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Laparoscopic Resection of Subclinical Functioning Para-aortic Paraganglioma

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Introduction: Extra-adrenal pheochromocytomas (paragangliomas) are neuroendocrine tumors derived from extra-adrenal chromaffin cells. Although laparoscopic resection of adrenal pheochromocytomas is a common procedure, there are few reports of the use of this approach in extra-adrenal para-aortic paragangliomas. Here, we report the case of a patient with a subclinical functioning para-aortic paraganglioma that was successfully resected laparoscopically.

Case presentation: A 58-year-old man was referred to our department for treatment of a para-aortic tumor after endoscopic submucosal dissection of early-stage colorectal cancer. Positron emission tomography-computed tomography showed abnormal accumulation by the para-aortic tumor. During its laparoscopic resection, the patient's blood pressure unexpectedly rose to over 180 mmHg, which suggested that the tumor was a paraganglioma. The diagnosis was confirmed by immunohistochemical staining, which showed chromogranin-positive cells forming a Zellballen pattern. The operation was successfully completed, and the patient's postoperative course was uneventful.

Conclusion: Laparoscopic resection may be a suitable procedure for the treatment of retroperitoneal paraganglioma.

Key words: Ectopic pheochromocytoma – Laparoscopic surgery – Paraganglioma

Paragangliomas are neuroendocrine tumors derived from extra-adrenal chromaffin cells. They most commonly occur in the retroperitoneum, along the aorta, in close association with the sympathetic chain. Unlike pheochromocytomas derived from the adrenal medulla, 40% of retroperitoneal pheochromocytomas lack hormonal activity.[1] Although laparoscopic resection of adrenal pheochromocytoma is

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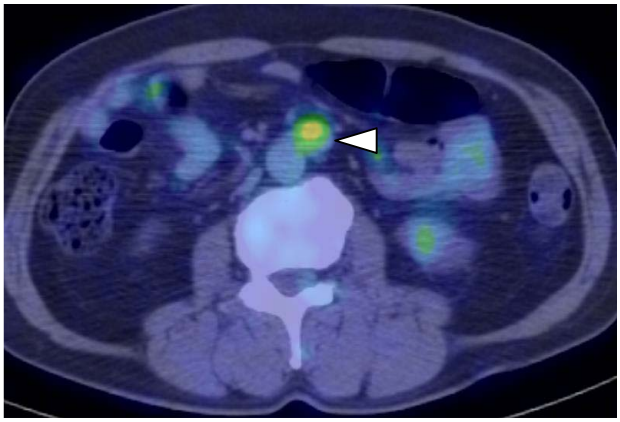

Fig. 1 PET-CT findings. Abnormal accumulation in the tumor can be seen (arrowhead).

a common procedure, there have been few reports of the use of this approach in the surgical treatment of extra-adrenal para-aortic paragangliomas.[2–4] In this report, we describe the successful laparoscopic resection of a subclinical functioning para-aortic paraganglioma.

Case Presentation

A 58-year-old man was referred to our hospital for endoscopic treatment of early-stage transverse colon cancer. Routine preoperative enhanced computed tomography (CT) revealed a para-aortic tumor. After endoscopic submucosal dissection of the transverse colon cancer, the patient was referred to our department. He had no familial history of hypertension and his blood pressure was within the normal range. Laboratory tests showed elevated carcinoembryonic antigen (4.7 ng/mL). Positron emission tomography (PET)-CT showed abnormal tracer accumulation by the tumor (Fig. 1). Because the transverse colon cancer was confined to the mucosa, the likelihood of lymph node metastasis was considered to be very low. Based on the imaging findings, malignant lymphoma was included in the differential diagnosis. Since the tumor was adjacent to the abdominal aorta and intestines, the patient did not undergo ultrasound- or CT-guided biopsy, given the anticipated difficulty in performing either procedure.[5] Instead, laparoscopic resection of the para-aortic tumor was planned, which would also allow a definite diagnosis.

The patient was placed under general anesthesia and in the supine position. The first 12-mm trocar was placed using a standard umbilical cut-down technique. Carbon dioxide (CO_2) insufflation was used to establish a pneumoperitoneum; intraabdominal pressure was maintained at 8 mmHg. Under laparoscopic guidance, two 5-mm trocars were inserted into the right upper and lower abdominal quadrants. The tumor was identified on the abdominal aorta, indenting the peritoneum, and was subsequently mobilized using laparoscopic coagulating shears (SonoSurg, Olympus Medical Systems, Tokyo, Japan) (Fig. 2a). However, just after initial manipulation of the tumor, the patient's blood pressure rose to $>$ 180 mmHg and then, after complete removal of the tumor, immediately fell to $<$ 100 mmHg. The operation was temporarily stopped to allow blood pressure control by the anesthesiologist. After its completion, the peritoneal defect was closed. The operative duration was 215 minutes, and total blood loss was 10 mL. The resected specimen was white, solid, and unencapsulated (Fig. 2b). The patient's postoperative course was uneventful.

Histopathologic examination of the specimen revealed large cells consistent with neuroendocrine tumor cells. They contained acidophilic granules and formed a Zellballen pattern. Immunohistochemical staining was positive for chromogranin,

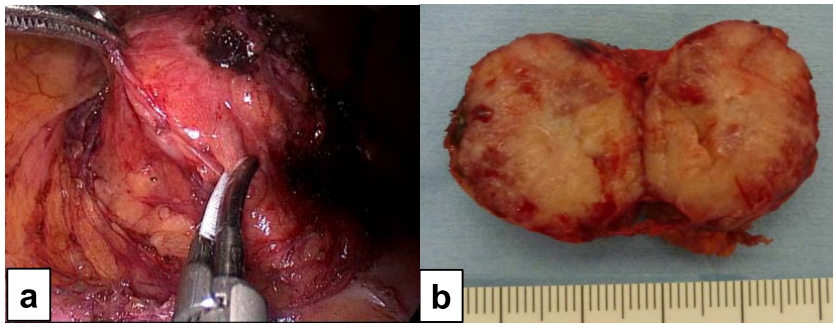

Fig. 2 Intraoperative findings and the resected specimen. (a) Tumor mobilization. (b) The white, unencapsulated specimen.

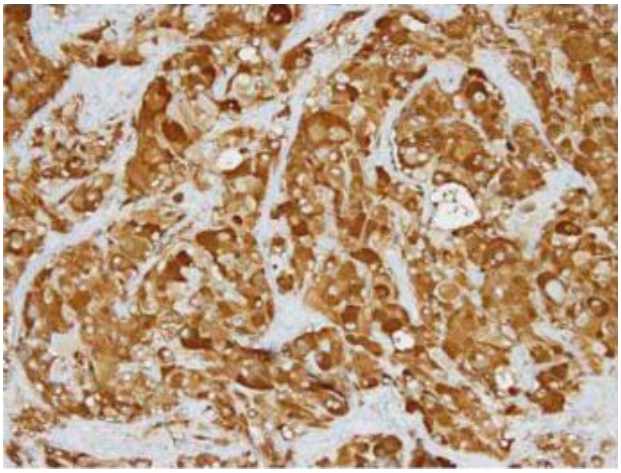

Fig. 3 Immunohistochemical findings. Chromogranin-positive tumor cells form a Zellballen pattern.

which confirmed the neuroendocrine origin of this tumor (Fig. 3). CT performed 22 months after surgery showed no tumor recurrence.

Discussion

Pheochromocytomas are derived from the chromaffin cells of the sympathetic nervous system and are usually located in the adrenal gland. Extra-adrenal pheochromocytomas are referred to as paragangliomas. In the pediatric population, primary adrenal pheochromocytoma is the most common presentation; however, pediatric paragangliomas are relatively rare and in approximately 50% of patients originate in the head and neck.[6] In adults, by contrast, paragangliomas originate in the head and neck region in only 3% of cases, whereas 85% of these tumors occur in the abdomen.[7] Abdominal paragangliomas are commonly located in the retroperitoneum and along the aorta, between the origin of the inferior mesenteric artery and the aortic bifurcation, where the organ of Zuckerkandl is located.[8]

Paragangliomas that secrete catecholamines cause characteristic symptoms, including headache, hypertension, palpitation, and sweating.[1] However, approximately 40% are not hormone-secreting and the patients are therefore asymptomatic, which complicates the preoperative diagnosis. Blood or urinary levels of catecholamines and metanephrines and their metabolic products are useful laboratory tests in the diagnosis of both adrenal and extra-adrenal symptomatic paragangliomas,[9] but hormonal measurements may be normal[1] and thus nondiagnostic. CT is able to localize extra-adrenal tumors, including paragangliomas, which commonly appear as hypervascular masses. On T2-weighted magnetic resonance imaging, paragangliomas will also be seen as hyperintense masses. I^{131}-MIBG (metaiodobenzylguanidine) scintigraphy is highly specific in localizing paragangliomas,[8] although in at least in 1 report[10] fluorodeoxyglucose (FDG)-PET was superior to MIBG scintigraphy.

Because our patient was normotensive and had no familial history of hypertension or paraganglioma, the preoperative differential diagnosis did not include this tumor. The preoperative assessment was therefore insufficient, which resulted in intraoperative hypertension, a very common but high-risk complication in patients undergoing surgery for pheochromocytoma. In our patient, despite the development of intraoperative hypertension, the operation was safely completed by stopping the procedure to allow blood pressure control by the anesthesiologist. Our experience is a reminder of the importance of close cooperation between the surgeon and the anesthesiologist to avoid intraoperative hypertension but also to allow its prompt and adequate control should it nonetheless develop. As paragangliomas are difficult to diagnosis preoperatively, we recommend the presurgical measurement of hormone levels in all patients with para-aortic tumors of unknown type, even in the absence of hypertension, to ensure the safe completion of surgery for these tumors.

The definitive treatment for retroperitoneal paraganglioma is surgical resection, as the efficacy of chemotherapy is limited. Although laparoscopic adrenalectomy is the most commonly used surgical approach for pheochromocytoma, it is not widely accepted for extra-adrenal paraganglioma. However, the local recurrence rate of these tumors is low and wide surgical margins are unnecessary during tumor resection. Therefore, in most cases retroperitoneal paragangliomas can be safely resected laparoscopically, as described in several recent reports.[2–4] Because laparoscopic resection is less invasive than laparotomy, the incidence of intraoperative hypertension is low.

Extra-adrenal paragangliomas are seldom malignant. However, the histologic diagnosis of malignant paragangliomas is difficult, and most are diagnosed based on clinical findings, such as the development of metastasis or recurrence.[8] Therefore, the long-term follow-up of these patients should include regular biologic and clinical exam-

inations aimed at detecting disease recurrence or metastasis.

This case demonstrates the feasibility of laparoscopic resection of a subclinical functioning para-aortic paraganglioma. Moreover, it highlights the importance of preoperative hormonal assessment to ensure the intraoperative status of patients undergoing resection of a para-aortic tumor.

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