Tonsillar Metastasis from Clear-Cell Renal Cell Carcinoma; A Case Report and Review of the Literature

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Abstract

Background
Metastasis to the oral cavity from renal cell carcinoma is very rare. The authors present a case of renal cell carcinoma metastatic to the palatine tonsil. Only six cases of metastatic renal cell carcinoma to the palatine tonsil have been reported. Common sites of RCC metastases are lungs, liver, bone, and brain. In the head and neck region, thyroid, paranasal sinuses, and parotid gland are the favoured sites.

Case Presentation
A 61-year-old male, 2 years post radical nephrectomy and adjuvant chemotherapy for metastatic Renal Cell Carcinoma (RCC), presented with new right sided throat pain and swelling to the Emergency Room. CT scan of the neck revealed an oropharyngeal tumor arising from the right tonsil; follow up otolaryngology exam and in-clinic biopsy of the mass showed clear cell nests consistent with metastatic RCC-clear cell subtype. He underwent an uncomplicated tonsillectomy for local disease control. The post-operative pathology report confirmed the diagnosis of tonsillar metastasis from RCC and the patient is currently without upper airway symptoms or pain.

Conclusion
Tonsillar metastasis from RCC is rare, however while assessing a tonsillar mass, the possibility of a metastatic lesion must be considered in the context of known prior malignancy. Biopsy with definitive histological diagnosis is imperative. Surgical treatment of the metastatic lesions of RCC should be considered in a multi-disciplinary oncology group setting based on the patient’s symptomatology and likelihood of tumor control.

Keywords
Renal Cell Carcinoma; Tonsil Mass; Tonsil Metastasis; Head and Neck Metastasis

Introduction
Renal Cell Carcinoma (RCC) accounts for more than 90% of kidney cancers, which in turn is responsible for about 2% of all cancer diagnoses worldwide [1]. RCC often metastasizes to lungs, lymph nodes, liver, bone, and brain as its preferred sites [2] with metastasis to the head and neck region reported as rare. RCC is the third most common infra-clavicular tumor to metastasize to the head and neck after only breast and lung [3]. In this region,
the common sites for metastases are the thyroid gland, paranasal sinuses, and parotid gland [4]. In this report, we describe a case of tonsillar metastasis from RCC in a 61-year-old male with known lung and liver metastases. RCC metastasis to tonsils are extremely rare with only 6 other case reports published in literature starting from 1997 [5-10].

Case Report

A 61-year-old patient visited the emergency department with a one-month history of right sided throat pain, dysphagia, and cough. 1.5 years previously, he was found to have a 15-cm left-sided renal mass extending to the left renal vein into the inferior vena cava, with cranial extension into the right atrium. There were also bilateral pulmonary and liver lesions present on the initial imaging, consistent with metastatic cancer. He subsequently underwent left radical nephrectomy, caval thrombectomy, sternotomy and resection of the right atrial thrombus. His pathology report revealed a clear cell RCC. Two months post nephrectomy, he was started on standard dose sunitinib chemotherapy, of which he received 6 cycles. He presented to the emergency room seven months after the last dose of sunitinib. At that point, he had shown a decreased burden of disease in his liver and stable pulmonary metastases, despite being off any chemotherapeutics.

While in the emergency department, a contrast-enhanced CT scan of the neck was performed (Figure 1), that showed a 2.3 x 1.3 x 2.9 cm soft tissue mass arising from right lingual tonsil causing mild airway narrowing. He was then referred to an Otolaryngologist for further assessment. Clinical examination of the oral cavity showed an exophytic right tonsillar mass that did not involve the palate (Figure 2). There was no palpable lymphadenopathy in the head and neck region.

CT scan imaging of the neck shows a 2.3 x 1.3 x 2.9 cm soft tissue mass arising from pharyngeal mucosal space of the right lingual tonsil causing mild airway narrowing

Figure 1: Sagittal, Axial and Coronal Views of Contrast-Enhanced CT scan of the Neck
Figure 2: Examination of the Oral Cavity

This figure shows an exophytic right tonsillar mass not involving the palate.

In-office biopsy of the lesion showed squamous epithelium with reactive changes and underlying stroma infiltrated by large cells with clear cytoplasm and uniform nuclei which stained positive for pancytokeratin, vimentin and PAX-8 consistent with metastatic clear cell RCC.

After a discussion with the patient and his oncology team, and due to intermittent bleeding and upper airway obstruction while lying supine, it was decided to proceed with a right radical tonsillectomy. Post-operative pathology report confirmed the diagnosis of metastatic clear cell RCC to the right tonsil with clear margins (Figure 3).

Figure 3: Post-Operative Histological Examination of Right Tonsil Specimen

(A) Right tonsil, 2X, H&E; Large nodular mass showing effacement of the normal tonsillar architecture. (B) Right tonsil, 10X, H&E; Well-circumscribed nest of clear cells abutting normal tonsillar parenchyma. (C) Right tonsil, 20X, H&E; Organoid nests of polygonal cells with clear cytoplasm, prominent round nuclei and distinct cell borders. (D) Right tonsil, 20X, PAX-8; Positive nuclear immunohistochemical staining for PAX-8

Discussion

In this paper, a rare case of tonsillar metastasis from renal cell carcinoma is described in a 61-year old patient with known metastatic RCC, status post radical nephrectomy and 6-months of sunitinib chemotherapy. The incidence of RCC has increased since 1975 partly due to earlier detection of low grade and indolent tumour, with the clear cell variant being the most common subtype of RCC [2]. However, one third of patients continue to present with regional or distant metastatic disease [2]. Of all patients with clear cell RCC who receive nephrectomy for localized disease, one third will also have distant metastases that becomes evident at a median of 1.3 years post nephrectomy [11].

The prognosis for RCC has improved with the introduction of novel chemotherapeutics. Currently, the 5-year survival rate in patients with localized disease is 74% and decreases drastically to 8% in patients with metastatic disease [2]. In a study of more than 11000 patients with metastatic RCC, Bianchi et al reported lung (45% of all metastases), bone (30%), lymph node (22%), liver (20%), adrenal (9%) and brain (8%) as the most common sites for metastases. Thirty-nine percent of their patient population had evidence of 2 or more metastatic sites. Metastases to the head and neck region, not involving brain and skull, was not reported in their study [12], likely due to its rare occurrence. In a review of case reports of rare metastatic sites of RCC published in 2011, Sountoulides, Metaxa and Cindolo described reported cases of head and neck metastases. They identified more than 150 cases of metastases to the thyroid gland, 50 cases of nose and paranasal sinuses, 28 cases of tongue, 26 cases of parotid gland, and lastly 2 cases of tonsils [4].

In our search of the literature, a total of 6 cases of tonsil metastasis from RCC were identified. In 4 cases, patients already had evidence of metastatic RCC elsewhere. The remaining 2 patients had nephrectomy with curative intent, and later presented with tonsilar metastasis as the first sign of widespread disease. Of these 6 cases, 5 were treated with tonsillectomy and 1 with radiotain therapy because of multiple comorbidities percluding a surgical treatment (Table 1).

As RCC metastases are considered radioresistant, the mainstay of treatment consists of chemotherapy. Recently, surgical resection of RCC metastases has been shown to improve survival as well [13]. In the head and neck region, surgical resection of RCC metastases should be considered and weighed against the risks of surgery.
Particularly in the tonsil region, surgical treatment can provide local control and prevent the progression of symptoms, and negate the need to continue with systemic chemotherapy and improve quality of life [14].

Several of the reported cases were originally misdiagnosed. This is a consequence of the rarity of tonsilar metastases from RCC. It is noteworthy, that less than 1% of malignant tonsilar neoplasms are of metastatic nature [15]. The majority of primary tonsilar malignancies are squamous cell carcinoma (72%) followed by non-Hodgekin (14%) and Hodgkin (2%) lymphoma as the less common possibilities [15].

When assessing a tonsilar lesion, tonsilar asymmetry or unilateral tonsilar enlargement alone is not a good predictor of malignancy [16,17]. A history of dysphagia or odynophagia combined with the presence of mucosal abnormalities in the tonsillar or peritonsillar area, and cervical lymphadenopathy should suggest further imaging workup and biopsy16. It has also been shown that a physician’s high clinical suspicion of the lesion was a good predictor of malignancy in assessing unilateral tonsilar enlargement [17]. In this case, the patient had odynophagia, and an exophytic mass. With a documented history of an infra-clavicular renal cell carcinoma the differential of the tonsillar mass included metastatic RCC as well as a second primary tonsillar malignancy. The patient is currently 3 months from tonsillectomy, has no upper airway obstructive symptoms or discomfort in the oropharynx. Because of the negative margins and the stability of his other metastatic sites he did not require adjuvant chemotherapy.

Conclusion
This case report highlights the importance of a broad differential diagnosis in clinical assessment of lesions in the oropharynx, specially in patients with known history of malignancy. Biopsy of these lesions have the potential to alter management and is therefore necessary. Surgical treatment of metastatic RCC in the head and neck should be considered to prevent disease progression and may defer treatment with systemic chemotherapy.

Declarations
Ethics approval and consent to participate: The UBC and affiliated investigators are not required to obtain Clinical Research Ethics Board approval for case reports. Consent to participate was not applicable for this case report.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and material: Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

Competing Interests
The authors declare that they have no competing interests.

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Authors’ Contributions
ME was a major contributor in writing the manuscript. AA and EP analyzed and interpreted the patient data, examination and investigations regarding the otolaryngeal disease and the prior cancer history. Both AA and EP contributed to writing and editing the manuscript. TN and AG performed the histological examination of the table.

### Table 1: Review of All Case Reports of Tonsillar Metastasis from RCC

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Previous Nephrectomy</th>
<th>Other Metastases</th>
<th>Treatment of Tonsillar Metastasis</th>
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tonsil, and contributed to writing the pathology sections of the manuscript. All authors read and approved the final manuscript.

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**References**


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