a valuable screening tool, with a detection rate of 90% for pheochromocytomas [16].

The judicious administration of preoperative medications is crucial for mitigating surgical risk. Alpha-adrenergic receptor antagonists play a pivotal role in the preoperative management of hypertension and the stabilization of blood volume. These agents should be administered 10–14 days prior to surgery to inhibit excessive catecholamine-induced stimulation of alpha receptors, thereby decreasing the likelihood of perioperative complications; examples include phenoxybenzamine and terazosin [20]. For patients with pheochromocytoma, the preoperative blood pressure should be maintained below normal systolic levels, with a heart rate controlled at 80–90 beats per minute [21]. The chronic elevation of catecholamines leads to the downregulation of alpha receptors, which can be reversed with alpha receptor blockers to prevent hypotension and inadequate response to vasopressors following renal vein clamping. Nonetheless, the preoperative use of these agents does not guarantee the prevention of hypotension post-tumor resection, highlighting the necessity for the timely administration of vasopressors in the postoperative period [20]. Once alpha receptor blockade is achieved, beta-blockers may be introduced to prevent reflex tachycardia and manage arrhythmias.

In this case, the patient underwent a 3-day preoperative volume expansion to mitigate potential vascular constriction and hypovolemia during surgery. However, recent studies have raised questions regarding the necessity of intravenous fluid resuscitation following the preoperative administration of alpha receptor blockers. One study reported that omitting intravenous fluid resuscitation after administering the alpha receptor blocker phenoxybenzamine did not independently elevate the risk of intraoperative hemodynamic instability [22]. Instead, tumor size emerged as a more significant risk factor for instability during the surgical procedure. Another study on the perioperative management of pheochromocytoma highlighted the importance of utilizing specific medications, such as magnesium sulfate and vasopressin, which can effectively manage hemodynamics without increasing fluid volume [23]. Vasopressin, a peptide hormone primarily synthesized in the supraoptic and paraventricular nuclei of the hypothalamus and released from the posterior pituitary into the bloodstream, plays a crucial role in maintaining fluid and circulatory homeostasis [24]. Preoperative management is crucial, but the role of fluid resuscitation may need reassessment for larger tumors.The patient exhibited significant hemodynamic instability both pre- and post-tumor resection, characterized by a peak systolic blood pressure of 250 mmHg. Blood pressure management was achieved through continuous intravenous infusion and intermittent administration of phenoxybenzamine and sodium nitroprusside. Following vascular ligation of the tumor, there was a precipitous decline in blood pressure, with the systolic pressure reaching a nadir of 50 mmHg. The response to high-dose norepinephrine administered via intravenous infusion was insufficient, leading to the consideration of an adrenal crisis. Consequently, 80 mg of methylprednisolone was administered intravenously, accompanied by a continuous infusion of epinephrine at a rate of 0.1 μg/kg/minute and intermittent boluses of 0.5 mg. Approximately 10 minutes later, the systolic blood pressure gradually stabilized at 90 mmHg. In the postoperative intensive care unit, vasopressin and norepinephrine were utilized to maintain the patient's blood pressure, in conjunction with continuous intravenous hydrocortisone

replacement therapy. The patient continued oral hydrocortisone therapy following discharge.

Surgical intervention is the preferred treatment modality for pheochromocytoma [16]. The resection of the tumor can effectively alleviate the symptoms and hypertension associated with pheochromocytoma. With ongoing advancements in minimally invasive techniques, laparoscopic surgery has increasingly supplanted open surgery [25]. Nevertheless, for pheochromocytomas measuring ≥ 5 cm in diameter, the selection of the surgical approach should be informed by the tumor's size, its characteristics, and the surgeon's expertise. In the present case, the substantial size of the tumor (7.8 cm × 5.9 cm × 6.4 cm) coupled with its compression of adjacent major vessels and proximity to the spleen and left kidney rendered a simple tumor excision potentially perilous. Consequently, we opted for an open abdominal exploration, which facilitated the complete excision of the left adrenal gland and tumor, a splenectomy, and the repair of the left renal artery and vein.

Intraoperative monitoring for pheochromocytoma primarily focuses on the real-time evaluation of blood pressure and heart rate fluctuations. Given the potential for significant hemodynamic instability during surgical procedures involving large pheochromocytomas, the administration of multiple vasoactive agents may be necessary to maintain intraoperative blood pressure stability [26]. To achieve precise hemodynamic control, the implementation of advanced monitoring techniques, such as invasive arterial pressure monitoring, central venous pressure monitoring, and transesophageal echocardiography (TEE), is crucial. TEE provides real-time visualization of cardiac anatomy and physiology, facilitating the assessment of left ventricular systolic and diastolic function as well as the evaluation of cardiac valve status. This information is instrumental in enabling surgeons to make timely and accurate intraoperative decisions [27]. In our case, the absence of TEE monitoring may have resulted in an inadequate assessment of cardiac function and volume status.

The utilization of combined epidural–general anesthesia in pheochromocytoma surgeries is of considerable clinical significance. A multicenter retrospective cohort study evaluated the outcomes of combined epidural–general anesthesia versus general anesthesia alone in surgeries for pheochromocytoma and sympathetic ganglioneuromas. The findings revealed a significant reduction in the incidence of intraoperative hypotension in the combined anesthesia group, whereas the general anesthesia group exhibited more pronounced blood pressure fluctuations [28]. This observation is corroborated by another study, which examined 146 patients undergoing open surgery for pheochromocytoma. The study demonstrated a significantly lower postoperative complication rate in patients who received combined epidural–general anesthesia compared with those who received only general anesthesia. These results suggest that combined anesthesia not only mitigates intraoperative blood pressure variability but may also decrease the risk of postoperative complications [29]. While combined epidural–general anesthesia offers advantages in managing intraoperative blood pressure variability, it is imperative to consider the patient's specific circumstances and the complexity of the surgical procedure when selecting an anesthetic strategy. Research indicates that combined anesthesia may exacerbate intraoperative hypotension in certain cases; thus, meticulous intraoperative monitoring and management are crucial to ensuring patient safety [28]. A study was conducted to compare the effects of selective versus non-selective alpha-adrenergic antagonists in patients undergoing surgical intervention for pheochromocytoma and paraganglioma. The findings demonstrated that non-selective alpha-adrenergic antagonists were associated with a reduced incidence of intraoperative hypertension compared with their selective counterparts. These results highlight the critical importance of preoperative preparation and elucidate the role of selective alpha-adrenergic antagonists in the management of intraoperative blood pressure during surgeries for pheochromocytoma [30]. Furthermore, the study investigated the potential advantages of utilizing the alpha-2 adrenergic receptor agonist dexmedetomidine to maintain hemodynamic stability during laparoscopic adrenalectomy for pheochromocytoma. The results indicated that dexmedetomidine infusion significantly decreased intraoperative maximum systolic blood pressure, diastolic blood pressure, mean arterial pressure, and heart rate, thereby enhancing hemodynamic stability throughout the surgical procedure [31].

The postoperative management of pheochromocytoma is a pivotal component of patient care due to the potential for hemodynamic instability and associated complications. Following the surgical resection of pheochromocytoma, patients may experience fluctuations in blood pressure and heart rate, necessitating meticulous monitoring and management. A primary postoperative concern is the risk of acute kidney injury (AKI), which is linked to intraoperative hypotension. Research indicates that maintaining the mean arterial pressure above a specific threshold is crucial for preventing AKI following adrenal pheochromocytoma resection. Therefore, optimizing hemodynamics, particularly after tumor removal, is essential to minimize the risk of postoperative complications such as AKI [32]. An essential component of postoperative management is the potential occurrence of persistent hypotension,

which may necessitate catecholamine support. Larger tumor volumes and elevated urinary catecholamine levels have been identified as predictive factors for persistent hypotension following laparoscopic adrenalectomy for pheochromocytoma. It is imperative for clinicians to be cognizant of these risk factors to enhance the anticipation and management of postoperative hypotension [33]. Additionally, the selection of surgical technique plays a critical role in influencing postoperative outcomes. Laparoscopic procedures, in comparison to open surgery, have demonstrated a reduction in morbidity and a decrease in hospital stay duration for patients with pheochromocytoma. This minimally invasive approach is both feasible and effective, providing opportunities for cure and hypertension control comparable to traditional open surgery [34].

Conclusion

In this particular case, the patient presented with a large tumor that was closely adhered to the spleen, kidneys, pancreas, renal arteries and veins, and splenic arteries and veins, which increased the likelihood of adhesions. Consequently, laparoscopic surgery was not performed. Despite thorough preoperative preparation, significant blood pressure fluctuations occurred during the surgery, including a severe hypotensive event following tumor resection. Postoperatively, the patient continued hormone replacement therapy, which was maintained after discharge.The perioperative hemodynamic management of large pheochromocytomas presents significant challenges, with the incidence of adrenal crises being closely associated with tumor size. The primary objective of perioperative management should be the maintenance of hemodynamic stability and the assurance of adequate perfusion to vital organs. To enhance patient prognosis, it is crucial to implement personalized and meticulous management strategies during the perioperative period, in conjunction with multidisciplinary collaboration.

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Author contributions
Jiyu Zeng collated case report data from patient records, carried out the literature review, and drafted the article. Ting Yang provided patient data and critically revised draft article. Yong Wang and Li Wu were the main contributors to the concept and design of the report and revised draft article. All authors critically revised and approved the final manuscript for publication.

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Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
None declared.

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