*Online Journal of Health and Allied Sciences*
Peer Reviewed, Open Access, Free Online Journal
Published Quarterly : Mangalore, South India : ISSN 0972-5997
Volume 12, Issue 2; Apr-Jun 2013

This work is licensed under a
Creative Commons Attribution-
No Derivative Works 2.5 India License

*Case Report:*

# Metastatic Renal Cell Carcinoma in the Sinonasal Region

**Authors**
**Jyothi A Raj,** Associate Professor of Pathology,
**V Mahantachar,** Professor of Pathology,
**T Rajaram,** Professor and Head of Department of Pathology,
**Rajarajeswari Medical College and Hospital, Mysore Road, Bangalore - 560074, India.**

**Address for Correspondence**
**Dr Jyothi A Raj,**
159, 43rd Cross, 2nd main,
8th block, Jayanagar,
Bangalore- 560082,
India.
**E-mail:** jyoki255@yahoo.co.in

**Citation**
Raj JA, Mahantachar V, Rajaram T. Metastatic Renal Cell Carcinoma in the Sinonasal Region. *Online J Health Allied Scs.* 2013;12(2):19. Available at URL: http://www.ojhas.org/issue46/2013-2-19.html

**Open Access Archives**
http://cogprints.org/view/subjects/OJHAS.html
http://openmed.nic.in/view/subjects/ojhas.html

Submitted: Jan 2, 2013; Accepted: Apr 1, 2013; Published: Aug 15, 2013

**Abstract:** Sinonasal region is an exceptional site for metastatic tumors. Renal cell carcinoma is known to metastasise to the most unusual sites, the sinonasal region being one of them. Clear cell carcinoma is its most common histologic variant. A sixty year old male presented with epistaxis and nasal obstruction. Clinical examination and CT scan revealed a vascular tumor in the right nasal cavity and maxillary sinus. The tumor was resected and sent for histopathological examination. A diagnosis of metastatic clear cell renal cell carcinoma was made and confirmed with immunohistochemistry (IHC). The pathologic diagnosis was made without prior knowledge of the primary tumor in the kidney. Very few cases of metastatic renal cell carcinoma in the sinonasal region have been reported in literature. We present this case to document its occurrence, highlight the rarity and briefly discuss the differential diagnoses of clear cell carcinoma in the sinonasal area, based on morphology and IHC.

**Key Words:** Sinonasal region; Metastatic renal cell carcinoma; Diagnosis

## Introduction

Renal cell carcinoma (RCC) is an aggressive tumor, representing approximately 3% of all malignant tumors.(1) Metastasis is common, seen in 20-50% of patients, at diagnosis or post-nephrectomy. Common sites include lungs, liver, bone, brain, and adrenals, although no site is excluded. RCC along with malignant melanoma and choriocarcinoma, are notorious for metastasising to the most unusual sites such as the larynx, parotid, thyroid, heart and pituitary.(2) Sinonasal region is an exceptional site, with very few cases reported in literature.(1,3)

Clear cell carcinoma is a rare morphologic pattern with an incidence of 9.6 per 100,000. Kidneys constitute the commonest primary site of clear cell carcinoma (85%).(1) It is rarely seen at other sites. Although primary carcinoma of the clear cell type is known to arise in the sinonasal area, metastatic RCC should be considered in the differential diagnosis of such tumors. Diagnosis of metastatic RCC is important as targeted therapies are now an important treatment modality.

## Case Report

A sixty year old male presented with recurrent bleeding from the right nostril and history of nasal obstruction. Local examination revealed a mass occupying the entire right nasal cavity. The left nasal cavity was patent. CT scan reported a heterogeneously enhancing mass, occupying the right nasal cavity and maxillary sinus, and extending into the nasopharynx. There was no obvious bone erosion. A vascular tumor was suspected clinically. Due to persistent epistaxis, exploration and sphenopalatine artery ligation was done. Two biopsies were taken, both of which were inconclusive. Subsequently, the mass was excised and sent for histopathological examination.

**Gross Findngs:** Multiple fragmented grey white tissue bits were received, largest measuring 3.0x2.0x1.0cm, and the smallest measuring 2.0x1.0x1.0cm. The external surface was mucoid, with foci of ulceration. Cut surface was grey white with areas of hemorrhage. Chips of bone were also received, which were grossly unremarkable.

The representative tissue was processed and the paraffin sections were stained with H&E.

**Microscopy:** Benign respiratory epithelium was seen lining the surface. The underlying stroma showed a tumor composed of cells with abundant clear cytoplasm, arranged in nests. The nuclei were small, centrally placed, with dense chromatin and inconspicuous nucleoli; mild pleomorphism was seen at places, with larger size and open chromatin. The cell nests were separated by vascular sinusoids lined by endothelial cells. There was very little stroma between the

cells (Fig. 1). The tumor was seen extending upto, but not involving the surface lining epithelium or the serous glands accompanying the lining mucosa. Adjacent salivary tissue and bone were uninvolved. The morphology was strongly suspicious of metastatic renal cell carcinoma. The tumor was positive for cytokeratin and vimentin; CD10 showed focal positivity (Fig. 2). With the above histologic findings and IHC profile, a diagnosis of metastatic renal cell carcinoma, of clear cell type, in the right sinonasal region was made. Further clinical details were sought and the patient disclosed having undergone nephrectomy for renal cell carcinoma six years back.

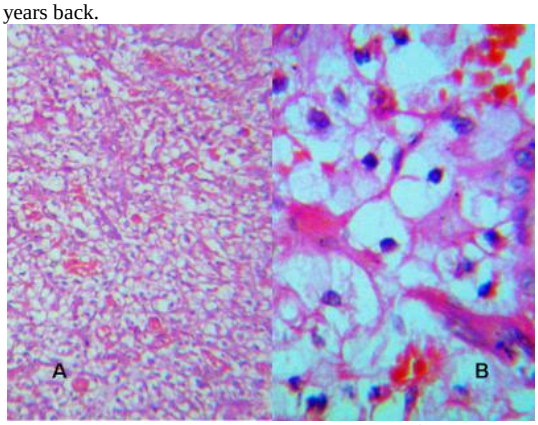


**Figure 1: Photomicrograph showing nests of clear cells surrounded by delicate vascular sinusoids (H&E; Figure 1A-10x, Fig 1B-40x)**

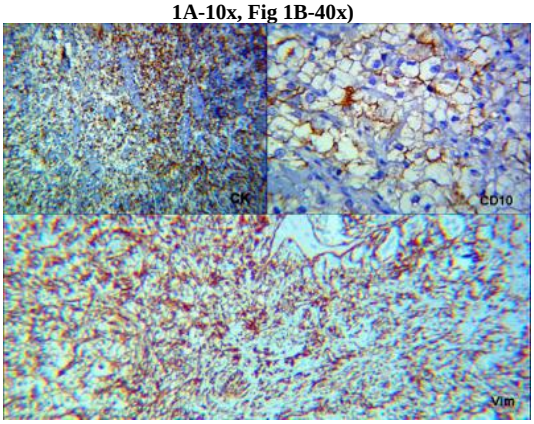


**Figure 2: Photomicrographs showing immunohistochemical stains in metastatic RCC**

**Discussion**

Sinonasal area is an unusual site for metastatic tumors. Renal cell carcinoma, in particular, is known to metastasise to the sinonasal region, although extremely rare. Nearly 50 cases of nasal metastases and about 105 cases of maxillary involvement have been reported in literature so far.(4,5)

Epistaxis is the most common presenting symptom in metastatic RCC. It should be included in the differential diagnosis of nasal bleeds, as experienced in the present case. The tumor is hypervascular due to the presence of abundant sinusoids, leading to persistent epistaxis. The high vascularity of the tumor can be explained by mutation of the VHL gene, which causes upregulation of hypoxia-induced factor 1a, which in turn leads to angiogenesis through VEGF upregulation.(4) In the case discussed here, sphenopalatine artery was ligated prior to biopsy which not only controlled the bleed, but also reduced the tumor size considerably.

The possibility of metastasis should be considered when carcinomas of unusual morphology are encountered in the sinonasal area.(2) Kaminski et al reported 46 cases of metastatic tumors in the head and neck region, of which four were in the nasal cavity and paranasal sinuses, with one case of RCC involving the maxillary sinus.(6) RCC is the most common primary tumor to metastasise to the paranasal sinuses, the maxillary sinus being most commonly involved.(1)

About 30% of patients with RCC present with metastasis at the time of diagnosis and another 30% develop metastasis after initial treatment. Late metastasis is not uncommon. The interval between nephrectomy for RCC and nasal metastasis was 6 years in the present case. Longer intervals of upto 17 years have been reported.(7) RCC spreads via the hematogenous route, although lymphatic metastasis is also known. Microvascular invasion plays an essential role in metastasis and is considered an important prognostic marker for recurrence. Tumor cells spread either through the inferior vena cava or through the Batson's paravertebral venous plexus, which allows the cells to escape the pulmonary capillary filter and spread to unusual sites.

Clear cell carcinoma accounts for 75% of all renal neoplasms. It is one of the great mimics in pathology. Tumor cells in clear cell RCC have abundant clear cytoplasm due to presence of lipid and glycogen. The nuclei are spherical and centrally placed. The chromatin could be dense or open, with inconspicuous to macronucleoli. The cells are arranged in nests and alveolar pattern, surrounded by a regular network of small thin walled blood vessels with little supporting fibrous tissue, a diagnostic feature of this tumor. Fuhrman grading system is a 4-tier grading system for nuclei in RCC. It grades tumors based on the size of the nuclei, their shape, chromatin pattern and presence and prominence of nucleoli. Those with low nuclear grade are less likely to metastasise.(8) Clear cell RCCs react positively for cytokeratin (CK), AE1, Cam5.2, vimentin, RCC marker, CD10 and EMA. MUC1 and MUC3 are consistently expressed. The tumor in the present case showed the above morphologic features with nuclear grade II. CK, vimentin and CD10 were the markers used and were positive.

The main differential diagnoses include hepatocellular carcinoma, clear cell sarcoma, hemangiopericytoma, and malignant melanoma.(3) In the present case, CK positivity indicates epithelial nature of the tumour. Vimentin was positive in the endothelial cells and smooth muscle cells in the sinusoids and vascular septae. CD10 positivity indicated metastatic RCC. CK and CD10 can be positive in hepatocellular carcinoma and melanoma. Co-expression of CK and vimentin, common in clear cell RCCs, is not seen in other carcinomas and should be taken as suggestive of a renal primary when found in metastasis of unknown origin.(9) This, considered with history of nephrectomy for RCC, clinched the diagnosis in favour of metastatic renal cell carcinoma.

Salivary gland tumors with clear cell change are excluded by the lack of relation between the tumor and salivary gland.(10) The salivary tissue in the vicinity of the tumor was uninvolved in our case. Rarely, primary clear cell carcinoma can arise from the respiratory epithelium in the sinonasal tract. Lack of transition from benign respiratory epithelium to malignant clear cells excluded this entity in the present case. Sinonasal adenocarcinoma is positive for CK and EMA, negative for S100, vimentin and CD10. Salivary gland tumors are positive for CK and S100, negative for CD10. Metastatic RCC is positive for CK, vimentin and CD10.

Sinonasal renal cell-like adenocarcinoma is an unusual neoplasm, described by Zur et al and Hadi et al, that is a histologic mimic of RCC. It is diagnosed by exclusion after ruling out metastatic RCC. RCC marker and vimentin are negative in this entity unlike RCC.(11) Sinonasal renal cell-like adenocarcinoma and low grade sinonasal adenocarcinomas are probably same entities, sharing similar morphologic and immunohistochemical profiles.

Clear cell RCCs carry worse prognosis. Nuclear grade, after stage, is the most important prognostic feature. Prognosis for metastatic carcinoma is poor despite advances in treatment like immunotherapy and mTOR kinase inhibitors. Median survival is about a year and expected 5-year survival is less than 20%.(12) Surgery with radiotherapy is the treatment of choice for metastatic deposits in the sinonasal region. It reduces the tumor burden and also controls epistaxis.

**Conclusion**

Renal cell carcinoma is an aggressive tumor with a propensity for distant metastasis. The patterns of spread are not well understood, leading to unusual metastatic sites and atypical presenting symptoms. The nasal cavity and paranasal sinuses are a rare site for metastatic deposits. Carcinoma in the sinonasal area, particularly clear cell variant, is very rare and is most often from a metastasising renal cell carcinoma; it carries a poor prognosis. Occult RCCs presenting as unknown primaries at distant sites or recurring years after radical nephrectomy pose unique problems in diagnosis. It has to be differentiated from salivary gland carcinomas and the rarer sinonasal adenocarcinomas of similar morphology. This case was diagnosed based on histopathological findings, without the prior knowledge of nephrectomy, which the patient had undergone for RCC 6 years back. We report this case to highlight an unusual site for metastasis from an RCC, 6 years after initial diagnosis and also to reinforce the view that a detailed history and morphology is as relevant as IHC in arriving at a diagnosis.

**References**


1. Bechara GR, Resende Junior JAD, Gouveia HA, et al. Metastasis to paranasal sinuses as the first presenting sign of renal cell carcinoma. *Open Journal of Urology*. 2012;2: 28-31.
2. Nasab MS, Jafari M, Bahar SHM, et al. Endoscopic management of unusual metastasis of renal cell carcinoma to the sinonasal area. *Acta Medica Iranica*. 2009;47(5):419-421.
3. Terada T. Renal cell carcinoma metastatic to the nasal cavity. *Int J Clin Exp Pathol*. 2012;5(6):588-591.
4. Sountoulides P, Metaxa L, Cindolo L. Atypical presentations and rare metastatic sites of renal cell carcinoma: a review of case reports. *Journal of Medical Case Reports.*2011;5:429. Available at http://www.jmedicalcasereports.com/content/5/1/429
5. Fyrmpas G, Adeniyi A, Baer S. Occult renal cell carcinoma manifesting with epistaxis in a woman: a case report. *Journal of Medical Case Reports.* 2011;5:79. Available athttp://www.jmedicalcasereports.com/content/5/1/79
6. Kaminski B, Kobirorska-Novak J, Bien S. Distant metastasis to nasal cavities and paranasal sinuses, from the organs outside the Head and Neck. *The Polish Otolaryngology.* 2008; 62(4): 422-425.
7. Ziari M, Shen S, Amaro RJ, et al. Metastatic renal cell carcinoma to the nose and ethmoid sinus. *Urology* 2006;67:199.
8. Amin MB, Tamboli P, Javidan J, et al. Prognostic impact of histologic subtyping of adult renal epithelial neoplasms: an experience of 405 cases. *Am J Surg Pathol.*2002;26:281-291.
9. Eble JN, Young RH. Tumors of the urinary tract. (Chapter 12, vol 1). In Fletcher CDM, editor. Diagnostic histopathology of tumors, 3rd ed. Philadelphia, USA: Churchill Livingstone (Elsevier); 2007. p 494
10. Negahban S, Daneshbod Y, Khademi B, et al. Sinonasal Clear Cell Adenocarcinoma: A case report. *Acta Cytol.* 2009;53:597-600.
11. Storck K, Moh'd Hadi U, Simpson R, et al. Sinonasal renal cell-like adenocarcinoma: A report on four patients. *Head Neck Pathol.* 2008 June;2(2):75-80.
12. Custodio S, Joaquim A, Peixoto V, et al. Metastatic renal cell carcinoma: The importance of immunohistochemistry in differential diagnosis. *Case Rep Oncol*. 2012 Jan-Apr;5(1):30-34.