



Renal Cell Carcinoma Metastasizing To Larynx: A Case Report

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Abstract

Renal Cell Carcinoma (RCC) is a malignant tumor occurring in 5th-6th decade of life with an increasing incidence reported in the US but stable in Europe. The metastasis of RCC to head and neck region is infrequent and very rarely seen in larynx. Very few cases of RCC metastasizing to larynx are reported in literature. We report a case of RCC in a middle aged male with metastasis to larynx, 7 years after initial diagnosis and nephrectomy. These unusual tumor metastases have unique pathobiology and route of metastasis, and there can be a long interval from initial diagnosis of primary tumor. The diagnosis of metastatic

RCC in unusual locations is often not easy. Treatment options include metastasectomy, radiotherapy and systemic chemotherapy but with a poor outcome. A differential diagnosis should always be considered in metastatic head and neck tumors. The need for prompt accurate diagnosis, risk stratification at initial primary diagnosis, surveillance, and long term regular follow up is emphasized.

Keywords

Metastatic RCC, Laryngeal metastasis, Royal Hospital Oman, Metastatic Ca, metachronous metastasis,

Introduction

Renal Cell Carcinoma (RCC) is reported as 2-3% of all malignant tumors (8th commonest in males and 14th in females), with incidence rising in the USA. The incidence is reported highest in North America and lowest in Asia and Africa. It is the 10th leading cause of cancer death worldwide. Head and neck region (HN) is known to have primary malignant carcinoma mostly confined within the region or metastasize to regional lymph node, usually a squamous or undifferentiated carcinoma ⁽¹⁾. A rare metastatic carcinoma in HN region from outside the area is an adenocarcinoma from gastrointestinal, pancreato-biliary, ovarian, endometrial, lung, renal and breast metastasizing to left supraclavicular (Virchow's) lymph nodes. An exception is right supraclavicular carcinomatous involvement of lower esophagus, right lung, and right breast tumors ⁽¹⁻²⁾. Some studies have shown frequency of RCC metastasis in the head

and neck region as high as 15.2% ⁽¹⁾.

Larynx is a very rare and infrequent site of involvement by a metastatic carcinoma from outside head and neck region. There are however few rare cases reported in literature of metastatic carcinoma to the larynx from rectum, pancreas, thyroid, and even lower extremity liposarcoma (1-8). Metastatic neoplasm in the larynx accounts for only 0.09% to 0.40% of all laryngeal tumors ⁽⁸⁾.

Renal cell carcinoma (RCC) accounts for about 2-3% of adult malignant tumor in 5th-6th decade with a reported rising trend in its incidence ⁽⁹⁾. About 25-30% RCC are metastatic at presentation being asymptomatic initially ⁽¹⁾. Seventy percent of RCC develop metastatic disease with a dismal 5 year survival of 5-15% only. The common metastatic sites from a primary RCC are regional lymph nodes, lungs (50-60%), liver (30-40%), bones (30-40%), suprarenal, pleura, brain (5%) and soft tissues ^(1, 8-9). The clinical features depend on site of metastatic involvement, size of metastasis, and the speed of tumor growth / tumor doubling

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time ⁽¹⁾. A post tumor nephrectomy metastatic disease after prolonged time interval is unusual ⁽¹⁰⁻¹²⁾, but nearly 20-25% can metastasize even 4 years after primary tumor nephrectomy ⁽¹⁰⁾. Some cases are reported even 132 months post nephrectomy. The metastatic potential depends on histological variant, tumor anaplastic grade, T stage, nodal involvement and Lymphovascular invasion. RCC when metastasize in head and neck region can involve lymph nodes, thyroid or rarely tongue ⁽⁶⁻⁷⁾.

Renal cell carcinoma, as a malignant disease, is one of the great imitators having an erratic clinical course and biological behavior. Rare involvement of larynx appears related to the terminal location of larynx in the lymphatic and vascular circulation.

Case Report

A 57 years old Sri Lankan male consulted local otorhinolaryngology clinic for hoarseness of voice of 2 months duration. There was a history of right tumor nephrectomy in 2003 in Sri Lanka. Histopathology showed clear cell carcinoma involving capsule and peri-nephric fat (pT4NxM0). The lymph node status was not known and molecular markers were not available, yet on this histology he was in high risk group for local or systemic relapse. He received local adjuvant radiotherapy (45 Gy/25 fractions) in June 2003. Bone scan done in July 2003 was normal. CT scan done in October 2003 and Ultrasound in March 2004 were normal. He was advised in 2003 adjuvant chemotherapy based on Vinblastine and alpha interferon. After discussion about the expected benefit and toxicity, the patient opted for observation and follow up.

There were no co-morbid conditions or associated diseases when he presented to us in 2010. An initial clinical evaluation and diagnostic work up was carried out. Laboratory investigations including complete blood counts, liver and renal functions were within acceptable range. A video laryngoscopy was carried out and revealed a right pyriform fossa ulcerating mass with contact bleeding involving the vocal cord completely (Figure 1). A biopsy was done only

due to excessive bleeding and a highly vascular nature of the tumor. Initial histopathology was reported as paraganglioma. CT scan chest showed small left supra clavicular, peritracheal and mediastinal lymph nodes largest being less than 1.5 cms. There was a static non-progressive 0.7 cm left lower lobe pulmonary nodule. CT scan abdomen revealed cholelithiasis, and empty right renal fossa, no abnormal mass or lesion, and no evidence of local recurrence. The patient was referred with this diagnosis of paraganglioma for further oncology review and management.

A histopathology review and immunocytochemistry was carried out. The tumor cells were positive for CK (cytokeratin), Vimentin, CAM 5.2, CK-18, EMA (epithelial membrane antigen) and negative for CD10 (Fig.1 and 2). Based on these results, final pathologic diagnosis was metastatic renal cell carcinoma in the vocal cord (Figure 2-4).

Clinically his performance status was 0 (PS=0) on WHO scale. There was no cervical adenopathy or mass. His general physical examination, respiratory, cardiovascular,

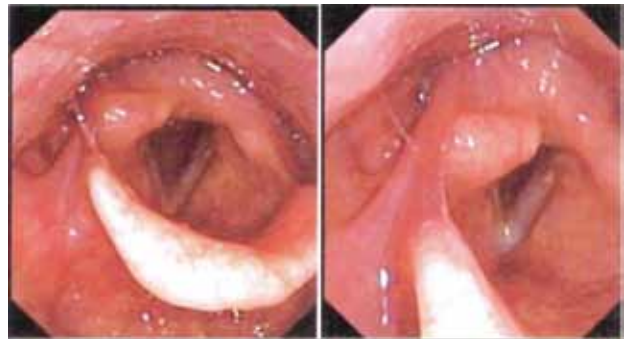


Fig. 1: Growth seen at Direct Laryngoscopy

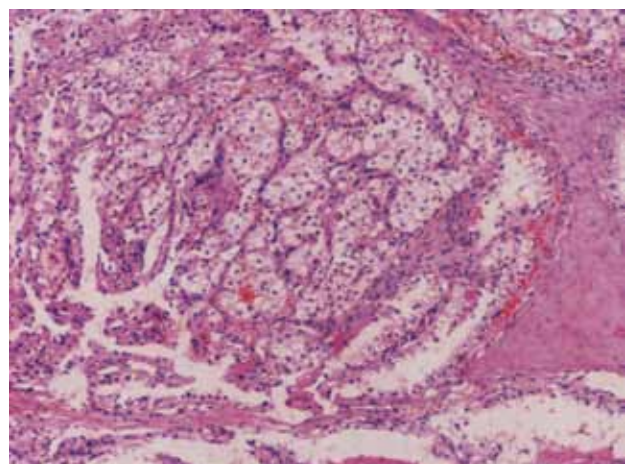


Fig. 2: Low power view of H & E stain Biopsy from Larynx

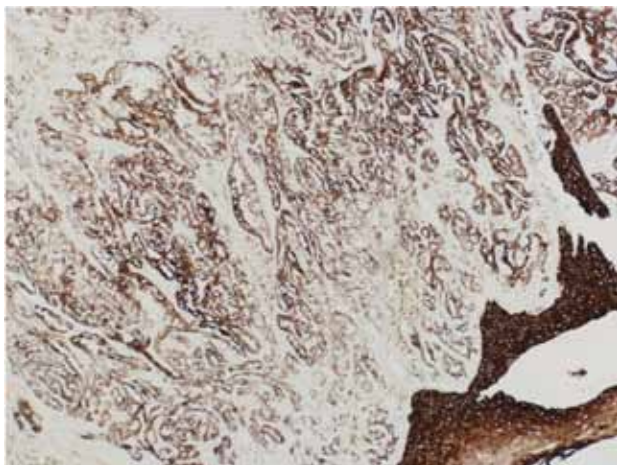


Fig. 3: Immunocytochemistry of tumor showing positivity for cytokeratin

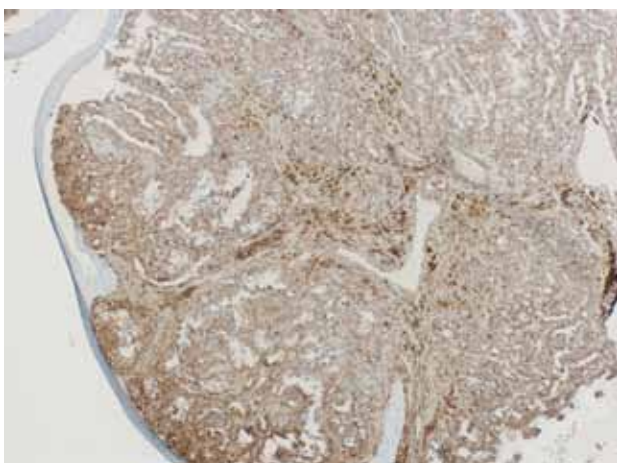


Fig. 4: Immunocytochemistry of tumor showing positivity for cytokeratin

abdominal, and CNS examination were unremarkable except a scar of right tumor nephrectomy. The case was discussed in multi-disciplinary oncology management team. A CT scans neck, and bone scintigraphy was advised to exclude any other metastasis. A PET-CT was advised to evaluate the status of lymph nodes. He was planned to be treated by local radiotherapy to larynx. The further management plan was to be decided after PET-CT evaluation. The patient during counseling agreed with this management plan but expressed his desire to return back to Sri Lanka for further management. He went to Sri Lanka where he had metastatic work up done by CT Scans and bone scan. There was no other site of metastatic disease involvement. He received local Radiotherapy to larynx at 65 Gy in 32 fractions. He came back and was seen in outpatient clinic, with no evidence of disease.

He was offered systemic chemotherapy as single agent Sunitinib, but he refused chemotherapy. He is in regular clinical follow up and radiological surveillance with no evidence of relapse until the last follow up (14 months from diagnosis). He has a performance status of 0 on WHO scale and he is on job with regular duty schedule.

This case report is prepared under the institutional ethical guidelines and with the consent and permission of the patient.

Discussion

RCC is the 3rd commonest tumor reported after breast and lung CA; which can metastasize to sites in head and neck region including paranasal sinuses, mandible, thyroid, parotid, nose, tongue, larynx and skin of the face or neck⁽⁶⁻⁷⁾. The number of metastatic RCC in head and neck region reported in literature are very few (less than 30), and to the larynx is less than 10⁽¹⁾. A head and neck metastasis combined with other sites of metastasis is 14-16% while isolated metastasis in head and neck is less than 1%⁽¹⁾.

Larynx is a very rare morphologic site to be involved by a metastatic tumor^(8, 12-15). There are however metastatic tumors to larynx reported scarcely in literature, the initial ones being in 1987 and 1992 presented with hoarseness and laryngeal symptoms⁽¹³⁾. These rare cases include metastasis from primary thyroid carcinoma⁽²⁾, rectal carcinoma⁽³⁾, pancreatic carcinoma⁽⁵⁾, and even a lower extremity liposarcoma⁽⁴⁾.

The pathogenesis of RCC metastasis to Larynx was postulated by Boles and Cerny, and Nahum and Baily implicating arterial, venous and lymphatic channels bypassing pulmonary artery filtration⁽¹⁾. A rich epidural, pre-vertebral and vertebral venous anastomosis and raised intra-abdominal pressure support this hypothesis/pathway of valve-less veins and least resistance. In the absence of hepatic or pulmonary metastasis, it is postulated that tumor cells migrate via Batson's venous plexus or thoracic duct. The site predilection of metastasis of RCC is similar in cases with or without initial nephrectomy^(1, 10, 12).

The potential for RCC to metastasize to the larynx years after nephrectomy necessitates

consideration of this entity during workup of a laryngeal lesion, or presentation with laryngeal symptoms like hoarseness in previously diagnosed RCC⁽¹³⁾. The patients with isolated laryngeal metastasis reportedly were treated with metastasectomy, radiation therapy or systemic treatment. The treatment was mostly individualized with no consensus standard approach. The treatment decision were guided by physician's discretion, patient's choice, risk assessment, nature of metastasis (isolated site or not, number, site, and size), co-morbidity, performance status, time from primary diagnosis, initial treatment for primary disease, initial response to treatment and expected survival. They reportedly had improved quality of life, better symptom control, improved time to disease progression, and a reasonably good survival of up to 16 months in pre-targeted therapy era^(8, 13-15).

The treatment of metastatic RCC in head and neck region include metastasectomy where ever technically feasible (small sized, solitary, resectable, and accessible metastasis) in eligible patient, palliative chemotherapy, radiotherapy or best support care^(1-2, 8-9, 11, 13-15). Although RCC is regarded as radio-resistant, good response rate are

seen in metastatic disease⁽¹⁴⁻¹⁵⁾. A good number of patients (66%) achieved complete response with chemotherapy and radiotherapy in a case study reported in 2006⁽¹⁾. Despite reported good initial response to treatment, a poor prognosis is seen with a 2 year survival of 41% and a 5 year survival of 13% only⁽¹⁾.

Conclusion

To conclude a differential diagnosis of metastatic RCC should not be overlooked in tumors of head and neck region in those with a history of RCC. All initially diagnosed RCC should be risk stratified using histological features and molecular markers for their metastatic potential in future. These cases should be followed for a prolonged course of time due to well-known tendency for late recurrences.

The availability of newer cytotoxic agents with better response rates (Tyrosine kinase inhibitors and mammalian target of rapamycin inhibitors), improved radiotherapy techniques (intensity-modulated radiotherapy and image-guided radiation therapy), and better laser assisted surgical procedures are likely to have a positive impact on prognosis even in these metastatic cases.

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