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Case Report

Adenoid cystic carcinoma metastasis to kidney disguised as primary renal cell carcinoma: a case report and review of literature

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Abstract: Adenoid cystic carcinoma (ACC) is a rare malignant epithelial tumor, mainly occurring in the salivary glands and characteristically showing infiltrative growth and perineural invasion. ACC tends to metastasize to the lungs, bones, liver and brain. However, ACC metastasis to the kidney is extremely rare. To our knowledge, only 11 cases of ACC metastasis to the kidney have been described in the English literature to date. Herein, we presented an additional case of a 65-year-old woman with renal metastasis of ACC in the right parotid which had been resected 9 years before. The patient was treated with successful left radical nephrectomy and postoperative chemotherapy. Up to now, the patient was followed-up regularly and without any evidence of local recurrence or new metastasis at 24 months after left radical nephrectomy.

Keywords: Adenoid cystic carcinoma, kidney, metastasis, prognosis

Introduction

Adenoid cystic carcinoma (ACC) is a malignant neoplasm, mainly affecting the major or minor salivary glands, and occasionally occurring in other locations. It constitutes approximately 10% of all tumors of the salivary glands, accounting for less than 1% of all malignant tumors of the head and neck [1]. ACC is characterized by slow development, perineural invasion, local and delayed recurrence after initial treatment. However, renal metastasis of ACC is extremely rare. Herein, we present such a case in a woman with renal metastasis of ACC to improve awareness of this extremely rare occurrence and also provide a brief literature review.

Case report

A 65-year-old woman was admitted with complaints of gross hematuria and left waist pain for 7 days in Mar 2015, without fever, anorexia, fatigue, general malaise, weight loss, urinary frequency, urgency and dysuria. Retrospective history data showed ACC of right parotid treated with right parotidectomy and local radiotherapy 9 years ago. Histologic analyses showed characteristic histopathological features of ACC with cribriform, tubular and solid growth pattern (**Figure 1**). Abdomen computed tomography (CT) revealed a solitary, round mass measuring 4.0 cm in diameter in the lower pole of left kidney (**Figure 2**). No additional mass, metastatic lesions or lymphadenopathy was detected by systematic clinical examinations, including ^{18}F-fluorodeoxyglucose whole body positron emission tomography scan. Laboratory examinations, such as routine blood tests, serum electrolytes, liver and kidney functions were unremarkable. Subsequently, the patient received a left radical nephrectomy as a primary renal carcinoma and her immediate postoperative course was uneventful.

Macroscopically, the nephrectomy specimen was 16.0 cm × 8.5 cm × 8.0 cm in size, with a

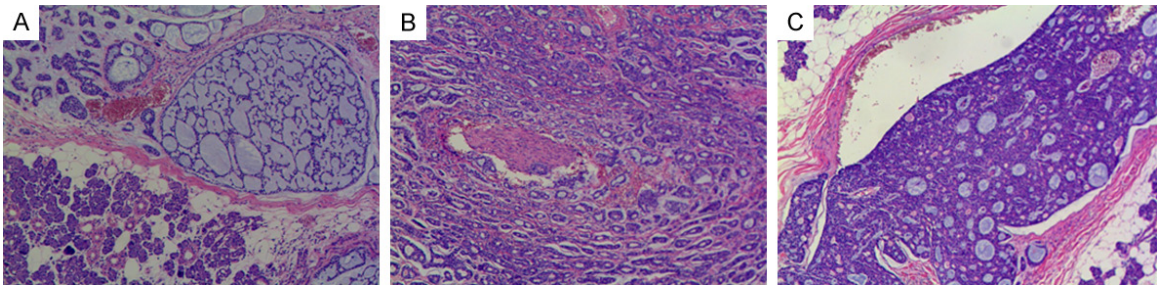

Figure 1. Histopathological analyses of the right parotid tumor. A. The tumor infiltrated parotid tissue with characteristic cribriform, tubular and solid growth pattern (100 ×). B. The tumor showed conspicuous feature of intraneural invasion (100 ×). C. Vascular invasion was observed in local region (100 ×).

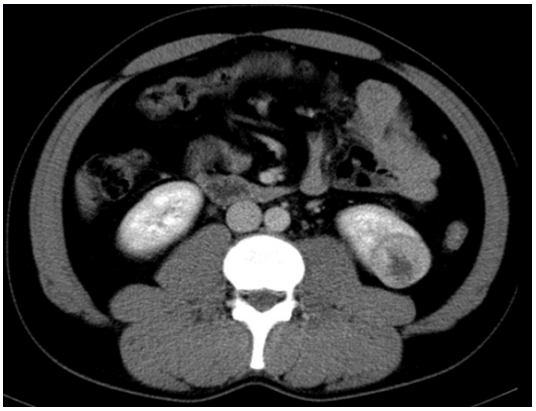

Figure 2. Abdominal CT scan revealed a well-defined, round mass in the lower pole of left kidney.

single mass measuring 3.8 cm × 3.7 cm × 3.7 cm, located in the lower pole of kidney. On the cut surface, the lesion was gray to whitish in color, with well-defined margin and mucoid areas. Microscopically, the tumor was well-circumscribed and consisted of two main cell types, including ductal and modified myoepithelial cells, with conspicuous features of cribriform, tubular and solid growth pattern (**Figure 3**). Immunohistochemically, the tumor cells were positive for AE1/AE3, CK7, CK5/6, Vimentin, CD117, P63, smooth muscle actin (SMA), and Calponin, whereas negative for CD10, PAX2, PAX8, CD56, chromogranin (CgA), synaptophysin (Syn), neuron-specific enolase (NSE), Wilms tumor-1 (WT-1), RCC marker, CD34, ER, PR, and E-cadherin. The Ki-67 labeling index was approximately 5% (**Figure 4**). Thus, a pathological diagnosis of metastatic ACC to the kidney was confirmed based on the patient's medical history mentioned before, histological appearance and immunohistochemical features. Twenty days after nephrectomy, the patient underwent six cycles of chemotherapy regimen that consisted of docetaxel and cisplatin. The patient was well without any evidence of local recurrence or new metastasis at 24 months of follow-up after left radical nephrectomy.

Discussion

Adenoid cystic carcinoma, also called cylindroma, is a relatively uncommon neoplasm, most frequently involving salivary glands, and accounting for approximately 10% of all tumors of the salivary glands. Although most commonly observed in salivary glands, ACC also can rarely arise in nose, sinuses, palate, tongue, nasopharynx, external auditory canal, lacrimal gland, bronchus, lung, breast, Cooper's gland, skin, oesophagus, vulva, cervix and prostate [2, 3]. ACC presents a widespread age distribution, with peak incidence occurring predominantly between the 5th and 6th decades of life. There is a slight sex predilection with a female to male ratio of 3:2. ACC is characterized by an indolent clinical course and has a tendency for delayed recurrence and metastasis after initial treatment. Five-year survival rates after surgical resection has been reported ranging between 68% and 90.3% [4, 5]. Thus, long-term follow-up is necessary for recurrence and metastasis may occur decades after treatment of primary ACC.

ACC characteristically shows infiltrative growth and perineural invasion, and tends to metastasize to the lungs, bones, liver and brain, less frequent to the pancreas, thyroid, spleen and breast [6]. Nevertheless, kidney metastasis of ACC is extremely rare. In 1984, Ladefoged et al. first described metastatic ACC of the kidney, 23 years after right pneumonectomy for ACC of

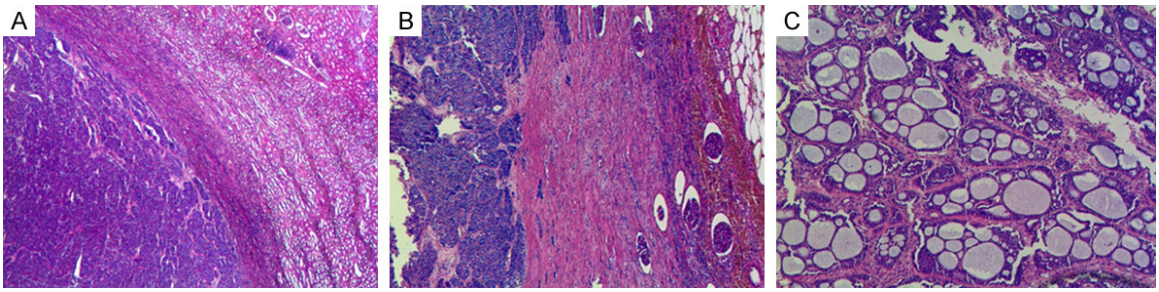

Figure 3. Histopathological analyses of kidney metastasis of ACC. A. The tumor was separated from the adjacent renal tissue by fibrous capsule (40 ×). B. The tumor infiltrated renal tissue in local region (100 ×). C. The tumor showed typical cribriform, tubular and solid growth pattern (100 ×).

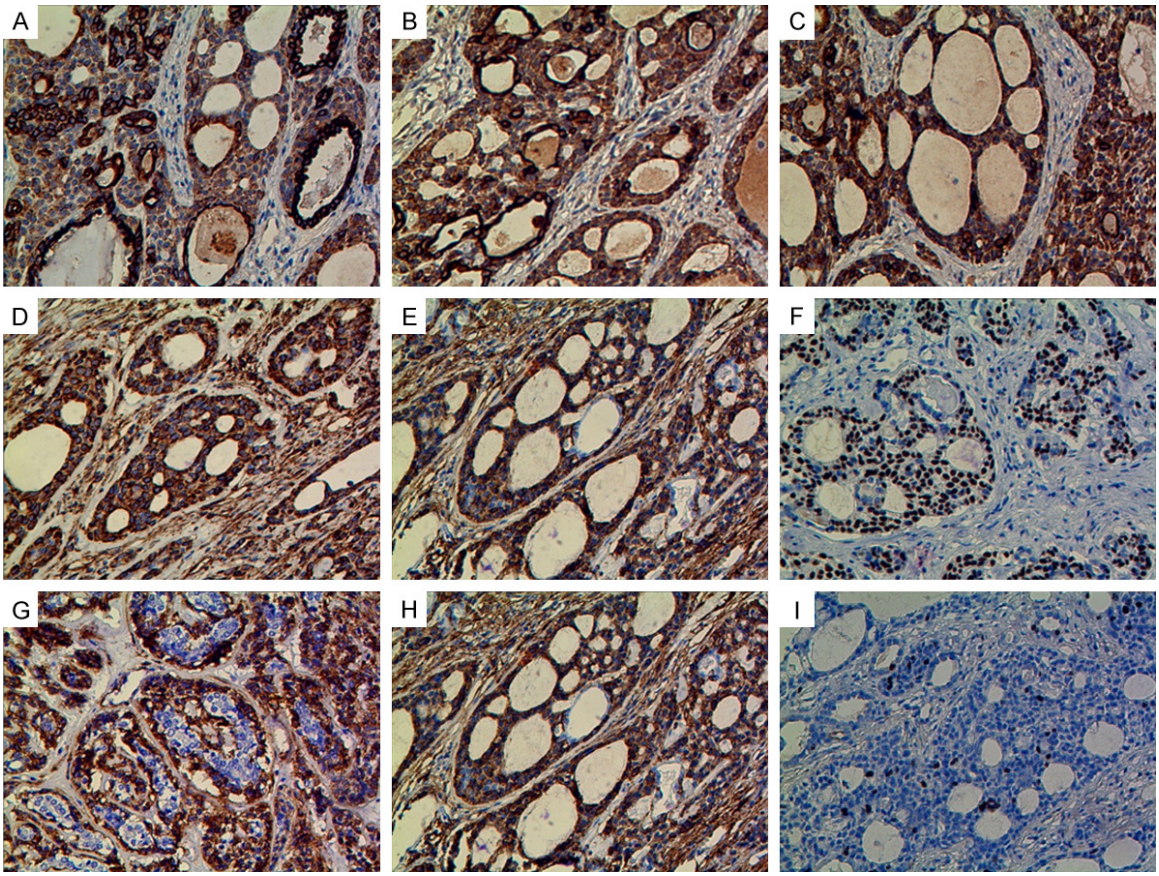

Figure 4. Representative cases of IHC staining. The tumor cells were positive for AE1/AE3 (A. 400 ×), CK7 (B. 400 ×), CK5/6 (C. 400 ×), Vimentin (D. 400 ×), CD117 (E. 400 ×), P63 (F. 400 ×), SMA (G. 400 ×), Calponin (H. 400 ×), and approximately 5% of tumor cells were positive for Ki-67 (I. 400 ×).

lung [7]. To our knowledge, only 11 cases of ACC metastatic to the kidney have been described in detail in the English literature to date [7-17]. The clinicopathogical features of the 12 cases including our case were summarized in **Table 1**, including 9 female and 3 male patients, with the mean age of 52.9 years old and median age of 53.5 years old (range 21~83 years). It seems that renal metastasis from ACC is more likely to occur in female, however, its underlying mechanism still remains unclear.

Among 12 cases, the primary tumor site includes 3 cases in the lung, 2 cases in the breast, 2 cases in the lacrimal grand, 2 cases (including our case) in the parotid, 1 case in the right palate, 1 case in the left submandibular gland, and 1 case in the salivary gland [13].

Table 1. Clinicopathogical features of 12 cases of ACC metastatic to the kidney

Reference	Age (y)/Sex	Clinical features	Primary tumor location/Size (cm)	Treatment of primary tumor	Kidney metastasis time	Metastatic tumor location/Size (cm)	Treatment of metastatic tumor	Follow-up
[7]	47/M	Hematuria	Between the middle and the lower lung lobe/not reported	Right pneumonectomy	23 years	Left kidney/9.0 cm	Radical nephrectomy	ANED after 12 months
[8]	57/F	Gross hematuria	Breast/1.5 cm	Modified radical mastectomy	12 years	Upper pole of the left kidney/6.5 cm	Radical nephrectomy	ANED after 20 months
[9]	83/F	Incidental	Left lacrimal gland/not reported	Excision and radiotherapy	25 years	Left kidney/two small tumors	Radical nephrectomy	Not mentioned
[10]	21/F	Incidental	Left parotid/not reported	Left parotidectomy and radiotherapy	7 years	Left kidney/9.0 cm	Radical nephrectomy	ANED after 4 years
[11]	76/F	Abdominal pain, hematuria and urinary frequency	Breast/1.8 cm	Mastectomy	5 years	Upper part of the right kidney/9.0 cm	Radical nephrectomy	Not mentioned
[12]	71/F	Not mentioned	Right palate/not reported	Right hemimaxillectomy	14 years	Right kidney/2.5 cm	Not reported	Not mentioned
[13]	35/F	Hematuria and right lumbar pain	Salivary gland/not reported	Surgical resection, chemotherapy and radiotherapy	8 years	Upper pole of the right kidney/6.0 cm	Radical nephrectomy	Not mentioned
[14]	50/M	Flank pain	Lower lobe of the right lung/not reported	Right lower lobectomy, radiotherapy and chemotherapy	7 years	Posterior of the right kidney/9.3 cm	Radical nephrectomy	Not mentioned
[15]	28/F	Abdominal pain	Lower lobe of the right lung/8.1 cm	Chemotherapy (cisplatin and doxorubicin)	Meanwhile	Both kidneys/ multiple lesions	Chemotherapy (cisplatin and doxorubicin)	3 months died of disease
[16]	26/M	Right waist pain	Left submandibular gland/not reported	Operation and radiotherapy	3 years	Right kidney/6.0 cm	Radical nephrectomy	Not mentioned
[17]	76/F	Hematuria and flank pain	Left lacrimal gland/not reported	Surgical resection	Lung metastases after 7 years, kidney metastases after 14 years	Lower pole of the right kidney/7.8 cm	Radical nephrectomy	Not mentioned
Our case	65/F	Gross hematuria and left waist pain	Right parotid gland/2.5 cm	Surgical resection and radiotherapy	9 years	Lower pole of the left kidney/3.8 cm	Radical nephrectomy and Chemotherapy	ANED after 24 months

F, female; M, male; ANED, alive with no evidence of disease

However, the size of primary tumor (range 1.5 cm to 8.1 cm) was described in only 4 cases including our case. To date, surgery and radiotherapy are major treatment for primary ACC developed at any site. **Table 1** showed that 5 cases underwent surgical treatment for primary tumors, 4 cases (including our case) treated with surgical resection and radiotherapy, 2 cases underwent surgical resection, radiotherapy and chemotherapy, and 1 case only received chemotherapy. Moreover, 11 cases developed kidney metastasis after 23, 12, 25, 7, 5, 14, 8, 7, 3, 14 and 9 years (mean time of 11.5 years), respectively, and one case of primary ACC of the lung in a 28-year-old female who presented with metastases to the liver and both kidneys meanwhile [15]. Limited data indicate that renal metastasis may occur years after surgery resection of the primary ACC.

As summarized in **Table 1**, the metastatic tumor was an incidental finding in 2 patients and clinical features were not described in one case, but 9 cases were symptomatic, including hematuria in 2 cases, abdominal/flank or waist pain in 3 cases, and abdominal/flank pain accompanied by hematuria in 4 cases. Furthermore, metastatic tumor of 11 patients was unilateral, with 5 cases located in the left kidney and 6 cases located in the right kidney. However, one case presented with multiple metastatic tumors in both kidneys. The size of metastatic tumor was reported in 10 patients (mean size of 6.9 cm, range 2.5 cm to 9.3 cm). Up to now, surgery is the main treatment method for ACC metastasis to the kidney. As showed in **Table 1**, nine patients underwent radical nephrectomy, but treatment information was not mentioned in one case, and one patient with multiple metastatic tumors in both kidneys only received chemotherapy. The present case received left radical nephrectomy and postoperative chemotherapy consisted of docetaxel and cisplatin. In addition, among previous 11 cases, only four patients were followed up for 3 to 48 months, and follow-up data were not described in seven cases. There is no clinical evidence of local recurrence or new metastasis at 24 months after left radical nephrectomy, and the present patient is still in follow-up currently.

Histologically, ACC consists of two main cell types, including ductal and modified myoepithelial cells, and the two different cell populations are essential histopathological features for the diagnosis of ACC [6]. There are three typically morphologic patterns in ACC: tubular, cribriform and solid. Each of these forms can be observed as the dominant component or more commonly as a part of a composite tumor. The stroma within the tumor is generally hyalinized and may manifest mucinous or myxoid features. Immunohistochemically, ductal cells are mainly positive for AE1/AE3, CK7, CEA and CD117, while myoepithelial cells are mainly positive for P63, SMA, Calponin, S-100, CK5/6, SMA, and Vimentin [18]. Immunohistochemistry (IHC) markers can highlight two different tumor cells differentiation, which provide an important clue for the diagnosis and differential diagnosis of ACC.

In conclusion, we report a case of renal metastasis after 9 years of right parotidectomy for ACC of parotid. The patient only presented with a singular metastatic neoplasm with well-defined margin in the lower pole of left kidney, which made it easily to be diagnosed clinically as a primary tumor of the kidney. Our case underscores the importance of performing lifelong follow-up of primary parotid ACC because metastasis may occur years after resection of the primary tumor. In addition, more cases of ACC metastasis to the kidney should be documented for further understanding of its epidemiological, clinical, imageological features, molecular genetic characteristics and pathogenesis due to its extremely rarity.

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Disclosure of conflict of interest

None.

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