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CASE REPORT

Improvement in renal dysfunction and symptoms after laparoscopic adrenalectomy in a patient with pheochromocytoma complicated by renal dysfunction

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Abstract A 70-year-old patient who was undergoing treatment for diabetes mellitus and chronic hepatitis was admitted to our hospital for evaluation of a tumor in the left adrenal gland (50 × 45 mm) and renal failure. On the basis of the patient's increased serum concentrations of catecholamines and other metabolites and the results of positron emission tomography (PET), the patient was diagnosed with a pheochromocytoma; iodinated metaiodobenzylguanidine ([^{131}I]MIBG) scintigraphy was insufficient to establish this diagnosis. Subsequently, he underwent surgery for tumor resection. Histological examination suggested the tumor to be a malignant pheochromocytoma. After left adrenalectomy was performed, the elevated catecholamine and metabolite concentrations and the blood pressure were restored to normal, and the patient's symptoms of severe headaches and vertigo reduced. Furthermore, his renal function improved (Cr 2.0–1.2 mg/dl). Our patient exhibited a rare condition of pheochromocytoma complicated by renal failure, which was successfully treated with laparoscopic surgery.

Keywords Malignant pheochromocytoma · Adrenal gland · Renal failure · Catecholamines · Laparoscopic surgery

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Introduction

Pheochromocytoma is an adrenal tumor that secretes catecholamines. It occurs in less than 0.6% patients with hypertension [1, 2]. Catecholamine hypersecretion is the most significant clinical manifestation of the tumor. The tumor can be detected by performing imaging tests such as computed tomography (CT) and magnetic resonance imaging (MRI) of the abdomen. Most pheochromocytomas are benign, with malignant ones accounting for only 10% of these tumors [3]. Clinically, malignancy is detected by the presence of distant metastases, mainly to the liver, lymph nodes, lung, and/or bone, either at the time of diagnosis or during follow-up [4]. Local invasion and various histopathological features can suggest the diagnosis of pheochromocytomas; however, these indicators are not widely accepted. Until recently, open surgery was the only approach for the resection of pheochromocytomas [5]. However, owing to technological advances and the experience gained in minimally invasive surgery, surgeons can now excise these tumors safely and successfully by performing laparoscopic surgery [6].

Here, we report the case of a patient with a diagnosis of pheochromocytoma complicated by the renal failure, with malignancy suspected on histopathological findings. Tumor removal by laparoscopic adrenalectomy improved the renal function and clinical symptoms of the patient.

Case report

A 70-year-old man was admitted to our hospital for the evaluation of a left adrenal tumor and episodic hypertension. He was diagnosed with chronic hepatitis B at the age of 56 years, and was treated with drugs. He complained of general fatigue, headache, and palpitations, and had a weight loss of 15 kg. The patient was admitted to another hospital for examinations to rule out malignancy; an abdominal CT scan was performed and revealed a left adrenal tumor. On admission, the results of his physical examination were normal and were as follows: height, 156 cm; weight, 50.5 kg; blood pressure, 184/115 mmHg; and the heart rate reflected a normal sinus rhythm. The results of laboratory examinations such as routine blood test and analyses for electrolytes, enzymes, and biochemical parameters are listed in Table 1. The results revealed chronic hepatitis B and renal dysfunction. The preoperative basal hormone expression values are shown in Table 2. The plasma levels of noradrenaline (but not adrenaline), urinary noradrenaline, metanephrine, normetanephrine, and vanillylmandelic acid were markedly increased. An abdominal CT scan obtained at the time of admission revealed a round, well-defined, and noncalcified mass (50 × 45 mm) in the left adrenal gland (Fig. 1a). However, a whole-body scan performed using iodinated metaiodobenzylguanidine ([^{131}I]MIBG) did not indicate sufficient ^{131}I accumulation in the adrenal tumor (Fig. 1b) to be suggestive of a pheochromocytoma. [^{18}F]Fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed significant uptake of the radiotracer in the left adrenal tumor (Fig. 1c); therefore, it was clinically diagnosed as a pheochromocytoma.

Pretreatment with α-adrenergic blockers is safe for most patients, even those with hypotension [7]. In the present case, the patient was administered an α-adrenergic antagonist (doxazosin) daily at increasing doses of 0.5–16 mg to increase the circulating blood volume; however, his blood pressure could not be controlled. Subsequently, the patient underwent a laparoscopic left adrenalectomy. The tumor in the excised sample measured 50 × 45 mm in diameter. Histopathological findings (Fig. 2a–h) revealed that the tumor satisfied many of the criteria for diagnosis as a malignant pheochromocytoma; it exhibited capsular and vascular invasion, large confluent nests, necrosis, increased cellularity, marked cellular and nuclear pleomorphism, and cellular monotony, with the smaller cells exhibiting a high nuclear to cytoplasmic ratio. The diagnosis of a pheochromocytoma was confirmed by histological examination, on the basis of which

Table 1 Laboratory data on admission

Blood chemistry	
CRP	0.04 mg/dl
TP	7.9 g/dl
ALB	4.6 g/dl
BUN	37.7 mg/dl
CRE	2.08 mg/dl
UA	6.5 mg/dl
T-Bil	0.5 mg/dl
GOT	128 U/I
GPT	221 U/I
ALP	287 U/I
LDH	394 U/I
GGTP	56 U/I
CHE	214 U/I
AMY	143 U/I
Na	140 mmol/l
K	5.6 mmol/l
Cl	101 mmol/l
Ca	9.6 mg/dl
IP	5.9 mg/dl
TCHO	186 mg/dl
TG	111 mg/dl
HDLC	43 mg/dl
CPK	66 U/I
BS	89 mg/dl
Blood count	
WBC	4,790 μl^{-1}
neu	56%
eos	2.5%
baso	1.5%
mono	5.5%
lym	34.5%
RBC	363×10^4 μl^{-1}
Hb	10.7 g/dl
Ht	33.6%
MCV	92.6 fl
MCH	29.5 pg
MCHC	31.8%
Plt	19.2×10^4 μl^{-1}
Tumor marker	
CEA	3 ng/ml
CA19-9	5 U/ml
HBV-Infection	
HBs-Ag	(+)
HBs-Ab	(−)
HBe-Ag	(−)
HBe-Ab	(+)
HBV-DNA	6.5 LC/ml

Table 2 Transition of the endoclinological findings and renal function

	Normal values	Preoperation	Postoperation
Basal hormonal values			
ACTH (pg/ml)	7–56	54.0	
Cortisol (μg/dl)	6.2–19.4	18.4	
PRA (ng/ml/h)	0.2–2.7	11.6	
Aldosterone (ng/ml)	56.9–150.3	132	
Calcitonin (pg/ml)		30	
Insulin (μIC/ml)	3.0–15.0	4.9	
Urine hormonal values			
17–OHCS (mg/day)	3.4–12.0	5.0	
17-KS (mg/day)	4.6–18.0	4.3	
Catecholamine fractions			
Adrenaline (μg/day)	3.0–15.0	19.2	2.7
Noadrenaline (μg/day)	26.0–121.0	8214	238.5
Dopamine (μg/day)	190.0–740.0	1672.8	826.8
Metanephrine fractions			
Metanephrine (mg/day)	0.05–0.23	0.2	0.07
Normetanephrine (mg/day)	0.07–0.26	11.3	0.44
VMA (mg/day)	1.3–5.1	50.8	3.7
Renal function			
BUN (mg/dl)	7.0–20.0	37.7	22.7
CRE (mg/dl)	0.70–1.30	2.08	1.26
UA (mg/dl)	0.70–1.30	6.5	5.8
CCr (ml/min		26.9	44.80
U-ALB (mg/g.cre)		209.7	81.7
Urinalysis			
pH		6.0	6.5
Pro		(+)	(−)
OB		(−)	(−)
Bil		(−)	(−)
Nit		(−)	(−)
Glu		(−)	(−)
WBC		(−)	(−)

malignancy without distant metastases was suspected. Following left adrenalectomy, the elevated catecholamine and metabolite concentrations returned to normal (Table 2); furthermore, his renal dysfunction improved postoperatively, but it is still under observation (Table 2). The patient's long history of hypertension may have contributed to the renal dysfunction noted postoperatively. However, we were unable to evaluate the mass effect of the pheochromocytoma on renovascular stenosis because renography could not be performed. During the 1-year annual follow-up visit, the catecholamine and metabolite concentrations in the plasma and urine were found to be normal. An abdominal CT scan revealed no abnormal masses.

Discussion

The precise incidence of pheochromocytoma is largely unknown. In one study, autopsies performed on the general population revealed pheochromocytoma in 0.13% cases, and it occurs in less than 1% patients with systemic hypertension [1]. Although hypertension is the most common clinical finding in patients with pheochromocytoma, it may not be uniformly present in all patients. Other findings and associated conditions include abdominal mass, postural hypotension (50–70%), weight loss, and metabolic disturbances, particularly hyperglycemia. In a study conducted at Mayo Clinic on 76 patients with pheochromocytoma, 20% of the patients with paroxysmal hypertension and 30% with

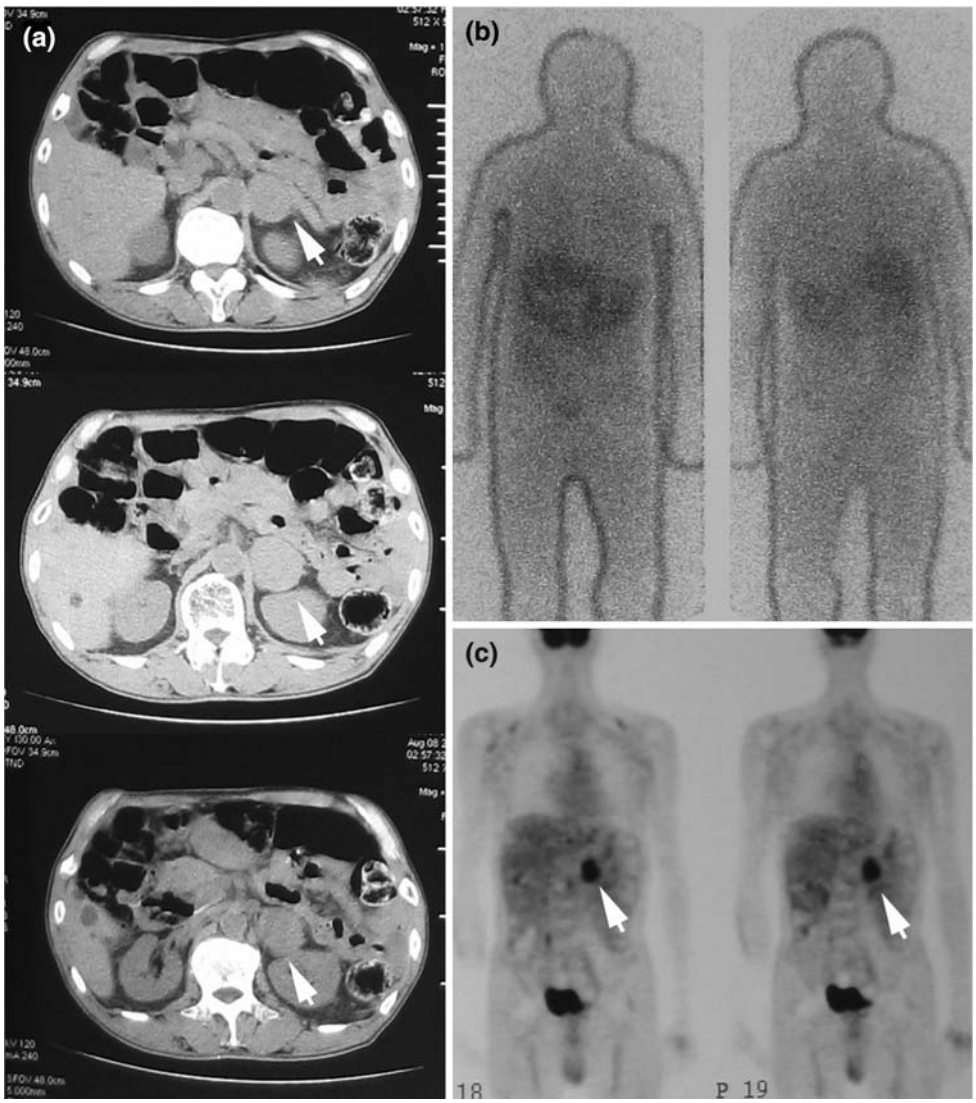

Fig. 1 **a** CT scans of the abdomen, the arrow indicates the left adrenal tumor. **b** [^{123}I]MIBG scintigraphy reveals no accumulation uptake. **c** [^{18}F]FDG-PET demonstrating the uptake in the left adrenal gland

persistent hypertension had fasting hyperglycemia [8]. Although pheochromocytoma complicated by renal dysfunction is rare, our patient had symptoms of renal dysfunction.

The introduction of techniques for precise localization of the pheochromocytoma, availability of new medications and procedures for safeguarding intraoperative hemodynamics, and the innovative surgical techniques dramatically altered the surgical approach adopted for resection of a pheochromocytoma. Until recently, open surgery was the only available approach for pheochromocytoma resection. With technological advances and the experience gained in minimally invasive surgery, surgeons can now excise the tumor safely and successfully by performing laparoscopic surgery [6]. In a previous study, perioperative hemodynamic variables were compared between 14 pheochromocytoma patients who underwent laparoscopic adrenalectomy (laparoscopic surgery group) and 20 patients who underwent open adrenalectomy by the traditional approach (open surgery group) [9]. The intraoperative hemodynamic values recorded during laparoscopic adrenalectomy were comparable to those recorded during open adrenalectomy. However, the patients who underwent laparoscopic surgery exhibited less severe intraoperative hypotension (mean lowest blood pressure levels, 98/57 and 80/50 mmHg for the laparoscopic surgery and open surgery group, respectively; $P = 0.05$) and the hypotensive episodes were less frequent (median number of episodes, 0 and 2 episodes for the laparoscopic surgery and open surgery group, respectively; $P = 0.005$). The median estimated blood loss was 100 ml (range, 100–200 ml) in the laparoscopic surgery group and 400 ml (range, 150–1,500 ml) in the open surgery group ($P = 0.001$). There was no difference in the duration of the surgery between the two groups (open surgery group, 196 $\pm$ 69 min; laparoscopic surgery group, 177 $\pm$ 59 min). Patients who underwent laparoscopic surgery had a shorter postoperative

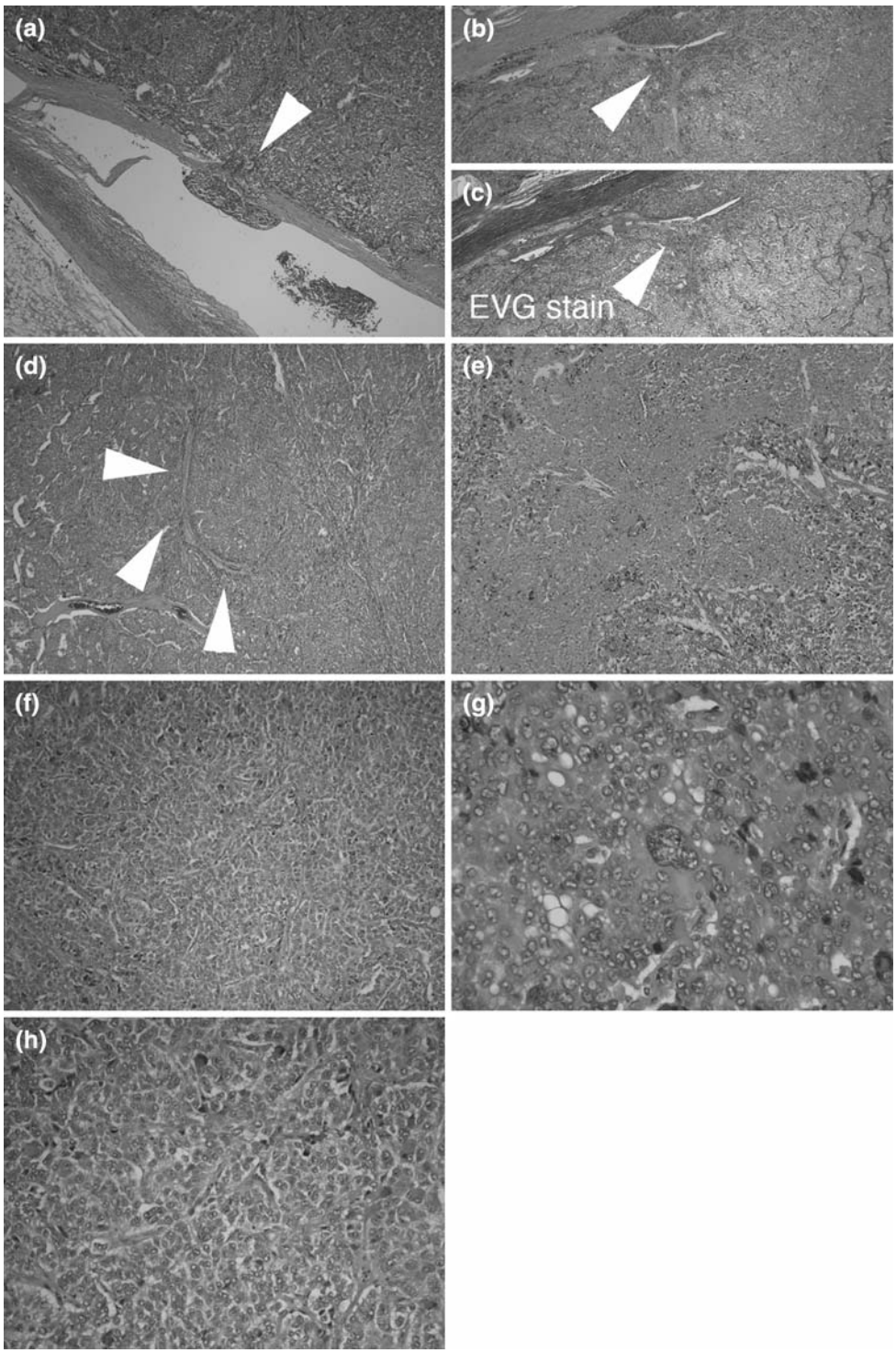

Fig. 2 Malignant pheochromocytoma. **a** Capsular invasion. **b** Vascular invasion (hematoxylin and eosin (HE) stain). **c** Vascular invasion (Elastic Van Gieson (EVG) stain). **d** Large and confluent nests. **e** Necrosis. **f** Increased cellularity. **g** Nuclear pleomorphism. **h** Cellular monotony with smaller cells having high nuclear to cytoplasmic ratio

course and were able to ambulate earlier (laparoscopic surgery group within 1.4 days and open surgery group within 4 days; $P = 0.002$), resumed oral food intake earlier (median duration, laparoscopic surgery group within 1 day and open surgery group within 3.5 days; $P = 0.001$), and were hospitalized for a considerably shorter duration (median duration, laparoscopic surgery group 3 days and open surgery group 7.4 days; $P = 0.001$). In addition, these patients resumed normal physical activity earlier (within 5–7 days) and had better cosmetic results when compared with those who underwent open surgery.

CT and MRI exhibit similar detection sensitivity (98% and 100%, respectively), but low specificity (70% and 67%, respectively) [10]. [^{123}I]MIBG-assisted scanning has excellent specificity (100%), but low sensitivity (78%). Further, PET performed using [^{18}F]fluorodopamine,

[^{18}F]fluorodopa, or [^{18}F]fluorodeoxyglucose is another functional imaging method that can be used as an alternative to [^{123}I]MIBG-assisted scanning or as an additional procedure in cases where [^{123}I]MIBG-assisted scanning yields negative results [10]. [^{18}F]fluorodeoxyglucose, the only compound that is widely available for PET imaging, is not recommended for initial diagnostic localization, since it is nonspecific for pheochromocytoma and has a low sensitivity [11]. However, it can be useful if other imaging procedures are negative, as is the case with rapidly growing dedifferentiated tumors that have lost the ability to absorb more specific drugs [11]. In the present case, the tumor characteristics were such that it showed positive uptake during FDG-PET but reduced uptake during [^{123}I]MIBG-assisted scanning. Interestingly, the findings of the histological examination suggest that the tumor may have been malignant. Despite the increasing availability of molecular diagnostic and prognostic markers, it is impossible to predict whether malignancy may develop at a later stage, on the basis of the histological findings from a resected tumor [12]. A single histological feature alone does not predict or provide unequivocal evidence of malignancy. The metastases of chromaffin tissue to sites where it is usually absent is the only strong indicator for a definite diagnosis of malignant pheochromocytoma. Thus, more sensitive and specific diagnostic techniques are required.

Conclusion

We report the case of a patient with a diagnosis of pheochromocytoma complicated by renal failure, with malignancy suspected on the basis of histopathological findings. Tumor removal by laparoscopic adrenalectomy improved the renal function and clinical symptoms of our patient. The findings of this study suggest that laparoscopic adrenalectomy should be considered in patients with pheochromocytoma complicated by renal dysfunction.

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