

CASE REPORT

Carcinoembryonic antigen-producing adrenal adenoma resected using combined lateral and anterior transperitoneal laparoscopic surgery

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Abstract

A 74-year-old woman presented with symptoms consistent with hyperadrenocorticism and hypercatecholaminism. She had a cushingoid appearance and her cortisol level was elevated. Her serum dopamine and noradrenalin levels were also elevated. Computed tomography detected a left adrenal mass measuring 3.5 cm × 3.0 cm in diameter. Metaiodobenzylguanidine scintigraphy was negative. Unexpectedly, the serum Serum carcinoembryonic antigen (CEA) level was

elevated. Fluorodeoxyglucose positron emission tomography showed increased uptake in the adrenal tumor only, with a maximum standardized uptake value of 2.8. Selective venography and blood sampling revealed that the concentrations of cortisol, catecholamines and CEA were significantly elevated in the vein draining the tumor. A diagnosis of CEA-producing benign adenoma was made. After preoperative management, we performed a combined lateral and anterior transperitoneal laparoscopic adrenalectomy. Her vital signs remained stable during surgery. Histopathological examination revealed a benign adenoma. Her cortisol, catecholamine and CEA levels normalized immediately after surgery. We present, to the best of our knowledge, the first case of CEA-producing adrenal adenoma, along with a review of the relevant literature, and discuss our laparoscopic surgery techniques.

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Key words: Carcinoembryonic antigen; Laparoscopy; Adenoma; Adrenal gland; Cushing syndrome

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INTRODUCTION

Serum carcinoembryonic antigen (CEA) level is widely used as a reliable tumor marker in cancer patients. CEA level is rarely elevated in benign disease, and to the best of our knowledge there have been no reports of CEA-producing benign adrenal tumors. We present the first reported case of a CEA-producing adrenal adenoma, along with a review of the relevant literature, and discuss a useful technique for the removal of adrenal tumors.

CASE REPORT

A 74-year-old Japanese woman was referred to our hospital

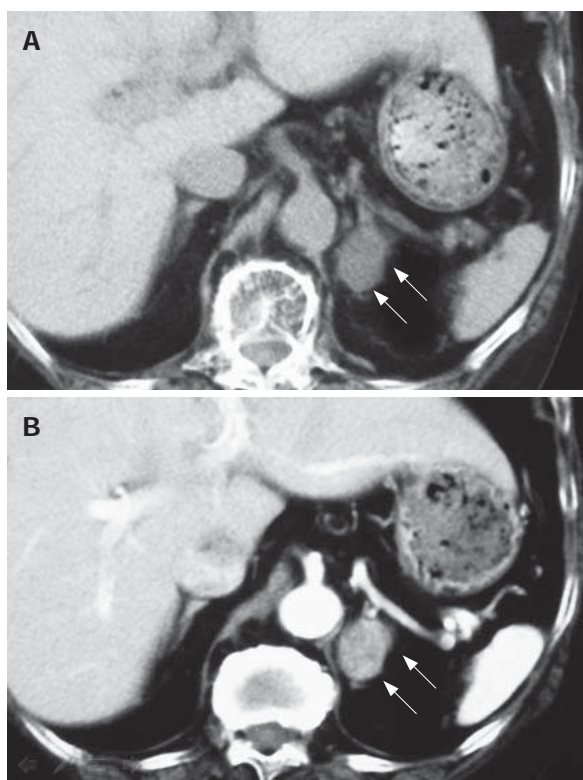


Figure 1 Abdominal CT. Plain (A) and enhanced (B) CT revealed a left adrenal mass (white arrows) measuring 3.5 cm × 3.0 cm in diameter.

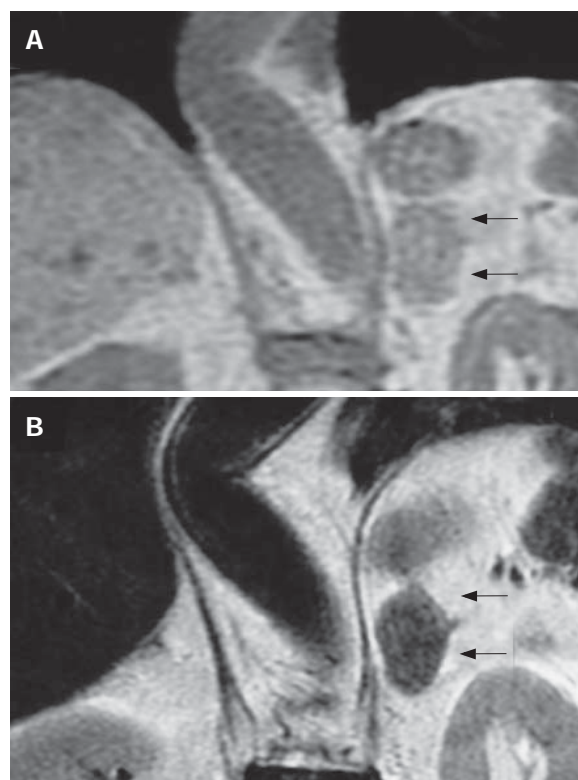


Figure 2 Abdominal MRI. MRI showed an adrenal mass (black arrow) with slightly low intensity on T1-weighted images (A) and low intensity on T2-weighted images (B).

because of fatigue and frequent episodes of palpitations, sweating, headache and weight gain over the past year. She had a history of hypertension and hyperglycemia, for which she had been treated at another hospital for 18 years. Although the number of medications and their dosages had slowly increased during the year before this consultation, her diseases and symptoms were not well controlled. Physical examination showed truncal obesity, moon face, buffalo hump and proximal muscle weakness. On admission, her blood pressure was 202/108 mmHg, and pulse rate 96 beats/min. X-ray images revealed osteoporosis. Serum biochemistry showed elevated levels of glucose (243 mg/dL; normal, 70-109 mg/dL), Hemoglobin A1c (HbA1c) (8.9%; normal, 4.3-5.8%) and total cholesterol (271 mg/dL; normal, 50-149 mg/dL), and reduced levels of total protein (5.5 g/dL; normal, 6.5-8.3 g/dL) and albumin (3.2 g/dL; normal, 3.7-5.3 g/dL). Abdominal computed tomography (CT) showed a left adrenal mass measuring 3.5 cm × 3.0 cm in diameter (Figure 1). Magnetic resonance imaging (MRI) showed an adrenal mass with slightly low intensity on T1-weighted images and low intensity on T2-weighted images (Figure 2). Her physical appearance was cushingoid, as described above. Adrenal cortical hormone analysis revealed a markedly elevated cortisol level, but aldosterone and estradiol levels were normal. The regulatory factors for these hormones were all within normal ranges (Table 1). Catecholamine analysis revealed markedly elevated dopamine and noradrenalin (NA) levels but the adrenalin level was within the normal range. The levels of catecholamine-breakdown products homovanillic acid (HVA) and vanillylmandelic acid (VMA) were both increased (Table 1). ^{123}I -metaiodobenzylguanidine scintigraphy showed

no adrenal or extra-adrenal hot spots.

Unexpectedly, the CEA level was also found to be elevated (Table 1), although other tumor markers including carbohydrate antigen (CA) 19-9, CA125, CA15-3, alpha-fetoprotein and squamous cell carcinoma antigen were all normal. Upper gastrointestinal and colorectal endoscopy, neck/chest CT, and genital and breast examination did not reveal any abnormal findings. F-18 fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT revealed increased FDG uptake in the left adrenal gland (Figure 3). The maximum standardized uptake value was 2.8, and there was no FDG uptake elsewhere. We performed selective venography and blood sampling at various locations around the inferior vena cava to measure the concentrations of factors not within a normal range. The left adrenal vein (AV) was the drainage vein of the tumor and flowed into the left renal vein (RV). Results from the selective blood sampling clearly showed that the concentrations of these factors were dramatically increased in the left adrenal 'drainage' vein. This revealed that the left adrenal tumor was an obvious source of the CEA (Figure 4).

We diagnosed the tumor as a benign adrenal adenoma, which caused hyperadrenocorticism and hypercatecholaminism^[1] and produced a large amount of CEA. After preoperative management^[2], we removed the tumor by combined lateral and anterior transperitoneal laparoscopic adrenalectomy (LA). The patient was placed in the right lateral position. A trocar was inserted at the umbilicus, and a carbon dioxide pneumoperitoneum (10 mmHg) was established. We introduced one trocar into the abdominal cavity through the lateral abdominal

Table 1 Time course of serum endocrine profiles and CEA levels before and after surgery

	Normal range	Before surgery	Postoperative day			
			1	3	5	7
Adrenal hormones						
Cortical secretion						
Hormones						
Aldosterone (pg/mL)	30.0-160.0	30.4	50.3	113.5	43.3	72.7
Cortisol (µg/dL)	5.0-15.0	<u>54.2</u>	11.2	9.9	10.6	7.2
Estradiol (pg/mL)	10.0-20.0	12.2	10.8	18.6	17.8	11.7
Regulatory factors for cortical hormones						
Adrenocorticotrophic hormone (pg/mL)	5.0-52.0	5.2	5.4	9.2	5.8	14.8
Angiotensin (pg/mL)	9.0-47.0	12.3	24.6	33.1	36.6	24.9
Renin (pg/mL)	2.5-21.4	3.7	13.9	16.1	8.9	17.6
Medullary secretion						
Catecholamines						
Dopamine (pg/mL)	< 14.0	<u>15.1</u>	6.5	8.5	6.2	11.5
NA (pg/mL)	46.0-60.0	<u>102.7</u>	52.7	47.1	50.9	59.1
Adrenalin (pg/mL)	< 70.0	40.0	45.8	65.2	64.6	61.2
Catecholamine breakdown products						
HVA (ng/mL)	4.0-7.8	<u>8.8</u>	4.5	4.2	5.2	6.5
VMA (ng/mL)	3.3-8.6	<u>24.5</u>	7.8	7.5	7.7	8.1
Tumor marker						
CEA (ng/mL)	< 5.0	<u>12.6</u>	4.5	2.5	2.1	2.2

Values outside the normal range are underlined.

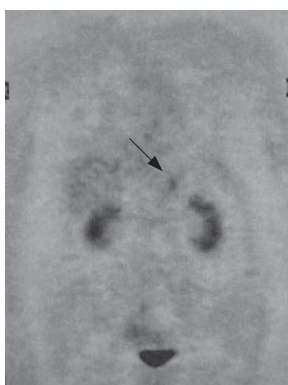


Figure 3 FDG-PET/CT. FDG uptake in the left adrenal gland (black arrow). The maximum standardized uptake value was 2.8, and no FDG uptake was seen anywhere else.

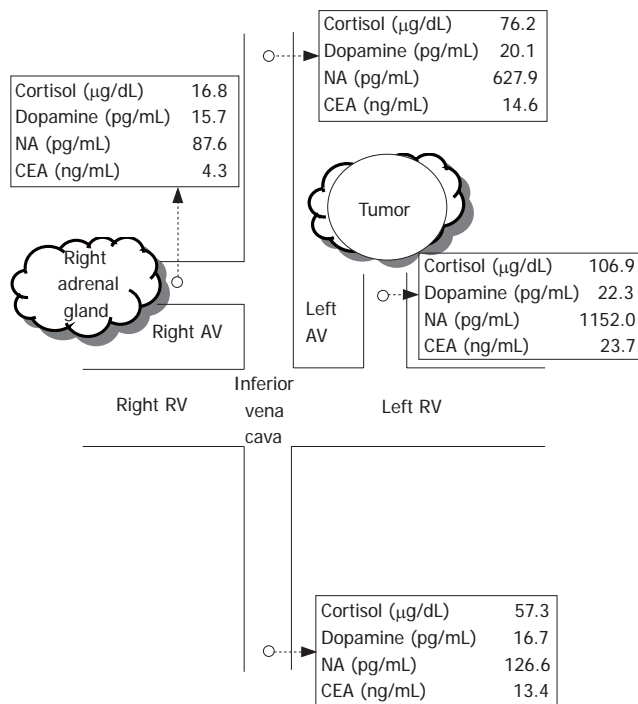


Figure 4 Selective venography and direct blood sampling. Measurements of serum cortisol, dopamine, NA and CEA were performed at four locations (proximal and distal inferior vena cava and both AVs). White circles represent sampling points.

wall, and two trocars through the subcostal wall. Using an electrothermal vessel sealing system (LigaSure, Tyco Healthcare, CO, USA), we isolated the spleen and distal pancreas by resecting the phrenic, colic and renal ligaments. The left RV and splenic vein were exposed by retracting the distal pancreas, spleen and left kidney. The left AV was separated from the surrounding tissue and ligated at its entry into the RV using a clip. The tumor was found to be located as indicated on preoperative imaging studies, without adhesion to the adjacent organ, and was removed with complete hemostasis. Vital signs remained stable during LA. Operative time was 2 h 45 m, and total blood loss was 85 mL. Histopathological examination of the resected specimen confirmed a benign adenoma. Chromaffin staining was negative. Cortisol, catecholamine and CEA levels normalized immediately after surgery (Table 1).

DISCUSSION

Based on hormonal evaluations of the adrenal cortex, we considered that this patient’s hyperadrenocorticism was

adrenocorticotrophic hormone-independent and renin-angiotensin-system-independent. Phenylethanolamine N-methyltransferase (PNMT), which is found in the adrenal glands, is required for the conversion of NA to adrenalin during catecholamine synthesis^[3]. Catecholamine metabolism produces the breakdown products HVA (from dopamine) and VMA (from NA). Hormonal evaluations of the adrenal medulla suggested that this adrenal

adenoma either lacked PNMT or the optimal environment for the activation of PNMT.

LA was first performed in 1992^[4,5], and this safe and effective treatment is now used worldwide for the management of functioning and non-functioning adrenal tumors for many reasons^[6]. The minimal skin incisions provide a sufficient surgical field, anastomosis and reconstruction are not required, hemostasis can be achieved using laparoscopic devices, and the resected tumor can be removed through the small skin incision. Many previous reports on LA have already described the advantages and shortcomings of the transperitoneal and retroperitoneal approaches. There are two transperitoneal approaches, lateral and anterior^[7]. Especially in left adrenal tumors and cases with more retroperitoneal fat, we have a clear impression that the combined lateral and anterior transperitoneal LA has the advantage of providing a sufficient surgical field and anatomical orientation in a timely manner. Surgery for catecholamine-releasing tumors differs from that for non-functioning tumors, because of the risk of intraoperative hypertensive and tachycardiac events^[8]. In the present case, the combined approach allowed easy and early ligation of the drainage vein, which was the source of the catecholamines. We suggest that this procedure is effective for avoiding intraoperative iatrogenic complications.

CEA, the first tumor-associated antigen to be described, has many features that make it attractive for active vaccination against cancer. This useful biomarker is expressed in > 50% of all human cancers^[9], including colorectal, lung, stomach, breast, pancreas, gallbladder, biliary tract, cervix, uterus, ovary, head/neck, bladder, kidney and prostate cancer. In the present study, we performed FDG-PET/CT to rule out adrenal cancer and to search for extra-adrenal tumors to explain the raised CEA level, as the conventional investigations for evaluation of an elevated CEA level showed no significant findings. We eventually hypothesized that the left adrenal tumor was producing a large amount of CEA, and performed selective venography and direct blood sampling of the drainage vein of the tumor to verify this. This method was useful for detecting the source of CEA in the present case. Previous reports have demonstrated that smoking, inflammatory diseases and benign tumors uncommonly produce CEA; but that benign tumors rarely progress to become malignant^[10,11]. We are unable to explain how this patient's benign adenoma acquired the ability to secrete CEA, even after reviewing the relevant literature. This appears to be the first reported

case of a CEA-producing adrenal adenoma. As a benign adrenal adenoma rarely secretes CEA, more cases need to be studied to better understand CEA production in benign adrenal tumors.

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