Oncocytic pheochromocytoma of the adrenal gland with preoperative endocrine examination

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Abstract We report a case of oncocytic pheochromocytoma of the right adrenal gland in a woman in her sixties with preoperative endocrine examination results. She had no clinical symptoms, but a large right adrenal mass (8.5×7.2 cm) was incidentally pointed out. Preoperative endocrine examination was within normal limits except for an increased dehydroepiandrosterone sulfate level. We removed the tumor surgically. It measured $10 \times 8 \times 5.5$ cm, weighed 260 g, and had a solid, bark-like cut surface. Microscopically, the tumor cells were highly eosinophilic, polygonal, and arranged in an alveolar pattern. Immunohistochemically the tumor cells were positive for chromogranin, synaptophysin and CD-56. Based on these results, the tumor combined oncocytoma and pheochromocytoma. Therefore we diagnosed it as oncocytic pheochromocytoma.

Keywords Adrenal · Oncocytic · Pheochromocytoma · Dehydroepiandrosterone sulfate

Introduction

Oncocytic pheochromocytoma of the adrenal gland is extremely rare. To our knowledge, only 3 cases have been

reported previously, but there were no preoperative endocrine examination data in those cases [1–3]. We report a case of oncocytic pheochromocytoma of the right adrenal gland in a woman in her sixties with preoperative endocrine examination results.

Case report

A female patient in her early sixties came to the hospital regularly for treatment of hypertension and dyslipidemia. She did not have any other symptoms such as headache, sweating, palpitation, or virilization. She had received valsartan 160 mg, benidipine 8 mg, and rosuvastatin calcium 2.5 mg orally, and her blood pressure was stable. In November 2010, she was incidentally found to have a massive, solid abdominal mass by ultrasonography. Contrast-enhanced computed tomography showed that there was a bulky tumor (8.5×7.2 cm) in the right adrenal gland that was very close to the liver and inferior vena cava (IVC) (Fig. 1). A nonenhanced, heterogeneous area existed in a portion of the tumor. There was no mass in the liver, lung, or other organs. Magnetic resonance imaging (MRI) with a contrast agent showed that medium or low intensity areas existed in most of the tumor. A high intensity area was dotted on a T2-weighted MRI sequence. Fluoro-18-deoxyglucose positron emission tomography revealed no emphatic finding except for an abnormal uptake in the right adrenal gland (Fig. 2). Routine laboratory data were within normal limits. Serum cortisol, adrenocorticotrophic hormone (ACTH), catecholamines, aldosterone, and plasma renin activity were also within normal limits. However, the dehydroepiandrosterone sulfate (DHEA-S) level was increased ($1590 \mu\text{g/dl}$, normal range for women in their sixties is $120\text{--}1330 \mu\text{g/dl}$). Twenty-four-hour urinary

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Fig. 1 Computed tomography of the abdomen. The right adrenal tumor is very close to the liver and inferior vena cava, and a nonenhanced, heterogeneous area exists in a portion of the tumor

catecholamines, metanephrines, vanillyl mandelic acid (VMA), and homovanillic acid (HVA) were within normal levels. A low dose dexamethasone suppression test revealed that serum cortisol and ACTH were suppressed normally.

According to these results, we considered that the tumor was nonfunctional. However, we could not deny adrenal

carcinoma because of the tumor size and the presence of a heterogeneous area. Therefore we suggested surgical removal to her and she received surgery in January 2010. During the surgery, the blood pressure did not fluctuate widely. The tumor size was $10 \times 8 \times 5.5$ cm, and its weight was 260 g. In macroscopic findings, the cut surface was bark-like, solid, and with some cystic changes (Fig. 3). Microscopic examination showed that the cells were in a polygonal, multiplied alveolar configuration. Their cytoplasm was remarkably eosinophilic, abundant, and protruded from nearly circular nuclei (Fig. 4a). These findings were characteristic of oncocytoma. There was very little abnormal mitosis. However, an area of hemorrhage, coagulation necrosis, and fibrotic degeneration existed. There was a tumor capsule structure, and a normal, atrophied adrenal cortex was located laterally to the capsule. This suggested that the adrenal gland was the origin of the tumor. Capsular invasion and lymphovascular invasion were not demonstrated. Immunohistochemically the tumor cells were positive for chromogranin (Fig. 4b), synaptophysin (Fig. 4c), and CD-56 (Fig. 4d). This indicated that the tumor had neuroendocrine granules characteristic of pheochromocytoma. Considering these results, we diagnosed it as oncocytic pheochromocytoma. Thirteen months

Fig. 2 Fluoro-18-deoxyglucose positron emission tomography. There is an abnormal uptake in the right adrenal gland

Fig. 3 Macroscopic examination shows the cut surface of the tumor as bark-like, solid, and with some cystic changes (*white arrows*)

after the operation, the patient had no clinical symptoms or evidence of disease. The DHEA-S level was improved to within the normal range.

Discussion

To our knowledge, only 3 cases of oncocytic pheochromocytoma were reported previously [1–3]. In 2 cases, the patients had no clinical symptoms such as headache, sweating, or palpitation and the tumor sizes were large (1150 and 275 g) [1, 3]. Those findings were similar to our case. In the other case, clinical presentation was not reported [2]. In this context, the tumor was considered to be clinically nonfunctional. However, there was no information about preoperative endocrine examinations in the previous cases. We herein reported an adrenal oncocytic pheochromocytoma with preoperative endocrine examination results, and showed that there was no abnormal finding in the endocrine data except for DHEA-S.

In this case, the differential diagnosis between pheochromocytoma and oncocytic pheochromocytoma is very important. Immunohistochemical study indicated that this tumor was pheochromocytoma because of the neuroendocrine markers, such as chromogranin, synaptophysin, and CD-56. However, histological examination revealed that

Fig. 4 Microscopic findings show tumor cells arranged in an alveolar pattern. Its cytoplasm is remarkably eosinophilic and abundant, protruding from nearly circular nuclei (**a**). Immunohistochemically the tumor cells were positive for chromogranin (**b**), synaptophysin (**c**), and CD-56 (**d**)

the findings were likely oncocytic tumor and these findings were rare as pheochromocytoma. This examination suggested that our case was oncocytic tumor because the tumor is characterized histologically [1].

The reason why oncocytic pheochromocytoma is clinically nonfunctional is unclear. Chang and Harawi [4] speculated that oncocytic changes were a cellular degenerative phenomenon, and that mitochondria accumulated to compensate for the uncoupling of oxidative phosphorylation. However, to clarify the characteristics of oncocytic pheochromocytoma seems to be very difficult because this tumor is exceedingly rare.

Histological examination revealed that the tumor cells had eosinophilic granular cytoplasm, a characteristic of the oncocytic tumor [1]. Oncocytic tumors are also derived from endocrine organs such as the thyroid, parathyroid, salivary glands, pituitary gland, and ovary [1]. Adrenal oncocytic tumors have been reported [5]. These reports suggested that the tumors were clinically nonfunctional, and the patients had an excellent prognosis. In this case, there was very little abnormal mitosis microscopically. Capsular and lymphovascular invasion were not demonstrated. On the other hand, microscopic examination revealed areas of hemorrhage, coagulation necrosis, and fibrotic degeneration. Therefore it was very difficult to diagnose whether the tumor was benign or malignant. It is known that 10 % of pheochromocytoma has a malignant potential [6]. Although there was no evidence of recurrence or metastasis 13 months after surgery, we should continue careful follow-up for the patient with abdominal imaging.

This case report has some limitations. One of these is that we did not evaluate surgical specimens with electron microscopic studies. Therefore, we could not determine ultrastructural findings such as cytoplasmic mitochondria. However, it was difficult to conduct full evaluation of this quite rare tumor preoperatively in the general clinical

setting. Those who encounter an unusual adrenal tumor in the future, should carry out more detailed differential diagnostic studies such as the fixation of the surgical specimen to be able to evaluate it with electron microscopic studies or fluorescence in situ hybridization with multiple bacterial artificial chromosome probes [7].

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Conflict of interest The authors declare that they have no conflict of interest.

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