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CASE REPORT

Solitary parotid metastasis 8 years after a nephrectomy for renal cell carcinoma

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Renal cell carcinoma is a common cancer, known for its aggressive behavior and ability to metastasize nearly every organ system in the body. While the cancer commonly spreads to a select few organs and metastasis usually develops within 5 years of diagnosis, there have been numerous case reports of atypical sites of metastasis and cases of relapse up to decades after treatment. We present a case a 65-year-old male who presented with right preauricular swelling 8 years after the initial diagnosis and right nephrectomy for clear cell renal cell cancer. We take a look at previous case reports with similar presentations.

Keywords: *renal cell carcinoma*; *parotid metastasis*; *head and neck metastasis*; *nephrectomy*; *Clear cell cancer*

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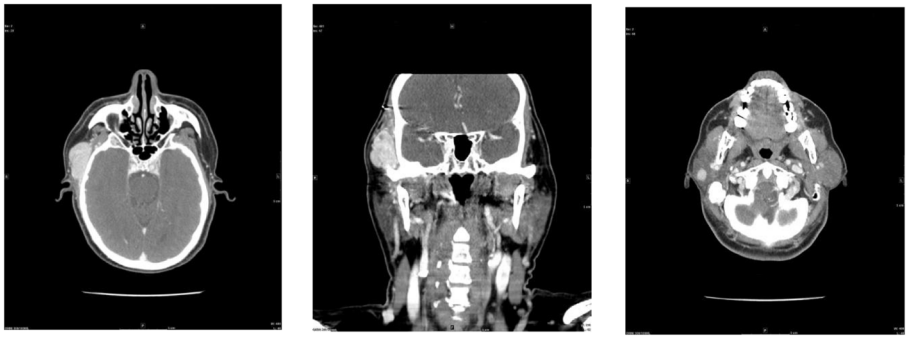
Renal cell carcinoma (RCC) is the ninth most common cancer in the United States. About 62,000 cases of renal cell carcinoma and 14,000 deaths occurred in 2016 (1). In the past, patients classically presented with hematuria, abdominal pain, and a palpable abdominal mass. Now, with the expanded use of imaging, more than 70% are found incidentally (2). RCC is known for its aggressive behavior. Approximately 20–30% of patients that presented with localized disease who underwent nephrectomy developed metastasis with a median time to relapse of 15–18 months, while 25–30% of patients with RCC were found to have metastatic disease at the time of diagnosis (3, 4).

Diffuse metastatic disease is usually treated with a combination of immunotherapy, chemotherapy, radiation, and hormonal therapy and is associated with poor outcomes and a median survival of less than 1 year (3, 5). About one third of patients with RCC eventually develop metastatic disease, most commonly affecting the lung, bone, adrenal, liver, brain, or contralateral kidney, and usually within the first 5 years of diagnosis. However, due to its aggressive and unpredictable behavior, there have been numerous reports of spread to atypical sites, and cases of late spread up to decades after treatment (2).

Here we present the case of a 65-year-old male who presented with right preauricular swelling 8 years after the initial diagnosis and right nephrectomy for clear cell renal cell cancer.

In April 2015, a 65-year-old Filipino male presented with complaints of swelling on the right side of his face for



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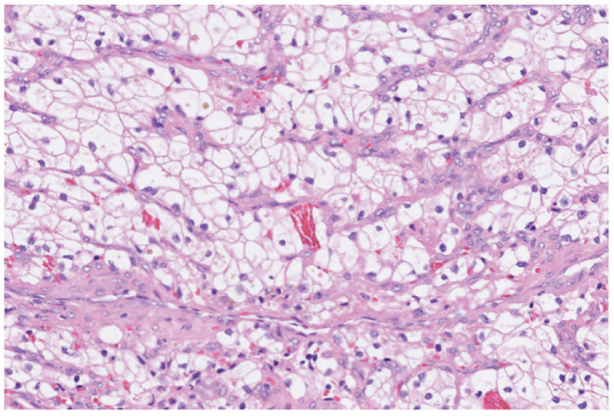
approximately 1 week. His past medical history was significant for right nephrectomy for renal cell carcinoma (RCC) (T3bN0, G2), clear cell type in 2007, and squamous cell carcinoma of the right pinna diagnosed in 2014 and treated with local excision. Total body skin was examined and the only pertinent finding was a right preauricular swelling. He was referred to ENT for further evaluation of the preauricular mass. Fine-needle aspiration was performed but was suboptimal for a definitive diagnosis. CT scan of the neck showed a homogeneously enhancing subcutaneous right preauricular mass (measuring 3.9 × 2.4 × 3.7 cm) and a homogeneously enhancing nodule in the superficial lobe of the right parotid gland. An ultrasound-guided biopsy of the mass was obtained, which showed fragments of predominantly fibrous tissue, scattered areas of fibrous tissue, and rare sebaceous fragments. The sample was negative for definitive evidence of malignant cells. The patient underwent surgical excision of the mass. The mass was noted to be hypervascular in nature and was located in the right temple area deep to the deep temporalis fascia overlying the temporalis muscle. Immunohistochemical examination was consistent with metastatic clear cell carcinoma, Fuhrman grade 2 of 4, lymphovascular invasion was identified, and the margin of resection was focally positive.

(a)



(b)

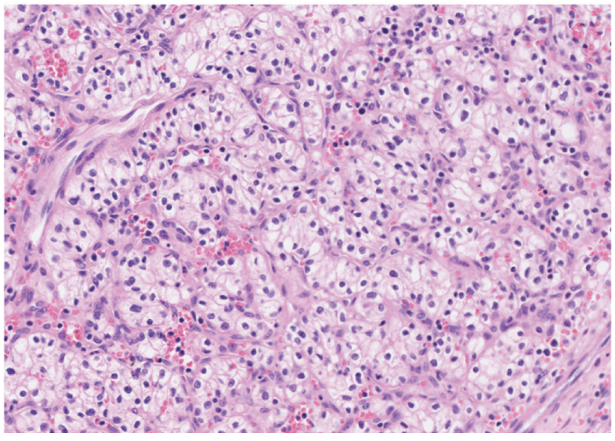


Fig. 1. Histology comparison between current temporal region mass (a) and original renal tumor removed 8 years ago (b). Both images show nests of clear cells with moderate nuclear pleomorphism (200 magnification). Tumor grading did not change (Fuhrman grade 2, ISUP 2013 grade 2).

Pathological description of clear cell renal cell carcinoma

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The removed mass was a 4.1 × 3.1 × 1.8 cm tan-pink encapsulated piece of soft tissue weighing 10.9 g. Its cut surface was approximately 50% tan-brown and 50% tan-white in color. Microscopically, it showed solid trabecular areas of clear cells with an intervening network of small thin-walled vessels (Fig. 1a). The nuclei appeared mostly round with some irregularities, and nucleoli seen at 400 × magnification were consistent with a simplified Fuhrman grade 2 of 4 renal cell carcinoma (RCC). Immunohistochemical staining of the mass for RCC and Carbonic Anhydrase IX (CAIX) antigens was positive. Slides from patients' previous nephrectomy in 2007 were obtained (Fig. 1b) and compared with this specimen and were shown to be similar in morphology.

The patient was referred to oncology for further management. PET/CT was done to evaluate for other metastatic deposits. No other obvious sites of metastatic disease were found. MRI of the face was completed, and an area of enhancement was seen measuring 42 × 32 × 16 mm. It was unclear what represented tumor versus scar. Given the focally positive margin, patient was referred to radiation oncology. He was treated with conventional external beam radiotherapy.

RCC is known for its aggressive behavior and ability to metastasize to nearly every organ system in the body. The most common sites for metastasis are the lung, bone, adrenal, liver, brain, and the contralateral kidney, but there also have been cases reported of metastasis to the head and neck, orbit, parotid gland, nasal and paranasal cavities, tongue, thyroid, heart, skin, muscle, and joints 6. Metastasis to the parotid gland in general is very uncommon but has been known to originate from hepatocellular carcinoma, squamous cell carcinoma, melanoma, retinoblastoma, carcinoma of the breast, urachus, prostate, stomach, lungs, and kidneys. A literature research done by authors of a review article in 2012 revealed a total of 45 reported cases and only 31 complete case presentations of RCC metastatic to the parotid gland (6). In 16 of these patients, parotid metastasis was the initial sign of the renal tumor. In 14 of the patients, parotid metastasis was

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found after treatment and diagnosis of RCC, at a time interval ranging from months to years, the longest interval being 19 years (6).

RCC is known to metastasize via hematogenous and lymphatic dissemination. The first major route is through the venous system. Tumor thrombi in the renal vein may spread to the Inferior vena cava then eventually into the lungs (the most common site of metastasis). The second route is through the lymphatic system. RCC is known to spread to the regional lymph nodes in about 21% of the instances. Once in the lymphatic system, it can spread to the thoracic duct and eventually to the lungs via the left subclavian vein. Tumor cells can also bypass the pulmonary capillary filtration altogether via Batson's plexus, a network of valveless veins that connect the deep pelvic veins and thoracic veins to the vertebral column or brain. This seems to be the case in our patient given the absence of lung involvement (7, 8).

Diagnosis of salivary gland tumors is somewhat controversial. Some question the utility of imaging or fine-needle aspiration biopsy, as the general consensus is that surgical resection is the optimal procedure, whether the tumor is benign or malignant. However, imaging (CT/MRI) can help assess for possible extension or invasion, and a biopsy could potentially change management. For example, if the results were consistent with lymphoma or sialadenitis, a large resection would be unnecessary (9). Fine needle aspiration biopsy (FNAB) is commonly non-diagnostic in the previously mentioned review; out of the 13 cases mentioned in FNAB, only three were diagnostic. Immunohistochemical staining is required even if the FNAB is diagnostic for clear cell, as it differentiates it from other types. RCC is known to stain positive for CD10 and Vimentin (6). CT and PETs scans are also useful in evaluating for other sites of metastasis.

Isolated parotid metastasis is ideally managed by local excision with disease-free margins and facial nerve preservation. In the review article by Lawlor and Wein, out of the 31 cases, 28 underwent local excision – superficial parotidectomies (15), total parotidectomies (5), parotidectomies with neck dissection (3), partial parotidectomy (1), deep parotidectomy (1), and facial nerve sacrifice (1). Traditionally in solitary metastasis from RCC, if operable the metastatic lesion operated upon (as in our case); however, there is a role for radiotherapy if the lesion is inoperable, or if the margins are positive (as in our patient). Depending on the radiation oncologist's preference, conventional radiation therapy (XRT) or stereotactic radiosurgery (SRS) can be used (10). Prognosis is difficult given the limited number of cases; however, the prognosis of solitary metastasis is favorable when compared with diffuse metastatic disease (5).

In our patient, while no other obvious metastatic deposit was found at the time of recurrence in the parotid, the patient, shortly after completion of radiation therapy, presented to an outside hospital with a gastrointestinal bleed. Imaging done at that time was notable for a soft tissue mass interposed between the pancreatic head and the second portion of the duodenum. A mass, measuring 6.6 cm in the greatest dimension, was originally reported as the pancreatic head occupying the right nephrectomy bed. It was further reported as eroding into the duodenal lumen. Upper gastroesophageal endoscopy revealed an ulcerated mass in the second portion of the duodenum. Endoscopic ultrasound with color doppler showed this mass to be a hypervascular lesion. Fine-needle aspiration was performed, and morphology and immunoprofile were consistent with a diagnosis of metastatic RCC. The patient was subsequently started on a tyrosine kinase inhibitor, sunitinib.

A consensus surveillance protocol does not exist for follow-up of RCC after nephrectomy; however, the longest duration of surveillance recommended is 5 years (National Comprehensive Cancer Network, American Urological Association). The greatest risk of recurrence for RCC occurs within the first 5 years after nephrectomy. About 43% recur within the first year, 70% within the second year, 80% within the third year, and 93% within the fifth year. The majority of recurrences are detected by surveillance laboratory or imaging studies in asymptomatic patients 50 to 80% of the time and the remainder by either workup of patient symptoms or physical findings (11). Metastatic RCC should be considered in the differential diagnosis in patients with a prior history of nephrectomy for RCC, regardless of how many years it has been since treatment. The extent of metastatic burden determines the approach to treatment and is directly associated with progression free survival.

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