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Malignant pheochromocytoma with liver invasion treated successfully by combined retroperitoneal laparoscopic control of arterial in-flow followed by open hepatectomy: A case report

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ABSTRACT

INTRODUCTION: Pheochromocytoma surgery is generally challenging for surgeons and anesthesiologists for cardiovascular complications.
PRESENTATION OF CASE: A 54-year-old Japanese man was found to have a large right pheochromocytoma infiltrating the posterior part of his liver and vena cava and multiple lung metastases. After retroperitoneal laparoscopic dissection of the dorsal side of the tumor and ligation of the feeding vessels, total resection of the primary tumor, extended posterior sectional hepatectomy, and partial vena cava resection were performed by open surgery via a thoracoabdominal approach. Abundant congestive bleeding with instability of vital signs occurred during transection. It could be finally controlled by dissect the remnant feeding artery in the inmost space. Prior control of arterial in-flow enabled successful completion of the planned surgical procedure. The patient has now survived for 27 months since resection of the primary lesion.
CONCLUSION: Ligation of the feeding arteries to this hypervascular catecholamine-releasing tumor via a retroperitoneal laparoscopic approach prior to performing combined organ resection facilitated successful excision of this large malignant pheochromocytoma.

1. Introduction

The WHO classification of 2017 recommends that PPGLs be managed as malignant neoplasms with some metastatic potential [1]. The standard first-line treatment for metastatic PPGLs is resection of the primary tumor [2]. This is generally challenging for surgeons and anesthesiologists because the procedure is complex and life-threatening cardiovascular complications may occur during it. Recent reports have described combined resection of adrenal gland or renal malignancies with surrounding affected organs, including the liver. Using a team comprising urological and general surgeons, we have also performed such aggressive surgery [3–6]. Despite remnant distant metastases, long-term survival with postoperative systemic therapy can be achieved. Therefore, we consider that reduction of the mass of primary urological malignancies is essential [4–6].

We herein report a patient with a large pheochromocytoma with liver invasion and lung and contralateral adrenal gland metastases. We succeeded in achieving total excision of the tumor by performing retroperitoneal laparoscopic dissection of the dorsal side of the tumor followed by excision with partial hepatectomy via a thoracoabdominal approach.

2. Presentation of case

A 54-year-old Japanese man with a history of intellectual disability and unattended hypertension presented with abdominal distention. His father had a history of a pheochromocytoma. Computed tomography (CT) revealed a large 14-cm diameter tumor in the right adrenal gland with direct invasion of the liver (Fig. 1A). Multiple metastases were also identified in the left adrenal gland and lung. His serum noradrenaline and dopamine concentrations were 22,621 pg/mL and 67 pg/mL, respectively. Metaiodobenzylguanidine scintigraphy and 18F-fluoro-2-deoxyglucose positron emission tomography/CT showed abnormal uptake in these tumors (Fig. 1B). Enhanced CT demonstrated multiple feeding arteries aris-

Abbreviations: WHO, World Health Organization; PPGLs, pheochromocytomas and paragangliomas; CT, computed tomography.

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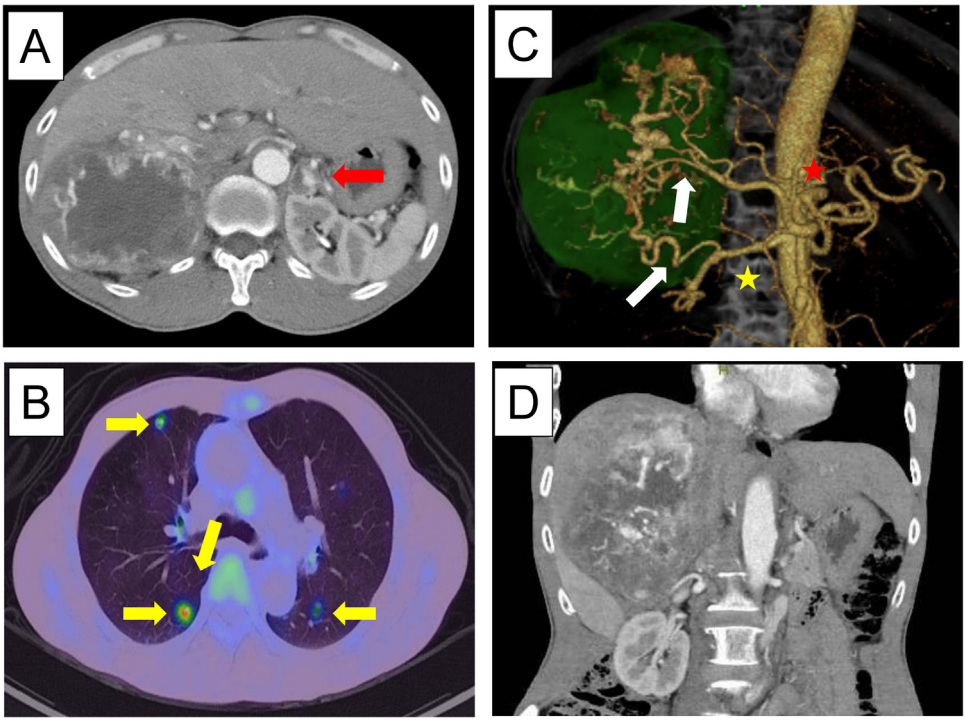

Fig. 1. **A**. Axial contrast-enhanced computed tomography (CT) image showing a 14-cm diameter right adrenal tumor and left adrenal metastasis (red arrow). **B**. Coronal CT showing feeding arteries arising from the renal artery (yellow arrows). **C**. Three-dimensional CT showing many feeding arteries (white arrows) branching from the celiac trunk (red star) and renal artery (yellow star). **D**. 18F-fluoro-2-deoxyglucose positron emission tomography/computed tomography showing abnormal uptake in lung metastases (yellow arrows).

ing from the celiac and renal arteries (Fig. 1C,D). Prior to surgery, administering of an alpha-blocker doxazosin was initiated to 12 mg/day, for blood pressure control and increasing of circulating blood volumes. Confirmation of maintenance of the functional reserve of the liver, it being anticipated that extended posterior sectionectomy of the liver would be necessary.

2.1. Surgical procedure

The patient was initially placed in a left lateral position under general anesthesia. Using a retroperitoneal laparoscopic approach and four-ports technique, the abnormal feeder adrenal arteries arising from the right renal artery were ligated with Hem-o-lok® clips

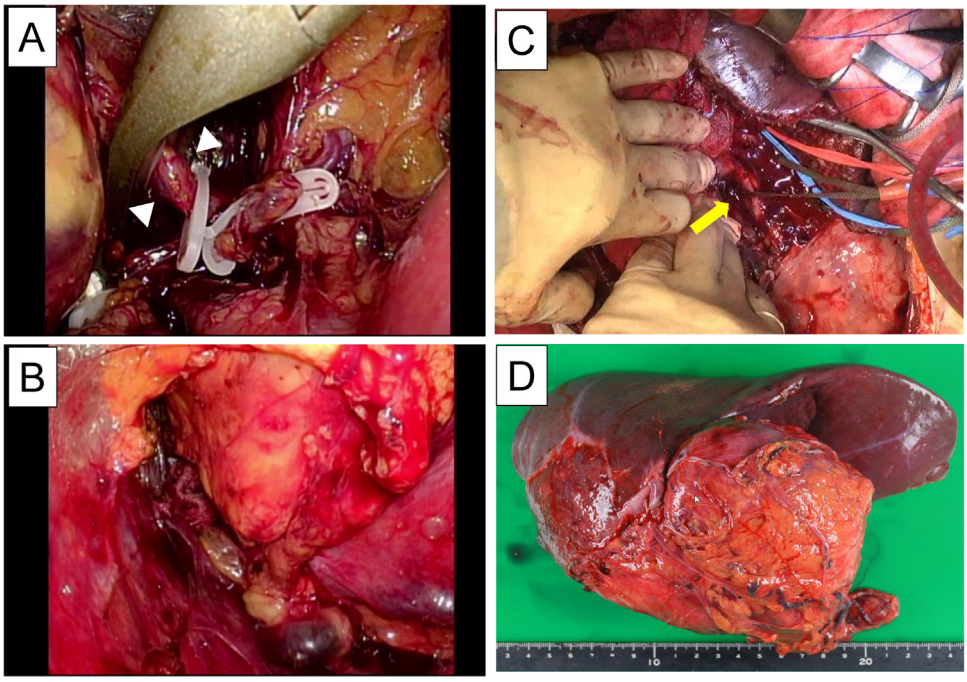

Fig. 2. **A**. The tumor's feeding arteries were ligated using Hem-o-lok clips. **B**. The dorsal side of the tumor was dissected via a retroperitoneal laparoscopic approach. **C**. A partial hepatectomy achieved complete resection of the tumor. The adrenal vein (yellow arrow), hepatic artery (blue tape), and portal vein (red tape) have been identified. **D**. Macroscopic appearance of the tumor with the posterior segment of the liver. Liver invasion is apparent (white arrow).

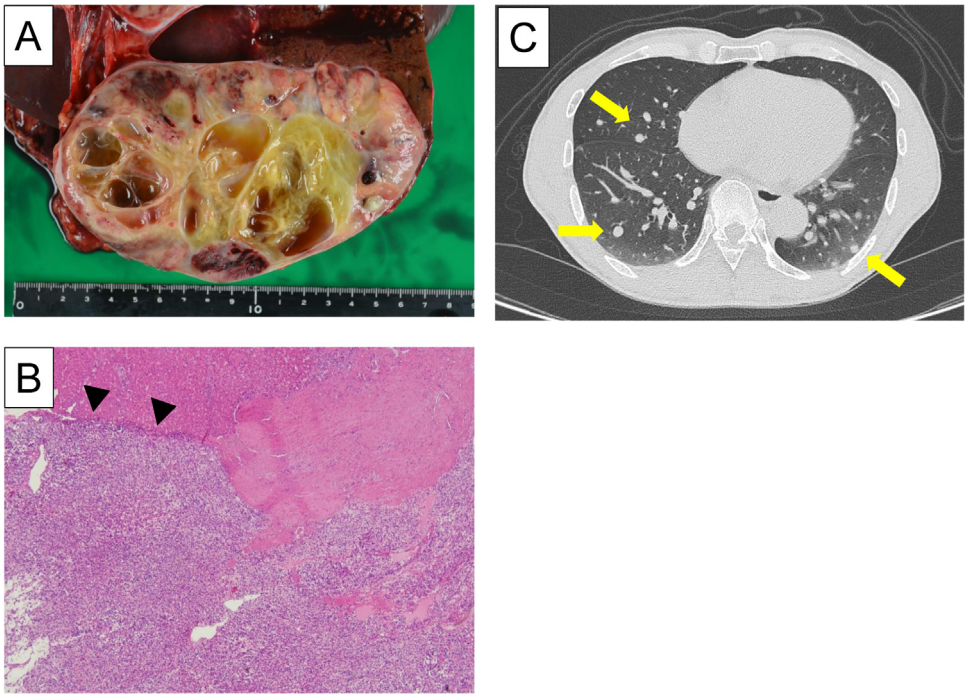

Fig. 3. A. Macroscopically, the tumor appeared as a gray and yellowish, well-circumscribed, cystic mass. **B**. Photomicrograph showing invasion of the liver parenchyma by tumor cells (black arrow) (hematoxylin–eosin, 40×). **C**. CT image showing progressive lung metastases 27 months after resection of the primary tumor (yellow arrows).

(Fig. 2A), after which the feeding arteries arising on the dorsal side of the tumor were ligated as completely as possible using LigaSure™ or clips (Fig. 2B). The patient was then placed in a left semi-lateral supine position and a thoracoabdominal incision made through the seventh intercostal space between the posterior axillary and median trans-rectal lines. This revealed extensive adhesions between the tumor and posterior segment of the liver, prompting a decision to perform a partial hepatectomy. Despite the retro-hepatic space having already been dissected during the initial laparoscopic procedure, mobilization of the liver around the subdiaphragmatic space was difficult because of tumor compression. We therefore decided on an anterior approach for the hepatectomy. The hepatic portal in-flow was transected and parenchymal resection performed using a hemi-hepatic in-flow occlusion procedure (Pringle's maneuver). Next, the posterior in-flow and hepatic veins were transected. However, subsequent massive congestive bleeding from the transected liver prevented transection of all feeder vessels. It was then found that the cranial space around the tumor behind the liver still harbored remnant arterial feeding vessels, which was poorly confirmed on preoperative images. These vessels were transected using LigaSure, achieving control of the congestive bleeding. The enlarged right adrenal vein was also transected (Fig. 2C), after which the tumor was removed en-bloc with the posterior segment of the liver (Fig. 2D). Thus, resection of multiple vessels enabled complete tumor resection, including all direct tumor invasion and thrombus in the right-sided vena cava. The total operation time was 420 min, including 146 min for the laparoscopic procedure. Direct manipulation of the tumor resulted in temporary hypertension, which the anesthesiologist was able to control. The estimated blood loss was 3500 mL because of the congestive bleeding, which necessitated blood transfusion. After the surgery, the patient had a normal blood pressure and plasma catecholamine concentrations and developed no serious complications.

Macroscopic examination of the operative specimen revealed a gray and yellowish, well-circumscribed, cystic mass (Fig. 3A). Microscopic examination resulted in a diagnosis of poorly-differentiated pheochromocytoma with malignant potential, classified according to the Adrenal Pheochromocytoma and Paraganglioma classification as 8, scores with liver invasion (Fig. 3B) and negative surgical margins.

The patient refused systemic chemotherapy for distant metastases. With a low dose of doxazosin (4 mg/day), normal blood pressure, and progressive lung metastases, he has now survived for 27 months since the surgery (Fig. 3C).

3. Discussion

PPGLs originate from chromaffin cells in the adrenal medulla or extra-adrenal autonomic paraganglia [1]. In approximately 30% of cases, PPGLs are associated with a genetic syndrome [2]. They have the potential to metastasize to non-chromaffin sites distant from the primary tumor, the common sites of metastases being lymph nodes, bone, liver, and lung [1]. The 5-year survival rate of metastatic PPGL is reportedly 50% or less [2]. It is considered that surgical excision can potentially improve overall survival of patients with metastatic PPGL [2]. In the present case, excision of the primary site achieved control of hypertension and normalization of catecholamine concentrations. Moreover, the patient has now survived without critical complications for over 27 months despite having progressive distant metastases. Ongoing surveillance is needed to gain these survival benefits.

Surgical management of gigantic PPGLs is currently controversial because their rarity means that surgeons have limited experience of dealing with them. Considerable surgical difficulties may be encountered as a result of hypervascularity, adhesion to adjacent organs, and serious adrenergic events, including cardiac arrest [7]. In the present case, we succeeded in safely transecting the adrenal feeder arteries and dissecting the dorsal side of the tumor via a retroperitoneal laparoscopic approach. To our knowledge, this is the first reported case of managing a patient with a PPGL and liver invasion using a laparoscope-assisted procedure. We have previously reported that retroperitoneal laparoscopic dissection can be an effective preparatory step toward total extraction of large malignancies originating in the retroperitoneum together

with involved surrounding organs, including the liver [3–6]. During surgery for large PPGLs producing a lot of catecholamines, direct manipulation of the tumor frequently precipitates a hypertensive crisis despite preoperative treatment with an alpha blocker. In this case, laparoscopic transection of adrenal arteries prior to excision of the tumor succeeded in preventing a severe hypertensive crisis during the invasive part of the surgery, which included partial hepatectomy.

A retroperitoneal laparoscopy-assisted approach has been already become standard in the urological surgery and a similar approach named "Retlap" was recently reported by Kiguchi et al. in the field of pancreatic surgery [8,9]. We here utilized the same strategy for liver surgery. The combination of a retroperitoneal laparoscopic procedure and open surgery may enhance safety and decrease blood loss. However, in the present case, feeding arteries originating from the aorta or sub-diaphragm vessels on the cranial side had been poorly detected by enhanced imaging. To start the liver transection without ligating these vessels resulted in out-flow block with congestive bleeding. Transection of too many out-flow vessels is a potential pitfall in patients with large hypervascular pheochromocytomas until complete ligation of in-flow; their drainage veins must be preserved as much as possible. This case has been reported in line with the SCARE guideline [10].

4. Conclusion

Resection of large PPGLs with invasion or metastasis is now considered indicated. A combination of early ligation of feeding arteries via a retroperitoneal laparoscopic approach followed by open surgery is a useful procedure for managing advanced adrenal gland malignancies.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

This report is not research studies involving patients.

Consent

The patient gave informed consent for publication of the details of his case, along with appropriate images. No information that would enable his identification has been provided.

Author contribution

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Registration of research studies

None.

Guarantor

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