—Case Reports—

Pediatric Retroperitoneal Paraganglioma Invading the Inferior Vena Cava: A Case Report and Literature Review

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Paraganglioma, a catecholamine-producing tumor originating in extra-adrenal paraganglion cells, is rare in children. Although diagnosis of paraganglioma is based on the presence of catecholamine symptoms, some patients lack such symptoms. Delayed diagnosis is associated with tumor growth and invasion of surrounding vessels. Herein, we report a case of pediatric retroperitoneal paraganglioma invading the inferior vena cava. The tumor was completely resected and the patient has been free of recurrence for 2 years. Our findings suggest that complete resection can help prevent recurrence in cases of invasion of the inferior vena cava. (J Nippon Med Sch 2024; 91: 554–559)

Key words: retroperitoneal paraganglioma, invasion, pediatric surgery

Introduction

Paraganglioma is a catecholamine-producing tumor originating from extra-adrenal paraganglion cells and is commonly characterized by concomitant catecholamine symptoms. However, some patients do not present with catecholamine symptoms. Paragangliomas grow silently and infiltrate surrounding vessels. Herein, we report a pediatric case of retroperitoneal paraganglioma that was completely resected despite invasion of the inferior vena cava and review the literature.

Case Report

A 15-year-old female presented with low back pain. A retroperitoneal tumor was detected on magnetic resonance imaging (MRI), and the patient was admitted to our hospital. Her past medical history and family history were unremarkable. The physical examination results were as follows: height, 163 cm; weight, 60 kg; body temperature, 36.8°C; blood pressure, 124/82 mm Hg; and pulse rate, 72 beats per min. Constipation was not observed. A mass was palpated at the right hypochondrium. The following findings were observed on a preoperative hormonal study: urinary adrenaline level, 19.4 (normal value: 3.4-26.9) μg/dL; and dopamine level, 1,453.5 (normal value: 365-961.5) μg/dL. Blood adrenaline and dopamine levels were normal at 52 (range: 0-100) pg/mL and 17 (range: 0-20) pg/mL. However, her urinary and blood noradrenaline levels were extremely high: 2,053.6 (normal value: 48.6-168.4) μg/dL and 5,294 (normal range: 0-450) pg/mL, respectively (**Fig. 1**).

MRI revealed a retroperitoneal mass (diameter, approximately 10 cm) at the right extra-adrenal gland. Computed tomography (CT) scanning revealed that the tumor was highly vascularized and invaded the inferior vena cava. Further, there was a satellite lesion at the left side of the aorta (**Fig. 2a, b**). The retroperitoneal tumor had a high ^{123}I-MIBG uptake on scintigraphy, but the satellite tumor had no ^{123}I-MIBG uptake (**Fig. 3**). The preoperative diagnosis was paraganglioma, and surgery was performed after the use of an alpha blocker and administration of normal saline solution to correct hypertension and hypovolemia caused by excess catecholamine activ-

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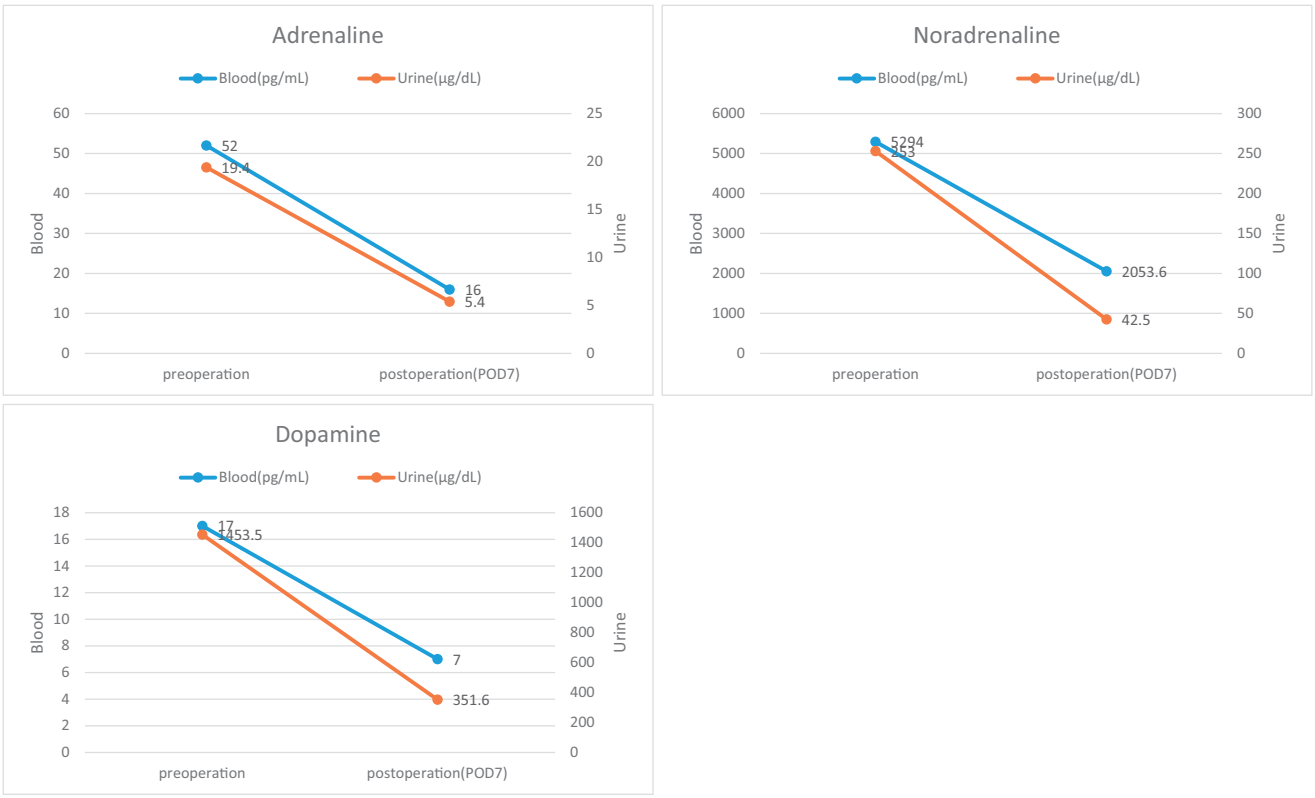

Fig. 1 Results of hormone testing

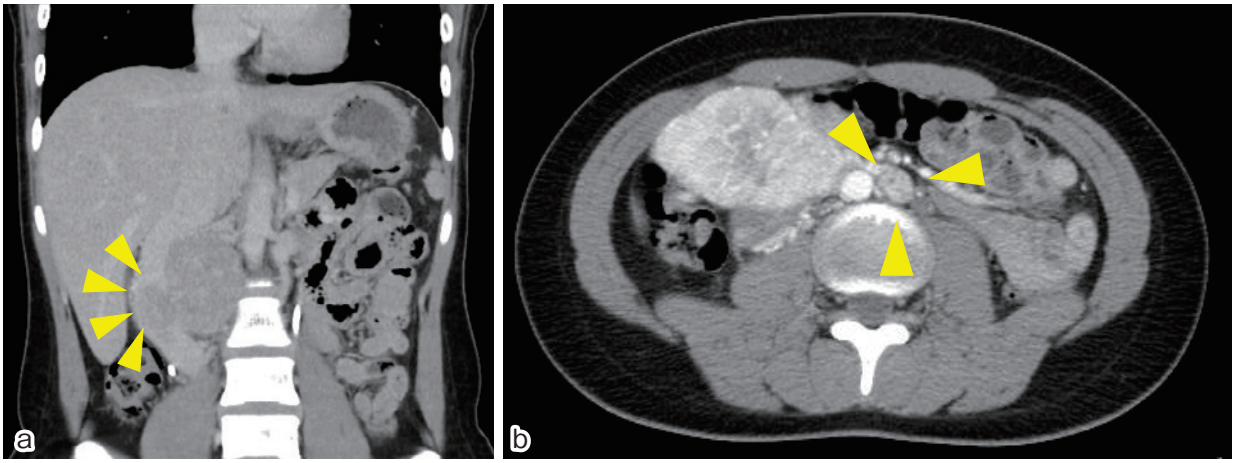

Fig. 2 CT scan showing tumor invasion of the inferior vena cava (a) and a satellite lesion at the left side of the aorta (b)

ity[1]. Specifically, she was started on doxazosin 1 mg at 7 days preoperatively, which was increased to 2 mg at 4 days preoperatively and 4 mg at 2 days preoperatively. A maintenance dose of normal saline solution was started on the day before surgery. Her blood pressure stabilized at 102/58 preoperatively.

Laparotomy showed that the mass was derived from the retroperitoneal space (**Fig. 4a**). Preoperatively, CT scanning and MRI revealed that the tumor invaded the inferior vena cava. Intraoperative ultrasonographic evaluation of the inferior vena cava confirmed invasion.

First, the tumor, excluding tissue invading the inferior vena cava, was cautiously resected from the surrounding areas. Second, the inferior vena cava was clamped, and a section of it was resected together with the tumor. Third, the inferior vena cava was reconstructed with 5-0

PROLENE running suture without a vascular graft. Finally, the satellite lesion at the left side of the aorta was excised, and the tumor was completely removed (**Fig. 4 b**). The operation time was 693 minutes and the inferior vena cava blocking time was 8 minutes. Intraoperative blood loss was 1,155 mL and intraoperative blood cell transfusion volume was 560 mL. Blood pressure was 110/90, preoperatively; 85/35 to 152/96, intraoperatively; and 92/42, postoperatively.

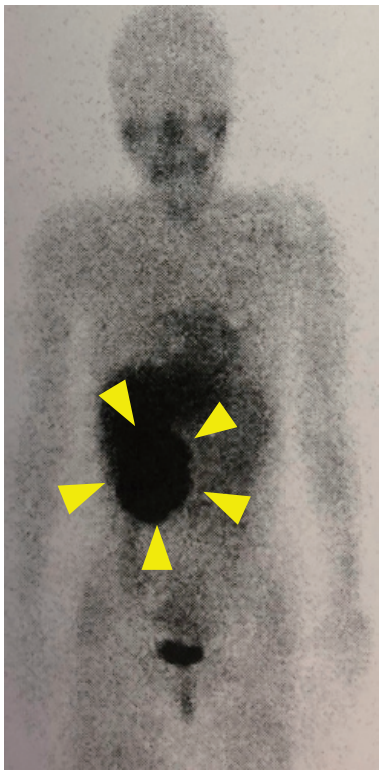

Fig. 3 ^{123}I-MIBG scintigram showing high uptake in the retroperitoneal tumor and no uptake in the satellite tumor

Immunohistochemical staining with chromogranin A and S100 yielded positive results, and the Ki-67 labeling index was 2.5%-2.7% (**Fig. 5**). The Grading System for Adrenal Pheochromocytoma and Paraganglioma (GAPP) score was 4, indicating a diagnosis of moderately differentiated sympathetic paraganglioma. The patient's postoperative course was uneventful, and her postoperative noradrenaline levels normalized (**Fig. 1**). At 2 years postoperatively, no recurrence has been observed.

Discussion

Paraganglioma is a catecholamine-producing tumor originating in extra-adrenal paraganglion cells. The incidence of paraganglioma is lower in children (1 per 3 million to 1 per 7 million) than in adults (1 per million)[2].

Few cases of pediatric paraganglioma have been reported[1–13]. Previous studies suggest that the average age at diagnosis in pediatric cases is 11 years and that the male-to-female ratio is 1:1 (**Table 1**)[4–13]. Concomitant catecholamine symptoms include hypertension, headache, excessive perspiration, palpation, tremor, and facial pallor. However, the primary symptom in children is hypertension. Secondary hypertension caused by paraganglioma is rare[1,14]. The tumor is primarily located at the retroperitoneum in children with paraganglioma[6,7,9,11,13]. Further, the risk of recurrence is believed to be high in patients with the succinate dehydrogenase B (SDHB) germline mutation[1–3]. Moreover, germline mutation and metastasis are more frequent in pediatric pheochromocy-

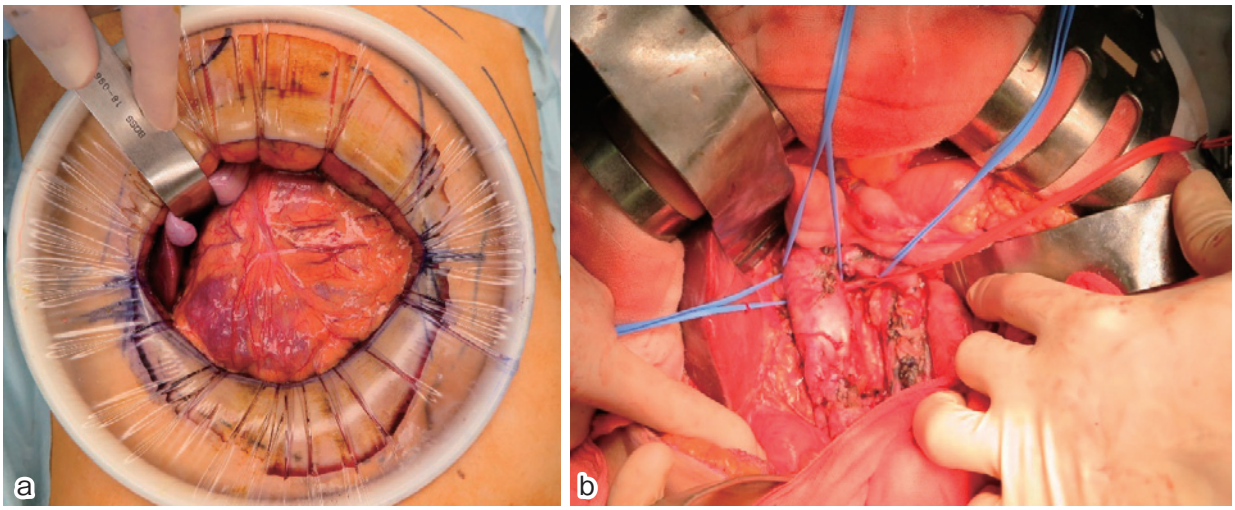

Fig. 4 Intraoperative findings before removal of the tumor (a) and after removal of the tumor (b)

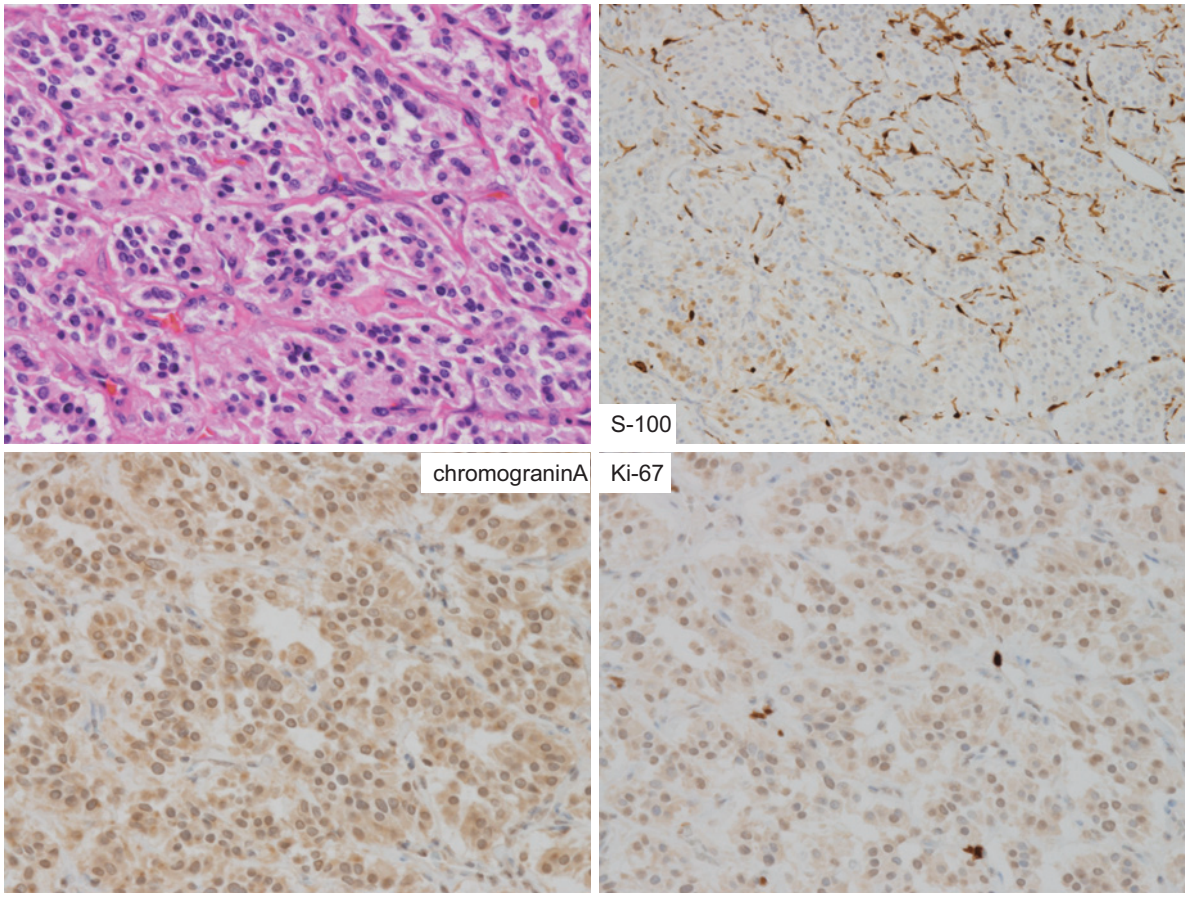

Fig. 5 Histopathological findings: Hematoxylin and eosin staining, immunohistochemical staining with chromogranin A, S100 and the Ki-67

tomas and paragangliomas than in adult cases[2].

According to the 2018 Japan Endocrine Society clinical practice guidelines on pheochromocytoma and paraganglioma[15], a paraganglioma diagnosis is confirmed on the basis of urinary metanephrine and catecholamine levels, ^{123}I-MIBG uptake in the tumor on scintigraphy, and pathological findings. Patients with paraganglioma test positive in immunohistochemical staining with chromogranin A. Our patient presented with high urinary noradrenaline levels and ^{123}I-MIBG uptake in the tumor on scintigraphy and tested positive on immunohistochemical staining with chromogranin, thus confirming a diagnosis of paraganglioma.

Preoperative CT scanning and MRI are convenient for evaluating tumor site, invasion of surrounding organs, and metastasis. Paraganglioma is a hypervascular tumor, and large tumors commonly become necrotic[16]. Malignant paragangliomas are usually larger, more heterogeneous, and more likely to have ill-defined margins[3,16]. In our case, MRI revealed a hypervascular retroperitoneal mass at the right extra-adrenal gland. However, necrosis was not observed on CT scan. A satellite tumor and invasion of the inferior vena cava were observed. Because the tumor was well-circumscribed and infiltration of surrounding organs was limited, complete resection was performed.

Surgery is the primary treatment for paraganglioma. However, indications are unclear for preoperative interventions such as chemotherapy and embolization. Preoperative chemotherapy and embolization of the feeding artery were attempted. Previous studies reported outcomes for cytoreduction[11,13]. However, these strategies increase the risk of hypertension crisis, and embolization is correlated with a risk of organ ischemia[13]. Although the tumor invaded the inferior vena cava in our patient, surgery was performed without preoperative intervention.

Long-term follow-up is needed because paraganglioma recurrence is a concern. If the patient's condition is stable, annual laboratory testing, including blood and urinary catecholamine, is essential. Imaging evaluation is recommended if the catecholamine level is high.

This case of pediatric retroperitoneal paraganglioma in-

Table 1 Characteristics of pediatric paraganglioma cases

Author	Age	Gender	Symptoms	Hyper-tension	Germline mutation	Size	Location	Metastasis at opera-tion	Vasucular reconstu-ruction	Follow-up time	Recurrence/Location
Takishima et al.[4]	9 y	female	vomiting, nocturia	(+)	no date	3×4 cm	Rt.abdominal cavity	(–)	(–)	about 1 year	(–)
Muhammad et al.[5]	13 y	female	hematuria	(+)	no date	no date	Bladder	(–)	(–)	no date	(–)
Mcgowan et al.[6]	13 y	male	headache, chest pain	(+)	SDHB	1.6 cm	Rt.retroperitoneum	lymph node	(–)	2 years	2 years later/Rt adrenal bed, lymph node
Luiz et al.[7]	12 y	male	headache, diphoresis, coma	(+)	SDHB	9 cm 2 cm	Retroperitoneum Rt.retroperitoneum	(–)	(–)	25 years	2 years later/bone, 14 years later/bones and lymph nodes
Cao et al.[8]	13 y	female	tachycardia	(+)	no date	4×6×4 cm	Abdominal cavity	(–)	(–)	3 years	3 years later/lymph nodes
Imamura et al.[9]	6 y	female	headache, convulsion, diphoresis	(+)	SDHB	4×9×3 cm	Lt.retroperitoneum	(–)	(–)	26 months	(–)
Cui et al.[10]	9 y	female	headache, weight loss	(+)	no date	4.6×3.1 cm	Rt.abdominal cavity	(–)	(–)	about 2 months	(–)
Bourke et al.[11]	10 y	male	back pain	no date	no date	12×14 cm	Rt retroperitoneum	(–)	(+)	3 years	(–)
Yuan et al.[12]	9 y	male	headache, vomiting	(+)	no date	7×5 cm	Posterior mediastinum	(–)	(–)	1 year	(–)
De Paula Miranda et al.[13]	11 y	male	headache, tachcardia	(+)	no date	12×9×7 cm	Retroperitoneum	bone	(–)	6 months	(–)
	12 y	male	headache, palpitation, left scrotal swelling	(+)	no date	12 cm	Lt.retroperitoneum	(–)	(–)	6 weeks	6 weeks later/bone
Our case	15 y	female	back pain	(–)	no date	11×9 cm 1.5 cm×1.5 cm	Rt.retroperitoneum Lt.retroperitoneum	(–)	(+)	2 years	(–)

vading the inferior vena cava suggests that complete resection is feasible even in cases of invasion of the inferior vena cava.

Conflict of Interest: None declared.

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