CASE REPORT

Synchronous renal cell carcinoma and adrenocortical carcinoma: a rare case report and clinicopathologic approach

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A case of synchronous adrenocortical carcinoma (ACC) and renal cell carcinoma (RCC) has not yet been described in the English medical literature, to our knowledge. We report a first such case of adrenocortical and renal cell carcinomas occurring simultaneously in a 53-year-old male. He presented with history of vague abdominal pain. Ultrasound followed by a computed tomography (CT) scan and a magnetic resonance imaging (MRI) examination revealed a 6.4 cm left adrenal mass and a 3.5 cm right renal mass. The patient had complaints of gastroparesis manifesting with constant nausea as well as intermittent abdominal bloating and abdominal pain. He also had history of profuse intermittent sweating. There was no history of palpitations or fluctuations in blood pressure. The patient's urinary vanillylmandelic acid (VMA) levels and serum cortisol levels were normal. His 24-hour urine metanephrine levels were slightly elevated. Left adrenalectomy and right partial nephrectomy were performed. In this case, it is important to determine whether these tumors represent metastases or two synchronous tumors, as this has implications on the patient's management and prognosis. Clinical and pathological clues that led to the diagnosis are discussed in detail.

Key Words: adrenocortical carcinoma, adrenocortical adenoma, renal cell carcinoma, synchronous tumors

Introduction

Presence of synchronous clear-cell malignancies in the adrenal gland and kidney are rare. The challenge that arises in such cases is to determine whether these tumors represent metastases or two synchronous, separate tumors. Nevertheless, such differentiation — the determination of whether the clear cell tumors are metastatic or are synchronous, separate primary tumors — is crucial, as it affects the patient's management and prognosis. Non metastasizing renal cell carcinoma (RCC) has a much better prognosis than does metastasizing cancer. Reported cases of synchronous adrenal and renal primary tumors are rare, and as far as we know, only one case of concurrent occurrence of kidney tumors and adrenal adenoma but not adrenocortical carcinoma (ACC) has been reported.[1] To our knowledge, the present case is the first case of synchronous RCC and ACC reported in the English medical literature .

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Case report

Clinical summary

A 53-year-old male presented with complaints of gastroparesis manifesting with constant nausea as well as intermittent abdominal bloating and abdominal pain. He also had history of profuse intermittent sweating. There was no history of palpitations or fluctuations in his blood pressure. His urinary vanillylmandelic acid (VMA) levels and serum cortisol levels were normal. His 24- hour urine metanephrine levels were slightly elevated. An abdominal computed tomography (CT) scan and

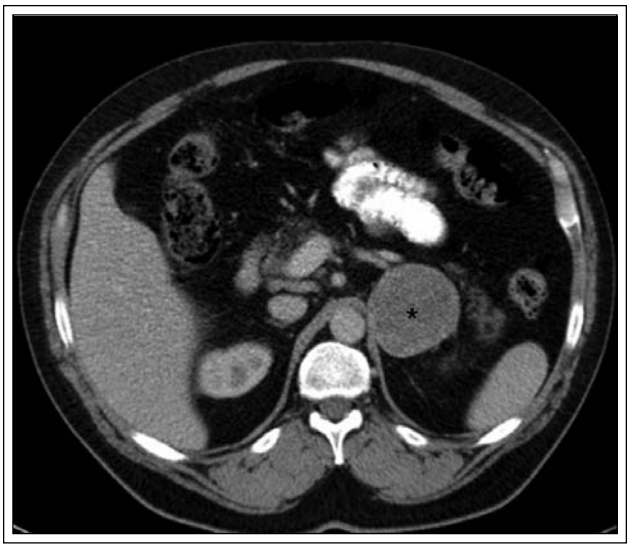

Figure 1. Abdominal CT scan showing large left-sided adrenal mass (with * marking the mass).

magnetic resonance imaging (MRI) revealed a 6.4 cm left adrenal and a 3.5 cm right renal mass, Figures 1 and 2. The former demonstrated irregular effacement, while the latter was enhancing. Based on such findings, concerns that the masses were malignant were raised. The left adrenal mass was suspected to be pheochromocytoma; however, the patient's serum cortisol level and urinary VMA levels were normal. His 24-hour urine collection revealed slightly elevated metanephrine levels. A left adrenalectomy and a right partial nephrectomy were performed. Postoperative follow-up for a year revealed that the patient was well and had no evidence of cancer recurrence.

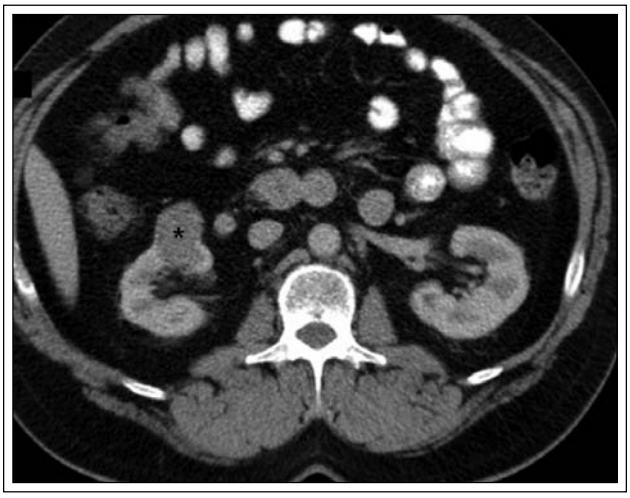

Figure 2. Abdominal CT scan showing right- sided renal tumor occupying the mid portion of the kidney (with * denoting the tumor).

Pathological findings

Gross examination of the left adrenal gland revealed a cortically centered, solid, multinodular mass measuring 6.5 cm x 6.0 cm x 5.0 cm and weighing 122 grams. The tumor was encapsulated but showed evidence of extraparenchymal penetration. The tumor had golden brown cut surface with areas of hemorrhage and necrosis. The partial nephrectomy showed a 3.0 cm x 3.0 cm x 3.0 cm yellow solid mass which did not invade into the perinephric adipose tissue.

Microscopically, the adrenal mass had predominant diffuse sheets and focal trabecular arrangements. The former pattern was present in about a third of the tumor. The cells had clear cytoplasm and round to ovoid nuclei with conspicuous nucleoli, Figure 3. The mitotic rate was 9/50 HPF and included atypical forms. Gross necrosis and capsular invasion were documented microscopically. There was no evidence of lymphovascular invasion. Considering the above-mentioned features, a Weiss histopathologic score[2] of 7/9 was applied.

Microscopic examination of the renal mass showed a vascular tumor with diffuse sheets of clear cells having Fuhrman grade II[3] nuclei, Figure 4. There was no evidence of necrosis within the tumor, and there was no evidence of extraparenchymal invasion.

The differential diagnosis included RCC with contralateral adrenal metastasis, ACC with contralateral renal metastasis, synchronous RCC and ACC, or synchronous RCC and adrenocortical adenoma.

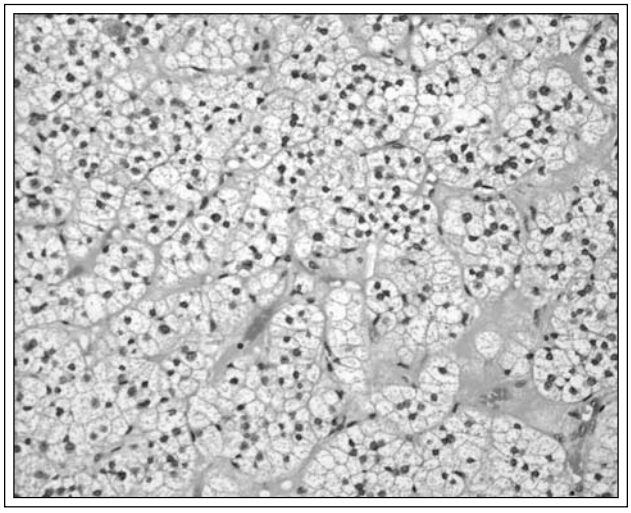

Figure 3. Adrenocortical tumor with clear cells having round to ovoid nuclei with conspicuous nucleoli of Fuhrman grade III, (HE X400).

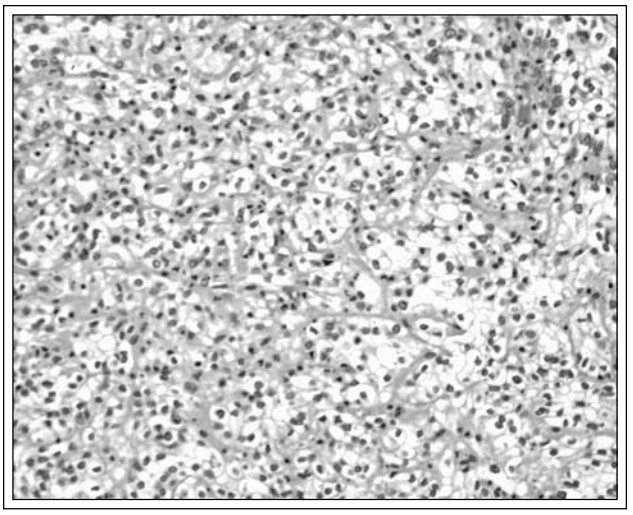

Figure 4. Renal cell carcinoma showing clear cells with Fuhrman grade II, (HE X400).

A panel of immunohistochemical stains was performed to determine the diagnosis.

The list of antibodies with their source, dilution and type of pretreatment methods used are described in Table 1.

Adrenal tumor demonstrated strong Vimentin positivity and is negative for CK7, CK20, E1/AE3, EMA, Synaptophysin and S100. Renal cell carcinoma was positive for CK7, AE1/AE3, EMA (weak) and Vimentin. It was negative for CK20, Synaptophysin and S100, Table 2.

Based on the integration of clinicopathological, morphological and immunophenotyping of both tumors, the diagnosis was renal cell carcinoma with contralateral synchronous adrenocortical carcinoma was established.

Discussion

RCC usually have excellent short term prognosis; however, long follow-up revealed that most of the cases showed remote metastasis in various organs. Thus, the prognosis of RCC is unpredictable. Metastasis of RCC to the contralateral adrenal gland has been diagnosed as late as 23 years after nephrectomy.[4] Radiological studies cannot determine with certainty whether an adrenal tumor in a patient with RCC is a primary adrenal neoplasm or a metastasis.[4] However, there are a few radiological clues from a CT scan and an MRI that may suggest the preoperative diagnosis. Metastatic RCC to the adrenal gland is usually a highly vascular tumor, compared to the relatively hypovascular adrenal cortical

TABLE 1. **Antibodies used in immunohistochemical tests**

Primary antibody	Marker/ clone	Supplier	Mono (M) Poly (P)	Dilution	Antigen retrieval
Calretinin	Clone: Calret 1	Dako	M	1/100	pH 9.0
CD10,(CALLA)	Clone: 56C6	Vector Lab	M	1/100	pH 9.0
EMA (epithelial membrane antigen)	Clone: E29	Dako	M	neat	
Cytokeratin 7	Transitional epithelium Clone: OV-TL 12/30	Dako	M	1/50	Enzyme proteinase K
AE1/3 (HMW Keratin)	Clone: AE1/3	Dako	M	1/100	Enzyme proteinase K
Inhibin	Clone: R1	Dako	M	1/25	pH 6.0
Melan-A	Melanocyte marker Clone: A103	Dako	M	1/25	pH 6.0
Cytokeratin 20	Gastric/bowel epithelium Clone: Ks 20.8	Dako	M	1/50	Enzyme proteinase K
S-100	S-100 Immunogen	Dako	P	_	
Synaptophysin	Immunogen	Dako	P	neat	pH 6.0
Vimentin	Clone: V9	Dako	M	_	pH 6.0

TABLE 2. **Results of immunohistochemistry in adrenal and renal tumors**

Immunohistochemical markers	Renal cell carcinoma	Adrenocortical carcinoma
CK7	Positive (+++)	Negative
EMA	Positive (+++)	Negative
CD10	Positive (+++)	Negative
AE1/AE3	Positive (+)	Negative
Inhibin	Negative	Positive (+++)
Calretinin	Negative	Positive (+++)
Melan A	Negative	Positive (+++)
CK20	Negative	Negative
S100	Negative	Negative
Synaptophysin	Negative	Negative
Vimentin	Positive (+++)	Positive (+++)

adenoma or carcinoma.[5] The presence of clinical or biochemical evidence of adrenocortical hormones hypersecretion can be helpful to determine whether an adrenal tumor is a primary and not secondary cancer, in the setting of present or past history of RCC. However, many of adrenocortical tumors are non secretory as was the tumor in this case. This patient's urinary VMA and serum cortisol levels were normal. Needle biopsy of adrenal masses may be helpful.[6] Still, the gold standard for such a distinction is made through pathological diagnosis of the resected tumors with the crucial aid of ancillary studies as immunohistochemistry and perhaps electron microscopy. In our case, the radiological findings and adrenal hormonal assays were not able to differentiate whether the two masses were metastatic or two synchronous primary tumors. Pathologically, both tumors showed clear cell carcinoma. Hence immunohistochemistry was very crucial in this case. The adrenal tumor demonstrated strong Vimentin positivity and was negative for CK7, CK20, AE1/AE3, EMA, Synaptophysin and S100. The renal cell carcinoma was positive for CK7, AE1/AE3, EMA (weak) and Vimentin. It was negative for CK20, Synaptophysin and S100. The different immunohistochemical profile of the two tumors documented that they originated from two different primary tumors.

The diagnosis of synchronous tumors rather than metastasis influences the prognosis. In one report, the longest disease-free interval after removal of a contralateral adrenal metastasis was 12.1 years,[7]and in another report, the longest crude survival was 14.3 years.[8] In contrast, non metastasizing RCC had an excellent prognosis if no metastasis developed.

Immunohistochemical analysis is not only helpful but is an essential part of a diagnostic work- up in cases of synchronous clear cell tumors of the kidney and adrenal gland. This can be very crucial in cases of biopsy or fine needle aspiration examination of these tumors. □

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