# Rapidly growing and ulcerating metastatic renal cell carcinoma of the lower lip: A case report and review of the literature

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Abstract. Renal cell carcinomas (RCCs) have a tendency to metastasize at an early stage, therefore, the patients frequently exhibit metastatic disease at the time of diagnosis. Common locations for the metastases are adjacent organs and abdominal lymph nodes; however, occasionally metastasis to the peripheral organs may be the initial clinical symptom. The 71-year-old male patient in the current case suffered from radioresistant and aggressively behaving RCC metastasis in the mandible and lower lip, which was successfully managed by surgical resection. RCC metastasis to the facial area is considered to be uncommon based on a review of the existing literature. RCC are somewhat radioresistant and therefore, palliative surgery must be considered when treating patients with this metastatic disease.

### Introduction

Renal cell carcinoma (RCC) is divided into clear-cell, papillary, oncocytoma and collecting duct subtypes which exert different invasion and metastatic potentials (1). The clear-cell carcinoma subtype represents <85% of reported cases, according to the United States National Centre for Health Statistics report (2). Recurrence of the disease following surgery can be observed in one-third of the cases and one-fourth of the patients exhibit metastatic disease at the time of a diagnosis (1,2). RCC metastases are often regarded as radioresistant tumors, which was observed in the present case (2-4). For this reason, metastases are usually treated with relatively high biologically effective doses. Metastasis to adjacent organs and bone are common, but distant metastases to the head and neck region are rare. Of these previously reported cases, the facial skin area has been

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the most common location. The present study demonstrates the case of rapidly growing and radiotherapy-resistant RCC metastasis to the lower lip and chin which was treated with surgery. The functional and esthetic outcome was satisfactory despite the large gap generated by the metastasis resection. This case provides evidence that palliative surgery may achieve a higher quality of life for end-stage oncological patients.

## Case report

The current study presents the case of a 71-year-old male patient who was diagnosed with RCC in September 2011. At that time, the disease was at an advanced stage. The primary tumor in the lower pool of the right kidney was infiltrating the adjacent structures and the patient exhibited synchronous mediastinal and pleural metastases, with the latter causing persistent pleural effusion and markedly declining lung function. Due to the poor performance status and risk of side effects, the patient refused to initiate the disease-controlling sunitinib treatment and chose to proceed to the optimum supportive care. The patient presented with subcutaneous metastases to the lower lip and back of the neck 11 months after the diagnosis. The patient received palliative radiotherapy (split course, 15/5 Gy) to the rapidly growing lower lip metastasis. The tumor diameter was 1.5 cm when the treatment was initiated. However, no clinical response to radiotherapy was obtained, and three weeks following the treatment the tumor had more than tripled in diameter. Thus, the patient was evaluated at the Department of Oral and Maxillofacial Diseases (Helsinki University; Helsinki, Finland). At the time of admission the patient had a spontaneously bleeding mass (size, 60x60 mm) in the lower lip and the anterior mandible area (Fig. 1A). In addition to this, there was a group of smaller subcutaneous metastases located at the subcutaneous nuchal area, which did not exhibit symptoms. Resection of the lip metastasis was performed with 5-mm clinical margins and for this reason, the resection was extended to the bony surface of the mandible. The lower lip was also partially resected as the small subcutaneous metastases had continued to spread into the lip mucosa (Fig. 1B). To prevent wound tension following closure, the skin was dissected subcutaneously from the resection line

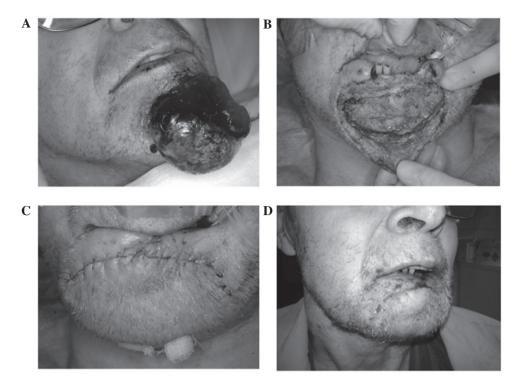


Figure 1. Labial and cutaneous renal cell carcinoma metastasis. (A) The patient exhibited a spontaneously bleeding mass, which had doubled in size within one week. (B) The tumor was resected with 5-mm clinical margins and transcutaneous sutures fixed to the titanium chin plate were used to support the skin and facilitate wound closure. (C) The lip was reconstructed and the skin was suspended by the titanium plate to support lip closure and prevent wound traction. (D) Postoperative follow-up at three weeks indicated no recurrent metastasis.

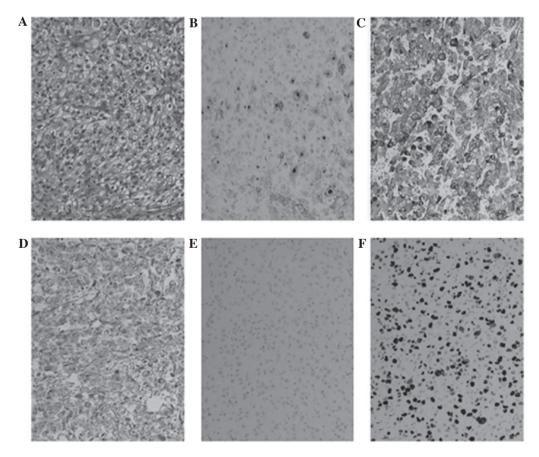


Figure 2. Histological analysis of the mass demonstrated renal cell carcioma metastasis. (A) Hematoxylin and eosin staining identified clear cell differentiation. Immunostaining revealed (B) some positivity for cluster of differentiation 10, in addition to (C) strong positivity for pan-cytokeratin (CK). The tumor was (D) positive for vimentin and (E) negative for CK7. (F) The Mib-1 proliferation index was high and in certain areas increased to  $\leq$ 70%. Magnification, x200.

Table I. Sites of renal cell carcinoma metastases in the head and neck area obtained from previous studies.

Location	Cases, n (refs)
Skin and subcutaneous	24 (4-11)
lymph nodes	
Parotid gland	10 (10,18,22,24,33,35,39,41,45)
Tongue	8 (14,15,19,23,31,36,48,51)
Oral mucosa	6 (20,29,30,34,36,40)
Tonsils, facial muscles and oropharynx	9 (21,27,32,34,36,40,50)
Nasal cavity and paranasal sinuses	10 (25,26,28,36,39,42,47,49)
Orbit	3 (15,17,43)
Mandible	3 (12,13,43)
Maxilla	2 (8,16)

The primary location of the renal cell carcinoma was included in the table when various locations were stated in a single study.

to the upper neck, pulled over the chin to cover visible bone, and resuspended with transcutaneous sutures to the titanium plate (MatrixMFACE Plating System; Synthes Holding AG, Solothurn, Switzerland) in the mandible (Fig. 1B and C). The patient was satisfied with the outcome at the three-week postoperative follow-up and no clinical sign of recurrence was observed (Fig. 1D). Histological examination via immunohistochemical staining (Fig. 2) identified the tumor as metastatic RCC and the mass was resected with clear lateral margins.

## Discussion

RCC commonly metastases to adjacent organs, and up to one-fourth of patients have metastases present at the time of the diagnosis (1,2). Four major subtypes of RCC exist (clear-cell, papillary, oncocytoma and collecting duct carcinoma), with different invasion and metastatic potentials. However, none of them have been reported to be particularly invasive to the head and neck region (1,2). Of the 75 previously reported cases of metastatic RCC to the head and neck region, the majority were already diagnosed with RCC, however, certain patients exhibited oral metastasis as the initial manifestation of the disease. This highlights the importance of full body imaging to identify whether the patient has previously undergone surgery for head and neck neoplasms, to avoid inaccurately diagnosing a newly formed metastasis as the recurrence of a former tumor. A third of the previously identified cases of patients with head and neck RCC metastases have been reported on the facial skin area (4-11), although the parotid gland, paranasal sinuses and tongue are also common locations. In addition, single cases of nephroblastoma (also termed, Wilms' tumor) and renal sarcomas have been reported in the head and neck area (12,13). According to earlier reports, none of the RCC subtypes preferentially metastasize to the head and neck area. The locations of previously reported metastases are listed in Table I (4-51).

In conclusion, surgery is rarely the first option when treating RCC patients with multiple metastases. However, it is important to consider palliative surgery for certain patients, as surgical management of the metastasis may provide an improved quality of life although this type of surgery does not affect the final outcome.

#### References

- Cohen HT and McGovern FJ: Renal-cell carcinoma. N Engl J Med 353: 2477-2490, 2005.
- 2. Jemal A, Siegel R, Ward E, Hao Y, Xu J and Thun MJ. Cancer statistics, 2009. CA Cancer J Clin 59: 225-249, 2009.
- 3. Owens RM, Friedman CD and Becker SP: Renal cell carcinoma with metastasis to the parotid gland: case reports and review of the literature. Head Neck 11: 174-178, 1989.
- Zhang Y, Gu ZY, Tian Z, Yang C and Cai XY: Oral metastasis from primary transitional cell carcinoma of the renal pelvis: report of a case. Int J ORal Maxillofac Surg 39: 737-739, 2010.
- Chauhan A, Ganguly M, Nath P and Chowdhary GS: Cutaneous metastasis to face and neck as a sole manifestation of an unsuspected renal cell carcinoma. Int J Dermatol 50: 81-84, 2011.
- Chhabra P, Bhatt V and Brown AM: Metastatic renal cell carcinoma in the neck: an unusual presentation. Dent Update 36: 511-513, 2009.
- Giuliani A, Caporale A, Borghese M, Galati G, Di Bari M and Demoro M: Papillary renal cell carcinoma presenting as nodal metastases to the neck. J Exp Clin Cancer Res 18: 579-582, 1999.
- 8. Langille G, Taylor SM and Bullock MJ: Metastatic renal cell carcinoma to the head and neck: summary of 21 cases. J Otolaryngol Head Neck Surg 37: 515-521, 2008.
- Mahmoudi HR, Kamyab K and Deneshpazhooh M: Cutaneous metastasis of renal cell carcinoma: case report. Dermatol Online J 18: 12, 2012.
- Mrena R, Leivo I, Passador-Santos F, Hagström J and Mäkitie AA: Histopathological findings in parotid gland metastases from renal cell carcinoma. Eur Arch Otorhinolaryngol 265: 1005-1009, 2008.
- Syryło T, Syryło A, Jurkiewicz D, Zieliński H and Pietka T: An upper lip tumour as the presenting symptom of metastatic renal cancer. Otolaryngol Pol 64: 318-319, 2010.
- 12. Florine BL, Simonton SC, Sane SM, Stickel FR, Singher LJ and Dehner LP: Clear cell sarcoma of the kidney: report of a case with mandibular metastasis simulating a benign myxomatous tumor. Oral Surg Oral Med Oral Pathol 65: 567-574, 1988.
- 13. Jia J, Chen XM, Sun ZJ and Zhang WF: Mandibular metastasis of nephroblastoma: a rare case. Int J Oral Maxillofac Surg 35: 1160-1161, 2006.
- Aguirre A, Rinaggio J and Diaz-Ordaz E: Lingual metastasis of renal cell carcinoma. J Oral Maxillofac Surg 54: 344-346, 1996.
- 15. Airoldi M, Succo G, Valente G, Cavalot A, Gabriele P and Bumma C: Head and neck metastases of renal cancer after nephrectomy: a report of 2 cases. Tumori 81: 213-214, 1995.
- Alvarez-Múgica M, Bulnez Vàzquez V, Jalón Monzón A, Gil A, Rodríguez Robles L and Miranda Aranzubía O: Late recurrence from a renal cell carcinoma: solitary right maxillar mass 17 years after surgery. Arch Esp Urol 63: 147-150, 2010.
  Bersani TA, Costello JJ Jr, Mango CA and Streeten BW: Benign
- 17. Bersani TA, Costello JJ Jr, Mango CA and Streeten BW: Benign approach to malignant orbital tumor: metastatic renal cell carcinoma. Ophthal Plast Reconstr Surg 10: 42-44, 1994.
- 18. Borghi L, Bianchini E, Ballotta MR and Reale D: Metastatic renal cell carcinoma presenting as a parotid tumor: a case report. Pathologica 87: 168-170, 1995.
- 19. Cochrane TJ, Cheng L and Crean S: Renal cell carcinoma: A rare metastasis to the tongue a case report. Dent Update 33: 186-187, 2006.
- Corsi A, Guerra F, Grippaudo G and Bosman C: Oral metastasis of renal cell carcinoma. Report of case and critical evaluation of morphologic features for differential diagnosis. Pathologica 86: 665-669, 1994.
- Dee SL, Eshghi M and Otto CS: Laryngeal metastasis 7 years after radical nephrectomy. Arch Pathol Lab Med 124: 1833-1834, 2000.
- 22. Deeb R, Zhang Z, Kini S and Ghanem T: Metastatic renal cell carcinoma to the parotid gland presenting 19 years after nefrectomy: case report and review of literature. Laryngoscope 120 (Suppl 4): S128, 2010.

- 23. Friedlander AH and Singer R: Renal adenocarcinoma of the kidney with metastasis to the tongue. J Am Dent Assoc 97: 989-991, 1978.
- Günbay MU, Ceryan K and Küpelíoğlu AA: Metastatic renal carcinoma to the parotid gland. J Laryngol Otol 103: 417-418, 1989.
- 25. Hamdoon Z, Jerjes W, Upile T, Akram S and Hopper C: Metastatic renal cell carcinoma to the orofacial region: A novel method to alleviate symptoms and control disease progression. Photodiagnosis Photodyn Ther 7: 246-250, 2010.
- 26. Homer JJ and Jones NS: Renal cell carcinoma presenting as a solitary paranasal sinus metastasis. J Laryngol Otol 109: 986-989, 1995.
- Kian A and Kato SN: Renal cell carcinoma metastatic to the base of tongue: a case report. Hinyokika Kiyo 50: 791-793, 2004 (In Japanese).
- Lee HM, Kang HJ and Lee SH: Metastatic renal cell carcinoma presenting as epistaxis. Eur Arch Otorhinolaryngol 262: 69-71, 2005
- 29. Maestre-Rodríguez O, González-García R, Mateo-Arias J, Moreno-García C, Serrano-Gil H, Villanueva-Alcojol L, Campos-de-Orellana AM and Monje-Gil F: Metastasis of renal clear-cell carcinoma to the oral mucosa, an atypical location. Med Oral Patol Oral Cir Bucal 14: e601-e604, 2009.
- 30. Makos CP and Psomaderis K: A literature review in renal carcinoma metastasis to the oral mucosa and a new report of an epulis-like metastasis. J Oral Maxillofac Surg 67: 653-660, 2009.
- 31. Marioni G, Gaio E, Poletti A, Derosas F and Staffieri A: Uncommon metastatic site of renal adenocarcinoma: the oral tongue. Acta Otolaryngol 124: 197-201, 2004.
- 32. Massaccesi M, Morganti AG, Serafini G, Di Lallo A, Deodato F, Picardi V and Scambia G: Late tonsil metastases from renal cell cancer: a case report. Tumori 95: 521-524, 2009.
- 33. Melnick SJ, Amazon K and Dembrow V: Metastatic renal cell carcinoma presenting as a parotid tumor: a case report with immunohistochemical findings and a review of the literature. Hum Pathol 20: 195-197, 1989.
- 34. Narea-Matamala G, Fernández-Toro Mde L, Villalabeitía-Ugarte E, Landaeta-Mendoza M and Rojas-Alcayaga G: Oral metastasis of renal cell carcinoma, presentation of a case. Med Oral Patol Oral Cir Bucal 13: E742-E744, 2008.
- 35. Park YW and Hlivko TJ: Parotid gland metastasis from renal cell carcinoma. Laryngoscope 112: 453-456, 2002.
- 36. Pires FR, Azevedo RS, Ficarra G, Cardoso AS, Carlos R, Kowalski LP and de Almeida OP: Metastatic renal cell carcinoma to the oral cavity and clear cell mucoepidermoid carcinoma: comparative clinicopathologic and immunohistochemical study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 109: e22-e27, 2010

- 37. Preechawai P, Amrith S, Yip CC and Goh KY: Orbital metastasis of renal cell carcinoma masquerading as cysticercosis. Orbit 27: 370-373, 2008.
- 38. Sarkis P, Bou-Malhab F and Mouaccadieh L: Solitary laryngeal metastasis from renal cell carcinoma of the kidney: clinical case and review of the literature. Prog Urol 22: 307-309, 2012 (In French).
- 39. Schantz JC, Miller SH and Graham WP III: Metastatic hypernephroma to the head and neck. J Surg Oncol 8: 183-190, 1976.
- Schwab B and Lee WT: Bilateral renal cell carcinoma metastasis in the oral cavity. Am J Otolaryngol 33: 154-155, 2012.
- 41. Seijas BP, Franco FL, Sastre RM, García AA and Lópexz-Cedrún Cembranos JL: Metastatic renal cell carcinoma presenting as a parotid tumor. Oral Surg Oral Med Oral Pathol Oral radiol Oral Endod 99: 554-557, 2005.
- 42. Sgouras ND, Gamatsi IE, Porfyris EA, Lekka JA, Harkiolakis GC, Nikolopoulou SM and Valvis PJ: An unusual presentation of a metastatic hypernephroma to the frontonasal region. Ann Plast Surg 34: 653-656, 1995.
- 43. Shetty SC, Gupta S, Nagsubramanium S, Hasan S and Cherry G: Mandibular metastasis from renal cell carcinoma. A case report. Indian J Dent Res 12: 77-80, 2001.
- 44. Simo R, Sykes AJ, Hargreaves SP, Axon PR, Birzgalis AR, Slevin NJ and Farrington WT: Metastatic renal cell carcinoma to the nose and paranasal sinuses. Head Neck 22: 722-727, 2000.
- 45. Spreafico R, Nicoletti G, Ferrario F, Scanziani R and Grasso M: Parotid metastasis from renal cell carcinoma: a case report and review of the literature. Acta Otorhinolaryngol Ital 28: 266-268, 2008
- 46. Susan LP, Daughtry JD, Stewart BH and Straffon RA: Palatal metastases in renal cell carcinoma. Urology 13: 304-305, 1979.
- 47. Vreugde S, Duttmann R, Halama A and Deron P: Metastasis of a renal cell carcinoma to the nose and paranasal sinuses. Acta Otorhinolaryngol Belg 53: 129-131, 1999.
- 48. Will TA, Agarwal N and Petruzelli GJ: Oral cavity metastasis of renal cell carcinoma: a case report. J Med Case Rep 2: 313, 2008.
- 49. Yeh HC, Yang SF, Ke HL, Lee KS, Huang CH and Wu WJ: Renal cell carcinoma presenting with skull metastasis: a case report and literature review. Kaohsiung J Med Sci 23: 475-479, 2007.
- Yiotakis J, Hantzakos A, Kostakopoulos A and Adamopoulos G: Intramasseteric metastasis of renal cell carcinoma. J Laryngol Otol 115: 65-67, 2001.
- 51. Yoshitomi I, Kawasaki G, Mizuno A, Nishikido M, Hayashi T, Fujita S and Ikeda T: Lingual metastasis as an initial presentation of renal cell carcinoma. Med Oncol 28: 1389-1394, 2011.