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

Qinqhong Liu1*, Xiaoqin Jiang2*, Ji Zhang3, Jingjing Bao2, Xiaowei Zhu2, Rongrong Dou2, Wenping Zhou4, Li Zhu4, Hong Yu2

Departments of 1General Surgery, 2Pathology, 3Image, Taizhou People’s Hospital, Taizhou, Jiangsu Province, China; 4Institute of Cardiovascular Diseases, Taizhou People’s Hospital, Taizhou, Jiangsu Province, China. *Equal contributors.

Received June 2, 2017; Accepted August 17, 2017; Epub December 15, 2017; Published December 30, 2017

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 18F-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
Metastatic adenoid cystic carcinoma of kidney

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

**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
Metastatic adenoid cystic carcinoma of kidney

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 ×).

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 clinicopathological 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].
# Metastatic adenoid cystic carcinoma of kidney

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

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

F, female; M, male; ANED, alive with no evidence of disease.
Metastatic adenoid cystic carcinoma of kidney

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, imagenological features, molecular genetic characteristics and pathogenesis due to its extremely rarity.

Acknowledgements

This work was supported by the Taizhou Social Development Project Foundation, Jiangsu, China (grant No. TS201625). The 333 Project of Scientific Research Project Foundation, Jiangsu, China (grant No. BRA2015224). The Peak of Six Talents Project Foundation, Jiangsu, China (grant No. 2016-WSW-148).

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Hong Yu, Department of Pathology, Taizhou People's Hospital, Taizhou, Jiangsu Province, China. E-mail: yuhongmiao-miao@163.com; Dr. Li Zhu, Institute of Cardiovascular Diseases, Taizhou People's Hospital, Taizhou, Jiangsu Province, China. E-mail: tzheart@126.com
Metastatic adenoid cystic carcinoma of kidney

References


