



# Minimally Invasive Management of Hemorrhagic Pheochromocytoma—A Rare Case Report

Ajay H. Bhandarwar, MS, FMAS, FAIS, FICS, FBMS, FLCS, FACS<sup>1</sup>

Amarjeet E. Tandur, MBBS, MS, FIAGES, FMAS<sup>1</sup> Keerthika Reddy Rachapalli, MBBS<sup>1</sup>

Amol Wagh, MBBS, MS<sup>1</sup> Abhijit Shah, MBBS, MS<sup>1</sup> Nikhil Dhimole, MBBS<sup>1</sup>

<sup>1</sup>Department of General Surgery, Grant Government Medical College and Sir JJ Group of Hospitals, Mumbai, Maharashtra, India

Surg J (NY) 2023;9:e52–e57.

**Address for correspondence** Keerthika Reddy Rachapalli, MBBS, 470/D, REDDYS, 15th cross, Idealhomes township, Rajarajeshwari nagar, Bengaluru- 560098, Karnataka, India (e-mail: keerthikareddy@gmail.com).

## Abstract

Pheochromocytoma is a rare catecholamine-secreting tumor derived from chromaffin cells. The diagnosis is usually suggested by its classic history, presence of a strong family history, or discovery of an incidental mass on imaging in an asymptomatic patient. Hemorrhage into an occult pheochromocytoma is a rare complication with ~1 to 2 per 100,000 individuals diagnosed annually. We report a case of a 29-year-old woman, who presented with abdominal pain (with no other significant history) due to a right hemorrhagic pheochromocytoma. Computed tomographic imaging and magnetic resonance imaging revealed the source of retroperitoneal hemorrhage as the right adrenal mass. They lacked the typical features of a pheochromocytoma which was eventually proven by the biochemical tests. The patient underwent preoperative stabilization with  $\alpha$  and  $\beta$  adrenergic receptor blockers for 7 days following which laparoscopic adrenalectomy was performed successfully with an uneventful postoperative period. This is the eighth reported case in literature managed laparoscopically. Histopathology confirmed it as pheochromocytoma. The treacherous and deceptive nature of pheochromocytomas and its hemorrhage make it crucial to detect and treat it promptly; otherwise, it will almost certainly be fatal from cardiovascular complications or metastasis.

## Keywords

- hemorrhagic pheochromocytoma
- minimally invasive surgery
- rare complication
- case report

Pheochromocytoma is a rare catecholamine-secreting tumor of the adrenal glands presenting with a myriad of clinical and imaging manifestations. It can lead to over whelming cardiovascular crises if left undiagnosed or if appropriate treatment is delayed.<sup>1</sup> Acute onset of abdominal pain and nausea may be the only presenting symptoms of spontaneous hemorrhage in a pheochromocytoma—a rare and highly lethal complication with atypical imaging findings, making its diagnosis challenging.<sup>2</sup> We report a case with spontaneous rupture of the right adrenal pheochromocytoma presenting with abdominal pain in a 29-year-old woman with no history of hypertension, paroxysmal headaches, or palpitations.

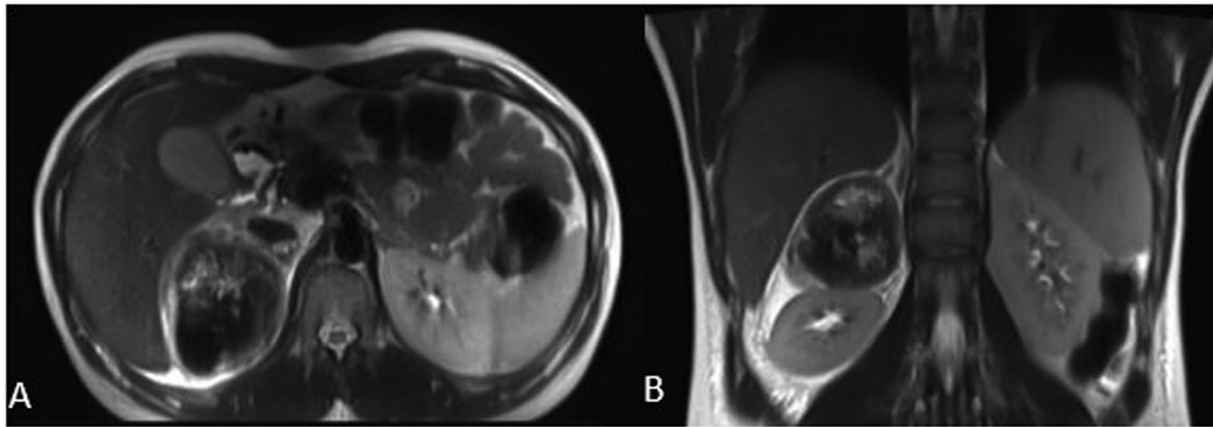
## Case Report

A 29-year-old female kabaddi athlete visited the outpatient department due to progressive upper abdominal pain for the past 4 months with no other complaints, no history of steroid use in the past, and no comorbidities of note. Clinical examination was unremarkable except for tachycardia. She was further evaluated with an ultrasonography of the abdomen and pelvis which was suggestive of a large right adrenal mass composed of hypoechoic fat with cystic areas and mild surrounding fluid extending into the right perinephric space and paracolic gutter. These findings being suggestive of a

received  
May 11, 2021  
accepted after revision  
January 2, 2023

DOI <https://doi.org/10.1055/s-0043-1762554>.  
ISSN 2378-5128.

© 2023. The Author(s).  
This is an open access article published by Thieme under the terms of the Creative Commons Attribution License, permitting unrestricted use, distribution, and reproduction so long as the original work is properly cited. (<https://creativecommons.org/licenses/by/4.0/>)  
Thieme Medical Publishers, Inc., 333 Seventh Avenue, 18th Floor, New York, NY 10001, USA



**Fig. 1** (A) Axial view and (B) coronal view of magnetic resonance imaging T2-weighted images showing a well-defined heterogenous hypointense lesion in the lateral limb of right adrenal gland.

ruptured adrenal myelolipoma with surrounding hemorrhage, a magnetic resonance imaging (MRI) of the abdomen was done for further evaluation and characterization. It showed a well-defined heterogenous lesion in the lateral limb of right adrenal gland  $\sim 6.7 \times 5.9 \times 6.4$  cm in size, hypointense on T1-weighted (T1W) and T2-weighted (T2W) sequences. No loss of signal is seen in the T1W out of phase images, representing no fat within the lesion with moderate free fluid in the right subhepatic, paracolic, and perinephric space suggestive of a hemorrhagic right adrenal adenoma (**► Fig. 1**). A coagulation profile and anticardiolipin antibody testing was further done (to rule out coagulation disorders and antiphospholipid antibody [APLA] syndrome) which were within normal range. Contrast-enhanced computed tomography (CT) of the abdomen showed a lesion likely arising from the lateral limb of the right adrenal gland showing central liquefaction and intralesional hemorrhage with rupture of the anterior wall leading to a walled off fluid

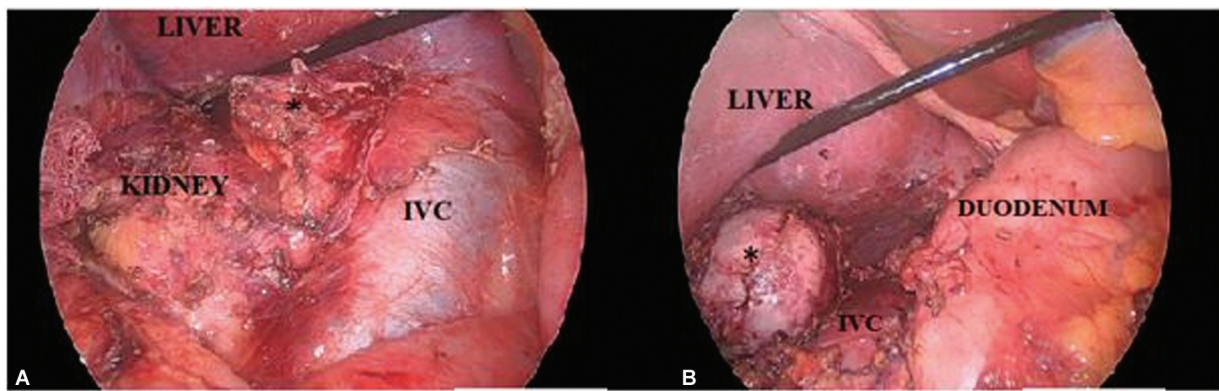
collection extending into the anterior pararenal and subhepatic space. The lesion showed a 60.2% absolute washout on delayed images. This mass was suspected to most likely be a lipid poor adenoma or a pheochromocytoma (**► Fig. 2**).

Accordingly, blood and 24-hour collection of urine for metanephrine were ordered. It returned with a marked elevation of plasma-free metanephrine (109 pg/mL, normal  $<65$  pg/mL), 24 hours urine metanephrine (833  $\mu\text{g}/24$  hours, normal  $<350$   $\mu\text{g}/24$  hours) and metanephrine to creatinine ratio (453.92  $\mu\text{g}/\text{g}$  creatinine, normal 33–109) confirming the diagnosis of pheochromocytoma.

The patient was optimized with preoperative prazosin ( $\alpha$ -1 receptor blocker) and metoprolol (selective  $\beta$ -1 receptor blocker) and fluid loading for 7 days. Thereafter, laparoscopic right adrenalectomy was performed successfully. Intraoperatively, the right adrenal gland was identified with dense adhesions around the hilum due to hemorrhage and subsequent fibrosis and with a contained retroperitoneal hemorrhage (**► Fig. 3**).



**Fig. 2** (A) Axial view and (B) coronal view of contrast-enhanced computed tomography showing a mass arising from the lateral limb of the right adrenal gland showing central liquefaction and intralesional hemorrhage with rupture (arrow) of the anterior wall leading to a walled off fluid collection extending into the anterior pararenal and subhepatic space.



**Fig. 3** (A) Intraoperative image showing an enlarged right suprarenal mass (\*) with contained retroperitoneal hemorrhage. (B) Completely dissected pheochromocytoma. IVC, inferior vena cava.

As the hilum was frozen, inferior dissection was done. An aberrant vein draining into the renal vein was identified. The rest of the hilar structures could not be identified due to the adhesions and was sheared with advanced bipolar device (►Video 1). During surgery, blood pressure was well controlled, although a few episodic rises required intravenous nitroglycerin. The total operative time was 3 hours (►Fig. 4).

#### Video 1

Hemorrhagic pheochromocytoma. Online content including video sequences viewable at: <https://www.thieme-connect.com/products/ejournals/html/10.1055/s-0043-1762554>.

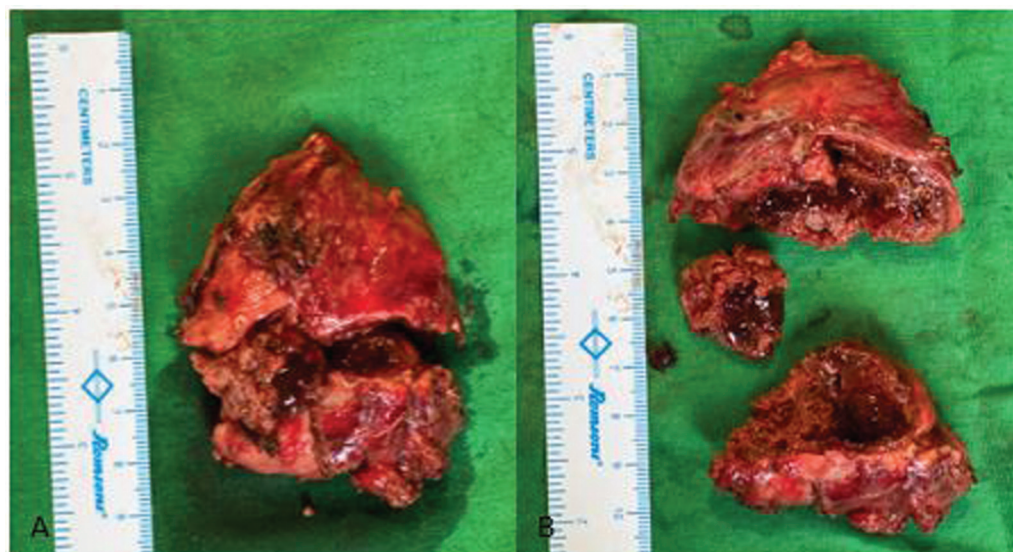
The patient's blood pressure was within normal range in the postoperative period eliminating the need for any anti-hypertensives. She was discharged on postoperative day 3.

Histopathological evaluation confirmed it as a PASS score (Pheochromocytoma of the Adrenal gland Scaled Score) of 2 and MIB1 proliferative index of 8% at the margin suggestive of a benign tumor (►Fig. 5). Immunohistochemistry showed positive for chromogranin A and synaptophysin (►Fig. 6).

Genetic testing ruled out suspected germline mutations. Patient has been advised about continued annual endocrinology follow-up with biochemical tests.

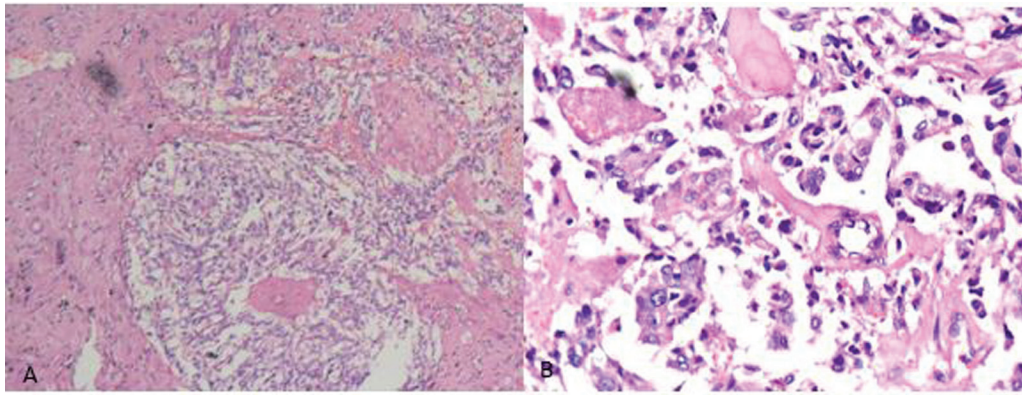
#### Discussion

Pheochromocytomas are rare, catecholamine secreting tumors with ~1 to 2 per 100,000 individuals diagnosed annually.<sup>3</sup> They are composed of chromaffin cells of the adrenal medulla derived from embryonic neural crest cells which were first described by Frankel<sup>4</sup> in 1886 in a young woman likely afflicted with Multiple Endocrine Neoplasia type 2.<sup>5</sup> They may be either sporadic or a manifestation of hereditary (familial) syndromes, which are transmitted in an autosomal dominant fashion.<sup>6</sup>

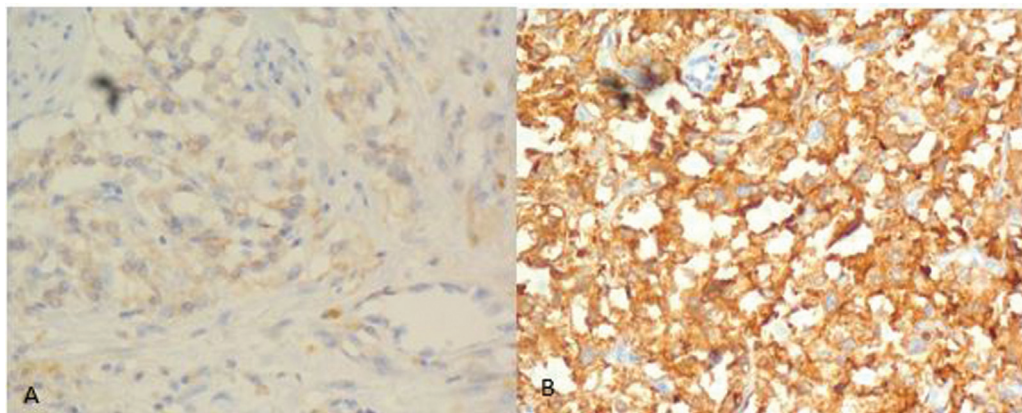


**Fig. 4** (A) Gross image of resected right adrenal mass. (B) Gross image of a cut open right adrenal mass showed variegated, partially cystic, and hemorrhagic cut surface.





**Fig. 5** Hematoxylin and eosin staining (A) shows a highly cellular tumor arranged in a diffuse form with focal Zellballen pattern and focal areas of necrosis and hemorrhage ( $\times 100$  magnification). (B) Individual tumor cells have moderate eosinophilic to clear cytoplasm, round to oval vesicular nuclei with inconspicuous nucleoli. Nuclear pleomorphism is present with tumor giant cells ( $\times 400$  magnification).



**Fig. 6** Positive staining for (A) chromogranin-A and (B) synaptophysin.

The key to diagnosing pheochromocytoma is to think of it first. Often referred to as “The Great Masquerader”<sup>7</sup> as it mimics various conditions, there is no single clinical finding that has significant value in diagnosing or excluding pheochromocytoma.<sup>8</sup> In two recent meta-analyses,<sup>8,9</sup> the symptoms with the greatest “pooled sensitivity” were hypertension (80.7%), headache (60.4%), palpitation (59.3%), and diaphoresis (52.4%). Pallor, nausea, flushing, anxiety or a sense of doom, palpitations, and abdominal pain can be part of the constellation of presenting symptoms.<sup>10</sup> It can rarely appear as “pheochromocytoma crisis,” a life-threatening condition<sup>11</sup> which presents with severe hypertension to circulatory failure and shock with subsequent involvement of multiple organ systems, including the cardiovascular, pulmonary, neurological, gastrointestinal, renal, hepatic, and metabolic systems.<sup>11</sup> Rarely, 1% is asymptomatic, representing an incidental discovery.

Several biochemical assays are available to facilitate diagnosis; however, plasma-free metanephrines have had the highest sensitivity and specificity in a recent multicenter cohort trial<sup>12</sup> in the detection of pheochromocytomas.

Once biochemical evidence of pheochromocytoma is obtained, imaging for localization should be undertaken to guide surgical resection (**► Table 1**).

Spontaneous rupture of pheochromocytoma is a rare event, with only ~83 cases reported in the literature. Its presentation being highly varied, ranging from nothing more than nausea and abdominal pain to hemodynamic shock and abdominal catastrophe, resulting in delayed diagnosis. The exact mechanism of pheochromocytoma rupture remains unknown. A massive release of catecholamines is probably associated with vasoconstriction in the tumor and subsequent necrosis and hemorrhage. Consequently, elevated intracapsular pressure may result in a tear in the capsule, causing further hemorrhage into the retroperitoneum.<sup>13</sup> Trauma,<sup>14</sup> medications,<sup>15,16</sup> coagulation disorders, and APLA syndrome have also been implicated in hemorrhagic complications.

Clinical diagnosis of a ruptured pheochromocytoma is difficult and only 30.2% of patients have been diagnosed preoperatively<sup>17</sup> due to the following reasons. First, metaiodobenzylguanidine (MIBG) and F-18-fluorodeoxyglucose do not accumulate to the mass with total coagulation necrosis. Second, previous case reports for ruptured pheochromocytoma often failed in proving elevated levels of catecholamines because of difficulty in performing hormonal examination under emergency situation<sup>18</sup> and early normalization in plasma and urinary levels of catecholamines.<sup>18,19</sup> Third, in the diagnosis process of the ruptured pheochromocytoma, there is

**Table 1** Different radiological modalities used in localizing a pheochromocytoma and paraganglioma and their typical imaging findings

1	Computed tomography	<ul style="list-style-type: none"> <li>- First choice</li> <li>- Excellent spatial resolution for thorax, abdomen, and pelvis</li> </ul>	<ul style="list-style-type: none"> <li>- Solid/cystic, homogenous <math>\pm</math> calcification</li> <li>- <math>&gt;10</math> HU</li> <li>- High attention due to hemorrhage</li> <li>- <math>&lt;50\%</math> washout</li> </ul>
2	Magnetic resonance imaging	<ul style="list-style-type: none"> <li>- In patients with metastatic pheochromocytoma</li> <li>- Detection of skull base and neck paraganglioma</li> <li>- Patients with surgical clips</li> <li>- Allergy to CT contrast</li> <li>- Where radiation exposure is to be limited (children, pregnancy, germline mutation)</li> </ul>	<ul style="list-style-type: none"> <li>- Low intensity at T1W imaging</li> <li>- High intensity at T2W imaging—light bulb appearance</li> <li>- Salt and pepper appearance on T1W and T2W in paraganglioma</li> </ul>
3	123I-MIBG scintigraphy	<ul style="list-style-type: none"> <li>- Patients with metastatic pheochromocytoma</li> <li>- When radiotherapy using 123I-MIBG is planned</li> <li>- Large sized tumor</li> <li>- Extra adrenal/multifocal/recurrent disease</li> </ul>	- MIBG, octreotide, FDG+
4	FDG-PET	- Preferred over 123I-MIBG in patients with known metastatic pheochromocytoma	

Abbreviations: CT, computed tomography; FDG, fluorodeoxyglucose; MIBG, metaiodobenzylguanidine; PET, positron emission tomography; T1W, T1-weighted; T2W, T2-weighted.

a strong correlation between hemodynamic instability and rate of misdiagnosis.<sup>18,20</sup>

In our experience with laparoscopic adrenalectomy, this is the first encounter with a ruptured hemorrhagic pheochromocytoma and the eighth documented case in literature managed laparoscopically.<sup>21</sup> In this case, we faced a unique set of circumstances. CT scanning is the diagnostic tool of choice, but the lesion in our case showed an absolute washout of  $\sim 60.2\%$  as opposed to a distinctive  $<50\%$  washout seen in a classical pheochromocytoma, thereby suggesting the possibility of it being a lipid poor adenoma. The lesion also failed to show a characteristic hyperintensity on T2W images on MRI, giving the impression of a ruptured adrenal hematoma. Hence, APLA syndrome (with a normal  $\beta_2$ -cardiolipin levels) and a history of steroid usage was ruled out. Pheochromocytoma can undergo a variety of pathological degenerations, which affect their imaging features. This varied and changeable appearance merits the “chameleon” epithet given to this tumor. Plasma-free and 24 hours urinary metanephrines were tested which were elevated confirming the diagnosis of pheochromocytoma.

The treatment and outcome of the 83 cases are summarized in ► **Table 2**. Mortality rate can be as high as 38.7% in patients with emergency adrenalectomy. However, there has only been 1 fatality (2.9%) reported among the 10 patients who underwent delayed surgery with transangiographic embolization (TAE).

Urgent surgery is not indicated even in the presence of hemorrhagic pheochromocytoma because it has been shown that delayed surgery is associated with fewer intraoperative and postoperative complications and also lower mortality rate.<sup>22</sup> In the setting of a contained hematoma (like in this case), every effort should be taken to avoid emergency surgical intervention. Adequate medical preparation results in a mortality rate similar to that observed for elective adrenalectomy in the absence of hemorrhage. Medical optimization should include adequate blood resuscitation, correction of any co-

agulopathy to limit continued hemorrhage, hemodynamic support as needed, and ultimately  $\alpha$ -blockade followed by volume expansion and  $\beta$ -blockade in an inpatient setting. Emergent surgical intervention may be considered in cases refractory to maximal medical management as recently described by May et al<sup>14</sup> with recognition of the high morbidity and mortality. In the absence of adequate adrenergic blockade in these extreme cases, the intraoperative and postoperative care must be tailored to the clinical picture as it evolves. Thus, the anesthesia and surgical teams must be prepared to manage sudden cardiovascular collapse, fulminant heart failure, massive pulmonary edema, and ongoing hemorrhage. If the tumor has been removed in toto, there is no need to continue antihypertensives postoperatively. Moreover, recent compelling data are emerging that in normotensive asymptomatic patients, preoperative  $\alpha$ -blockade may not be necessary.<sup>23</sup> Although these data are provocative, they require validation from other centers, ideally in a prospective randomized fashion. It is the view of the committee that for such patients, preoperative blockade remains recommended to prevent unpredictable increases in blood pressure during surgery.<sup>24</sup>

An alternative that has been receiving attention is TAE of the adrenal vessels which provides good control of ongoing

**Table 2** Summary of treatment, outcome and mortality rate of the 83 cases of ruptured pheochromocytoma

Treatment	Emergency surgery 36 (43.3%) Elective surgery 24 (28.9%) Conservative surgery 13 (15.6%) Elective surgery after TAE 10 (12%)
Outcome	Survived 63 (75.9%) Died 20 (24.0%)
Mortality rate	Emergency surgery or conservative treatment: 38.7% Delayed with or without TAE: 2.9%

Abbreviation: TAE, transangiographic embolization.

hemorrhage in a patient who is unstable and unprepared for an exploration.

A large pheochromocytoma (>5 cm) warrants an  $^{123}\text{I}$ -MIBG scan to look for metastasis.<sup>25</sup> The scan showed no metastasis. According to Endocrine Society Clinical Practice Guidelines, it is recommended that all patients with (pheochromocytomas and paragangliomas (PPGLs) should be engaged in a shared decision-making for genetic testing with a clinical feature-driven diagnostic algorithm to establish the priorities for specific genetic testing of suspected germline mutations.<sup>26</sup> Specifically, pretest and posttest counseling should be available. All tests for PPGL genetic testing should be performed by accredited laboratories.<sup>26</sup>

## Conclusion

Spontaneous intraperitoneal hemorrhage remains a rare complication of pheochromocytoma, though the physiologic consequences present considerable medical and surgical challenges. Unfortunately, emerging clinical scenarios do not allow for optimal preoperative medical preparation with  $\alpha$ -adrenergic blockade, and are associated with a high mortality rate. In the present case, as the patient was hemodynamically stable, she was optimized with antihypertensives preoperatively and managed through elective laparoscopic approach. Most importantly, a high index of suspicion must be maintained in similar cases so that the highly lethal hemodynamic sequelae may be anticipated and managed with the appropriate pharmacologic agents to ensure optimal outcomes. In unstable patients, a trial of TAE can be done.

### Funding

None.

### Conflict of Interest

None declared.

### Acknowledgments

We hereby acknowledge the efforts of Bharat Shah, Professor of Anaesthesiology for providing skillful and apt anesthetic support and intensive care management for the patient. Sanjay Navani's histopathology analysis of the specimen is also worth mentioning.

## References

- Blake MA, Kalra MK, Maher MM, et al. Pheochromocytoma: an imaging chameleon. *Radiographics* 2004;24(Suppl 1):S87-S99
- Yeong-Chin Jou, Wei-Hao Chen, Jiann-Der Wu, Shu-Hua Lin, I-Mo Chiu, Bo-Jung Chen. Spontaneous rupture of adrenal pheochromocytoma. *Formosan Journal of Surgery* 2013;46(02):48-51 ISSN 1682-606X, <https://doi.org/10.1016/j.fjs.2012.11.002>
- Bravo EL, Tagle R. Pheochromocytoma: state-of-the-art and future prospects. *Endocr Rev* 2003;24(04):539-553
- Frankel F. Ein Fall von doppelseitigem, völlig latent verlaufenen Nebennierentumor und gleichzeitiger Nephritis mit Veränderungen am Circulationsapparat und Retinitis. *Arch Pathol Anat Physiol Klin Med* 1886;...:244-263
- Neumann HPH, Vortmeyer A, Schmidt D, et al. Evidence of MEN-2 in the original description of classic pheochromocytoma. *N Engl J Med* 2007;357(13):1311-1315
- Kantorovich V, Pacak K. Pheochromocytoma and paraganglioma. *Prog Brain Res* 2010;182:343-373. Doi: 10.1016/S0079-6123(10)82015-1. PMID: 20541673; PMCID: PMC4714594
- Reyes HA, Paquin JJ, Harris DM. Pheochromocytoma, "the Great Masquerader," presenting as severe acute decompensated heart failure in a young patient. *Case Rep Cardiol* 2018;2018; 8767801
- Pourian M, Mostafazadeh DB, Soltani A. Does this patient have pheochromocytoma? A systematic review of clinical signs and symptoms. *J Diabetes Metab Disord* 2016;15:11
- Soltani A, Pourian M, Davani BM. Correction to: does this patient have Pheochromocytoma? a systematic review of clinical signs and symptoms. *J Diabetes Metab Disord* 2017;16:42
- Chen H, Sippel RS, O'Dorisio MS, Vinik AI, Lloyd RV, Pacak K. North American Neuroendocrine Tumor Society (NANETS) The North American Neuroendocrine Tumor Society consensus guideline for the diagnosis and management of neuroendocrine tumors: pheochromocytoma, paraganglioma, and medullary thyroid cancer. *Pancreas* 2010;39(06):775-783
- Tschuor C, Sadri H, Clavien PA. Pheochromocytoma crisis. *Clin Case Rep* 2014;2(01):14
- Lenders JWM, Pacak K, Walthers MM, et al. Biochemical diagnosis of pheochromocytoma: which test is best? *JAMA* 2002;287(11): 1427-1434
- Tanaka K, Noguchi S, Shuin T, Kinoshita Y, Kubota Y, Hosaka M. Spontaneous rupture of adrenal pheochromocytoma: a case report. *J Urol* 1994;151(01):120-121
- May EE, Beal AL, Beilman GJ. Traumatic hemorrhage of occult pheochromocytoma: a case report and review of the literature. *Am Surg* 2000;66(08):720-724
- Delaney JP, Paritzky AZ. Necrosis of a pheochromocytoma with shock. *N Engl J Med* 1969;280(25):1394-1395
- Van Way CW III, Faraci RP, Cleveland HC, Foster JF, Scott HW Jr. Hemorrhagic necrosis of pheochromocytoma associated with phentolamine administration. *Ann Surg* 1976;184(01):26-30
- Kobayashi T, Iwai A, Takahashi R, Ide Y, Nishizawa K, Mitsumori K. Spontaneous rupture of adrenal pheochromocytoma: review and analysis of prognostic factors. *J Surg Oncol* 2005;90(01): 31-35
- Maruyama M, Sato H, Yagame M, Shoji S, Terachi T, Osamura RY. Spontaneous rupture of pheochromocytoma and its clinical features: a case report. *Tokai J Exp Clin Med* 2008;33(03):110-115
- Jee YS. Spontaneous ruptured pheochromocytoma: an unusual case report and literature review. *Ann Surg Treat Res* 2017;93 (03):170-172
- Kobayashi T, Iwai A, Takahashi R, Ide Y, Nishizawa K, Mitsumori K. Spontaneous rupture of adrenal pheochromocytoma: review and analysis of prognostic factors. *J Surg Oncol* 2005;90(01):31-35
- Arora E, Bhandarwar A, Wagh A, et al. Role of indo-cyanine green (ICG) fluorescence in laparoscopic adrenalectomy: a retrospective review of 55 cases. *Surg Endosc* 2018;32(11):4649-4657
- Scholten A, Cisco RM, Vriens MR, et al. Pheochromocytoma crisis is not a surgical emergency. *J Clin Endocrinol Metab* 2013;98(02): 581-591
- Shao Y, Chen R, Shen ZJ, et al. Preoperative alpha blockade for normotensive pheochromocytoma: is it necessary? *J Hypertens* 2011;29(12):2429-2432
- Williams DT, Dann S, Wheeler MH. Pheochromocytoma—views on current management. *Eur J Surg Oncol* 2003;29(06):483-490
- Alexander Kutikov, Paul L. Crispin, Robert G. Uzzo. *Pathophysiology, Evaluation, and Medical Management of Adrenal Disorders*. Wein Alan J. Louis R. Kavoussi Alan W. Partin and Craig Peters. Campbell-Walsh Urology. Eleventh ed. Philadelphia PA: Elsevier; 2016:1548
- Lenders JW, Duh QY, Eisenhofer G, et al; Endocrine Society. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2014;99 (06):1915-1942