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【 CASE REPORT 】

# Optimizing Hemodynamics with Transcatheter Arterial Embolization in Adrenal Pheochromocytoma Rupture

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**Abstract:**
Pheochromocytoma rupture is rare, and emergent adrenalectomy is associated with a high mortality. We herein report a patient with pheochromocytoma rupture who was stabilized by transcatheter arterial embolization (TAE) and subsequently underwent elective surgery. A 45-year-old man presented with the sudden onset of left lateral abdominal pain, headache, chest discomfort, high blood pressure, and adrenal hemorrhaging on enhanced abdominal computed tomography. TAE was performed under a provisional diagnosis of pheochromocytoma rupture. Following oral doxazosin, he underwent elective left adrenalectomy four and a half months after TAE. Stabilizing the hemodynamic status by TAE before adrenalectomy is a viable option for treating pheochromocytoma rupture.

**Key words:** pheochromocytoma, transarterial chemoembolization, rupture, hemorrhaging

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## Introduction

Rupture or hemorrhaging is a rare complication of adrenal tumors. Only a few dozen cases of adrenal hemorrhaging have been reported in patients with pheochromocytoma. Emergent adrenalectomy in such cases is known to be associated with a high mortality.

We herein report a patient with pheochromocytoma rupture who was stabilized by transcatheter arterial embolization (TAE) before undergoing elective surgery.

## Case Report

A 45-year-old man with a history of sleep apnea, non-ischemic chronic heart failure, diabetes, and dyslipidemia presented to an emergency hospital with the sudden onset of left lateral abdominal pain, headache, and chest discomfort. High blood pressure (181/142 mmHg) and adrenal hemorrhaging on enhanced abdominal computed tomography (CT) were observed (Fig. 1), and he was transferred to our hospital. A physical examination upon admission was unremarkable except for a blood pressure of 142/102 mmHg (treated with 8 mg/h of nicardipine) and a heart rate of 107 beats-per-minute. The laboratory findings including hormonal data are shown in Table 1. Enhanced abdominal CT performed at the previous hospital showed left intratumoral hemorrhaging with a 6.5-cm adrenal mass. Under a provisional diagnosis of pheochromocytoma rupture, TAE was performed in order to restore hemodynamic stability (Fig. 2). After embolization, his systolic blood pressure rose to 240 mmHg, and he was treated with intravenous phentolamine followed by oral doxazosin. In addition, severe constipation persisted for about one week.

Four and a half months after TAE, the patient underwent elective left adrenalectomy. During the period between TAE and surgery, the catecholamine level peaked 3 days post-TAE before decreasing to around 0.085 μg/mgCre of urine metanephrine and 2.3 μg/mgCre of urine normetanephrine 1 month post-TAE and remained flat thereafter (Fig. 3). A his-

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tological examination of the resected tumor confirmed the diagnosis of pheochromocytoma (Fig. 4) and showed several small arteries with irregular fibrous thickening and a collection of small vessels in the tumor (Fig. 5).

Since the surgery, he has been in good health, only taking 10 mg/day of carvedilol for non-ischemic chronic heart failure. At 1 year postoperatively, his urinary metanephrine and normetanephrine were 0.063 μg/mgCre and 0.29 μg/mgCre, respectively, and adrenal magnetic resonance imaging revealed no signs of local recurrence.

## Discussion

Xarli et al. proposed a treatment algorithm for patients with adrenal hemorrhaging (1). However, treating pheochromocytoma rupture, which severely affects the hemodynamics, can be challenging. The clinical profiles of 74 cases reported in the literature are summarized in Table 2. The mortality rate can be as high as 40% in patients that subsequently undergo emergency adrenalectomy. However, there has only been 1 fatality (4%) reported among the 7 patients who underwent delayed surgery with TAE (Table 3). The patient who died had pheochromocytoma rupture presenting as acute abdomen. Despite TAE, his blood pressure remained unstable, and emergency surgery was performed two hours later. However, he ultimately died six days after the surgery (2).

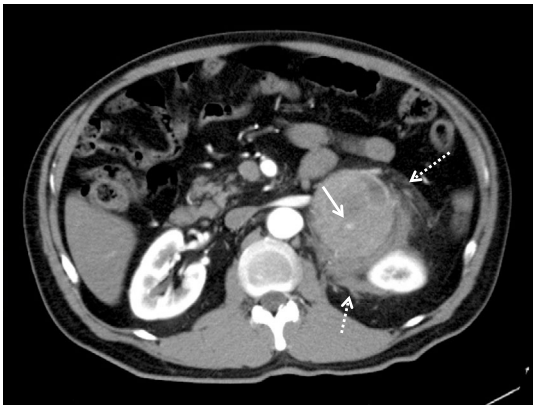

**Figure 1. Enhanced abdominal computed tomography showing a 6.5-cm left adrenal mass with cystic components and intratumoral extravasation of the contrast agent (solid arrow). Also, increased density of the peritumoral fat tissue was found (dotted arrows).**

While TAE is considered an effective and minimally invasive option for arterial bleeding due to pheochromocytoma, emergency surgery might be unavoidable in some cases, as in the above-mentioned patient. Therefore, excluding the cases in which emergency surgery is necessary, TAE is a suitable option for the management of active bleeding from pheochromocytoma. In addition, even in the absence of active hemorrhaging, it may be beneficial to perform TAE to achieve hemodynamic stability in patients with fulminant cardiogenic shock (3) or to reduce perioperative blood loss from a giant hypervascular pheochromocytoma (4).

In the present case, the catecholamine level of the patient peaked at three days post-TAE, declined, and then remained flat from one month post-TAE. Severe but transient constipation, which was present for about one week after TAE, may reflect the post-TAE elevation in the levels of noradrenaline, the predominant catecholamine secreted by this patient's tumor, as noradrenaline plays an important role in causing constipation in pheochromocytoma (5). There have only been two reports evaluating the changes in the catecholamine levels around TAE. Bunuan et al. reported that, in their patient, the urinary vanillylmandelic acid level increased after TAE was performed for non-hemorrhaging pheochromocytoma (from 38.5 mg/24 hours before TAE to

**Table 1. Laboratory Data after Hospital Transfer and Administration of 8 mg/h of Nicardipine.**

| Blood Cell Count | | Biochemistry (continue) | | Endocrinology | | Blood Gas Analysis | |
|---|---|---|---|---|---|---|---|
| WBC | 19,600 /μL | TP | 8.5 g/dL | ACTH | 97.8 pg/mL | pH | 7.482 |
| RBC | 590×10⁴ /μL | Alb | 4.7 g/dL | Cortisol | 55.7 μg/dL | $pO_2$ | 119.0 Torr |
| Hb | 19.0 g/dL | Glu | 126 mg/dL | TSH | 3.290 μIU/mL | $pCO_2$ | 31.6 Torr |
| Hct | 54.0 % | UA | 7.6 mg/dL | Free T4 | 1.26 ng/dL | $HCO_3^-$ | 23.1 mEq/L |
| MCV | 91.5 fL | BUN | 15.8 mg/dL | Free T3 | 1.78 pg/mL | BE | 0.9 mEq/L |
| MCH | 32.2 pg | Cre | 0.92 mg/dL | PRA | 120 ng/mL/h | | |
| MCHC | 35.2 % | Na | 137 mEq/L | Aldosterone | 506 pg/mL | | |
| Plt | 29.2×10⁴ /μL | K | 4.7 mEq/L | Adrenaline | 0.06 ng/mL | | |
| | | Cl | 99 mEq/L | Noradrenaline | 8.87 ng/mL | | |
| Biochemistry | | Ca | 9.7 mg/dL | Dopamine | 0.07 ng/mL | | |
| T-bil | 1.34 mg/dL | P | 3.4 mg/dL | Calcitonin | 19 pg/mL | | |
| D-bil | 0.18 mg/dL | T-Chol | 199 mg/dL | CEA | 3.3 ng/mL | | |
| ALT | 113 IU/L | TG | 117 mg/dL | DHEA-S | 1,332 ng/mL | | |
| ALP | 245 IU/L | HDL-C | 45.0 mg/dL | A1c(NGSP) | 6.6 % | | |
| γGTP | 153 IU/L | CRP | 0.44 mg/dL | u-MN | 0.25 μg/mgCre | | |
| | | | | u-NMN | 11.0 μg/mgCre | | |

DHEA-S: dehydroepiandrosterone sulfate, u-MN: urinary metanephrine, u-NMN: urinary normetanephrine

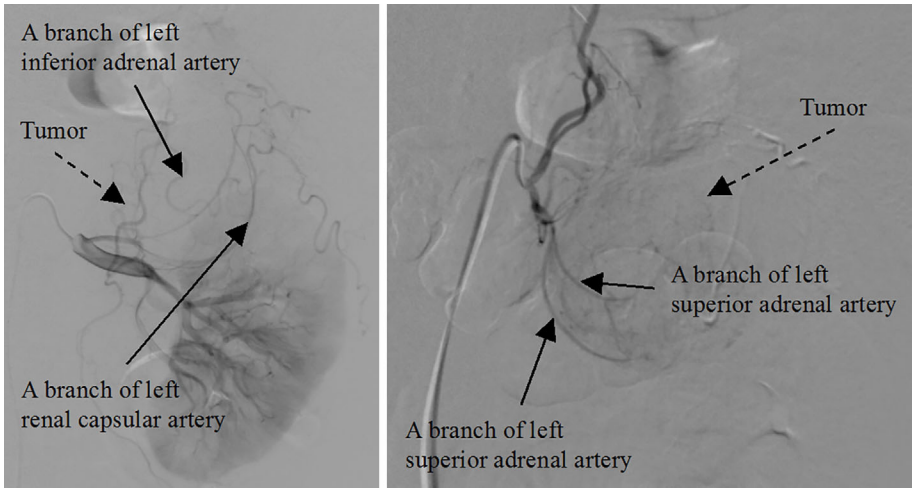


**Figure 2.** **Transcatheter artery embolization (TAE). TAE of arteries (arrows) was performed.**

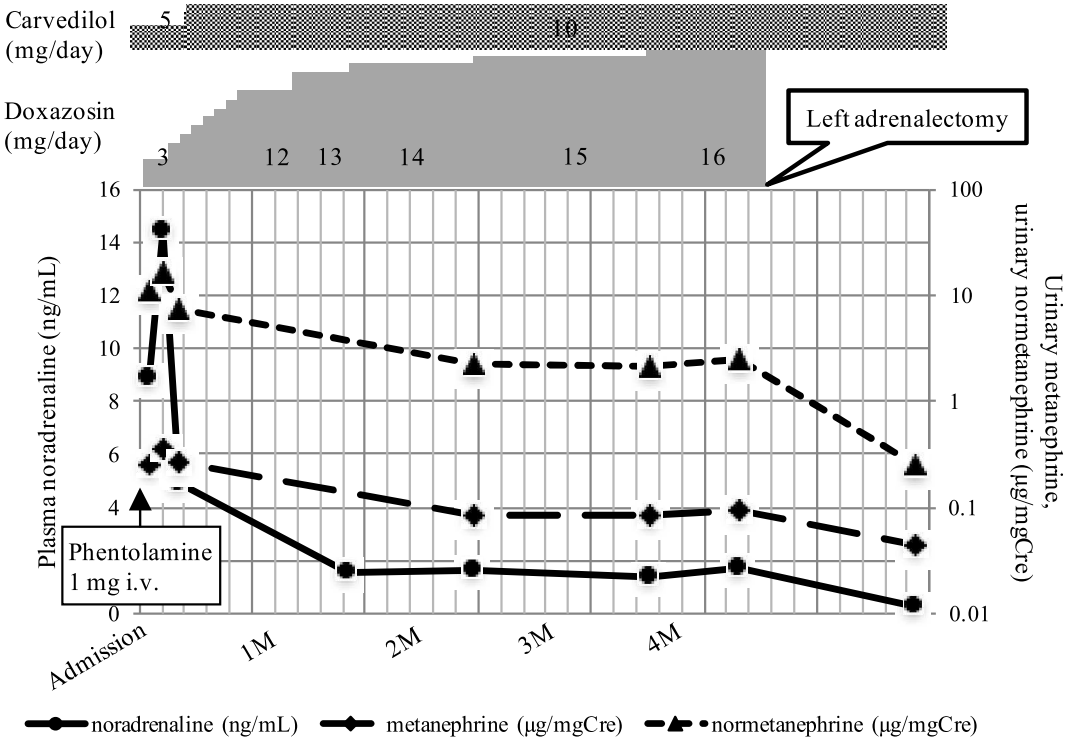


**Figure 3.** **Clinical course and changes of catecholamine levels after TAE.**

>200 mg/24 hours at 1 day after TAE). Their patient complained of nausea and epigastric pain a few hours after TAE (6). In contrast, Teranishi et al. reported that the plasma noradrenaline level decreased after TAE of a catecholamine-secreting Glomus jugulare tumor (7). Changes in the catecholamine levels and symptoms might be dependent on the histology of the tumor, the bioactivity of the secreted catecholamine, and the technique of TAE. The further accumulation of cases may help predict changes in the catecholamine levels and symptoms after TAE.

The exact mechanism underlying pheochromocytoma rupture is unknown. In the present case, a pathological evaluation of the resected left adrenal gland showed several small arteries with irregular fibrous thickening and a collection of small vessels in the tumor. The fibrous thickening of small arteries indicates heterogeneous arterial repair, which may suggest the influence of localized endothelial cell dysfunction and/or persistent mechanical stimulation (e.g. hypertension and/or mass effect). In addition, endothelial cell dysfunction and heterogeneous remodeling may be associated with microthrombogenesis as well (8). The collection of small vessels in the tumor may indicate angiogenesis and the formation of granulation tissue, which reflects the remodeling process following intratumoral hemorrhaging and necrosis. Further histological studies are needed to clarify the mechanism underlying pheochromocytoma rupture.

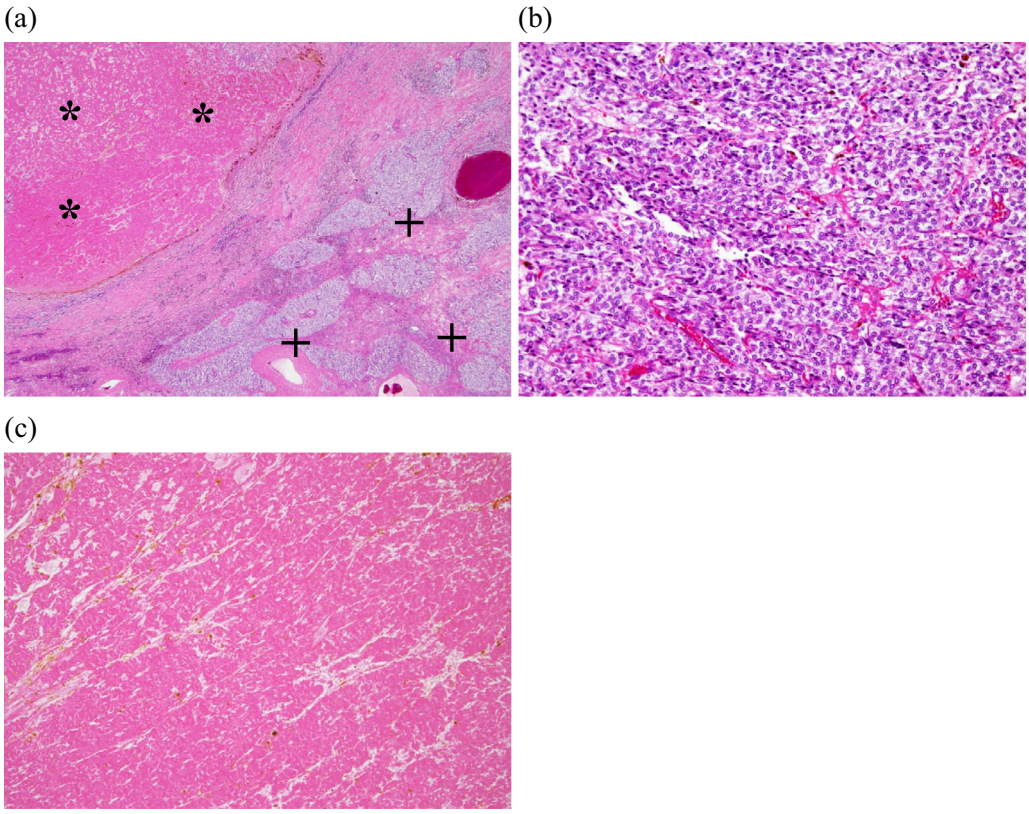


**Figure 4.** **Histology of the resected tumor. (a) The tumor consists of viable (+) and necrotic regions (*) (×20). (b) Viable tumor cells a Zellballen architecture, which is a small compartmentalized nest of tumor cells, infiltrated by a fibrovascular stroma (×200). (c) Ghost cells and vascular stroma are found in some areas of necrosis (×100).**

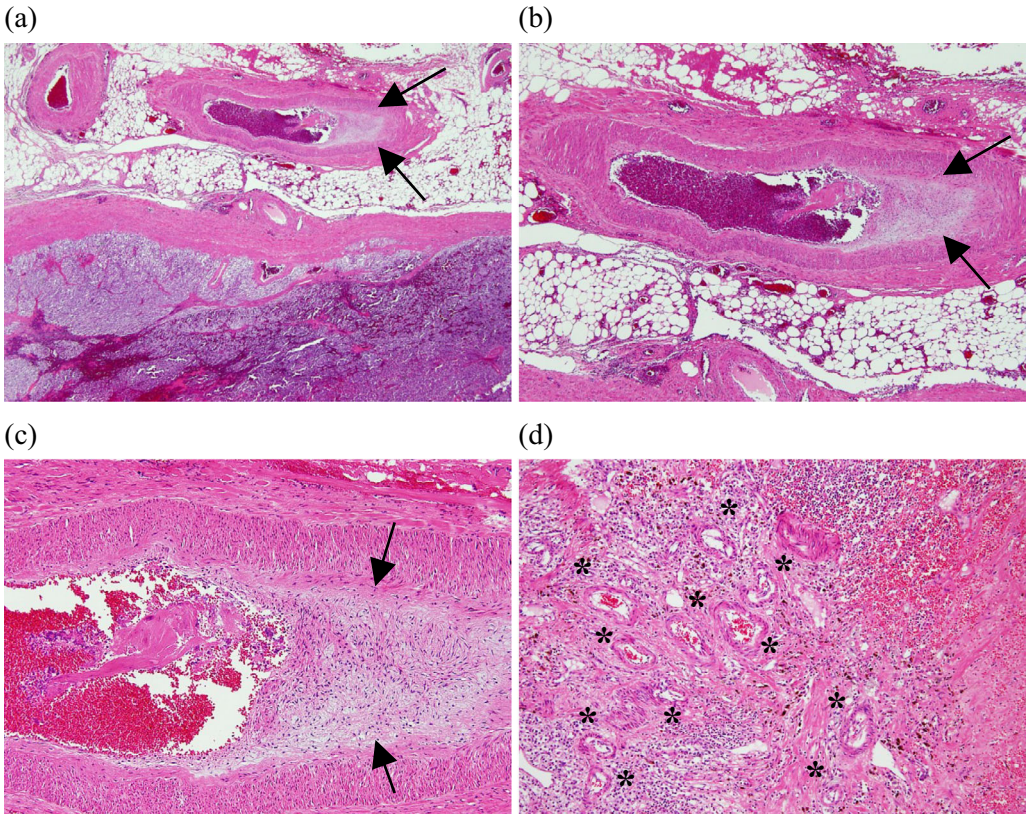


**Figure 5.** **Histology of the resected tumor. There were several small arteries with irregular fibrous thickening (a: ×20, b: ×40, and c: ×100), and a collection of small vessels (*) in the tumor (d: ×100).**

**Table 2. Clinical Profiles of 74 Cases of Pheochromocytoma Rupture.**

| | |
|---|---|
| Age | 15-84 years. (average, 50.5 years) (our case, 45 years) |
| Gender | Male 41 (55%), Female 33 (45%) |
| Side | Right 39 (53%), Left 33 (44%), Bilateral 2 (3%) |
| Symptom | Abdominal pain 58 (78%), Shock 38 (51%), Chest pain 16 (22%), Lumbar pain 13 (18%) |
| Bleeding site | Retroperitoneal 41 (55%), Intratumoral 18 (24%), Intraperitoneal 15 (21%) |
| Treatment | Emergency surgery 35 (47%), Elective surgery 20 (27%), Conservative 12 (16%), Elective surgery after TAE 7 (10%) |
| Outcome | Survived 54 (73%), Died 20 (27%) |
| Mortality Rate | Emergency surgery or conservative treatment: 40%<br>Delayed surgery with or without TAE: 4% |

**Table 3. Details of Cases with Delayed Surgery after TAE.**

| Reference | Age Gender | Catecholamine levels upon admission | Side (Bleeding site) | Interval | Note |
|---|---|---|---|---|---|
| (9) | 68 F | NA 4.90 ng/mL<br>DA 61.0 ng/mL<br>(on dopamine) | Left<br>(RP) | 3 months | Blood and urinary catecholamine levels were normal. |
| (10) | 32 M | A: 68.0 pg/mL<br>NA: 8,529.0 pg/mL<br>u-MN: 8.2 mg/day | Right<br>(IT) | 21 days | Bilateral adrenal enlargement |
| (11) | 67 M | u-MN: 33,376 nmol/day<br>u-NMN: 14,919 nmol/day | Right<br>(RP) | 2 months | n.p. |
| (12) | 42 M | u-VMA: 31 mg/day | Right<br>(RP+IT) | 1 month | n.p. |
| (13) | 38 M | s-MN 14.0 nmol/L<br>s-NMN 24.3 nmol/L | Left<br>(IP) | 4.5 months | MEN 2A. Bilateral adrenal enlargement. Damage control surgery for hemorrhage. |
| (14) | 63 M | Not measured<br>(Pathological diagnosis only) | Left<br>(RP) | 1 month | At preoperative evaluation, $^{131}$I-MIBG was positive, but urinary catecholamine levels were normal. |
| (2) | 40M | A: 8.83 ng/mL<br>NA: 45.99 ng/mL<br>DA: 6.5 ng/mL | Left<br>(RP) | 2 hours | Dead six days after surgery. |

A: adrenaline, DP: dopamine, F: female, IP: intraperitoneal, IT: intratumoral, M: male, MEN 2A: multiple endocrine neoplasia type 2A, $^{131}$I-MIBG: 131I-meta-iodobenzylguanidine, NA: noradrenaline, RP: retroperitoneal, u-MN: urinary metanephrine, u-NMN: urinary normetanephrine, u-VMA: urinary vanillylmandelic acid

In conclusion, stabilizing the hemodynamic status with TAE followed by adrenalectomy may be a suitable option for treating pheochromocytoma rupture. However, a careful evaluation is important, as there are some cases in which hemodynamic stabilization is difficult to achieve with TAE alone.

**The authors state that they have no Conflict of Interest (COI).**

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