ORIGINAL ARTICLE

Tongue metastasis as an initial presentation of renal cell carcinoma

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ABSTRACT

Aim Distal metastases to oral cavity are very rare. Adenocarcinoma, renal cell carcinoma (RCC) and squamous cell carcinoma are the most common metastatic tumours. The aim of this study was to assess the diagnostic relevance of metastatic renal cell carcinoma on tongue manifestations in large patient series.

Methods A patient with distal RCC metastases to the tongue and neck lymph nodes as the first manifestations of malignancy was presented. Also, all reports described during 106-year period relating to distal RCC metastasis to the tongue were evaluated.

Results In the presented patient, initial presentation of RCC was metastasis to the tongue. Three months after nephrectomy, tongue tumour resection and radical neck dissection were performed. Histopathological analysis confirmed RCC metastasis. Postoperatively, the patient underwent radiotherapy and polychemotherapy. Tongue metastasis from RCC is extremely rare with only 51 cases reported during the 106-year period. In only 7 patients tongue metastasis was reported as an initial presentation of RCC.

Conclusion The RCC metastasizing to the tongue is extremely rare and thus it poses a diagnostic challenge especially when it is the first sign of malignancy. Therapeutic decisions should maximize patient comfort and minimize morbidity considering the poor long-term prognosis.

Key words: oral cavity, renal carcinoma, metastasis

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INTRODUCTION

The incidence of lethal cases due to oral carcinoma remains rather high not because it is difficult to detect or diagnose, but because this carcinoma is routinely detected in the advanced stage of the disease (1). The tumour is frequently diagnosed when local or distal metastases are already present, or the presence of metastases is the first sign of malignant disease (2). Squamous cell carcinoma, mostly malignant, is the most common primary carcinoma of oral cavity accounting for more than 90% of all tumours, whereas metastatic tumours to oral cavity account for 1%-1.5% of all tumours (1). The incidence of metastasis to the maxillofacial region is 2.1% (3). Almost all types of malignant tumours can metastasize to oral cavity (3). According to histopathologic types adenocarcinoma, renal cell carcinoma (RCC) and squamous cell carcinoma are the most common metastatic tumours (4). They are usually detected in the fifth and sixth decade of life with slight predominance in males (3). Numerous single case reports and small series of metastasis into the head and neck region are available in the literature (2-5).

The prevalence of oral metastases frequently differs from the prevalence of primary tumours; it also varies significantly according to primary tumour localization and tumour histopathology, pointing to different metastatic potential of tumours (5). In addition, significant differences are also found in the prevalence of metastases and geographic origin of patients (4). Shen et al. reported the lung, breast, kidney, liver and prostate carcinomas to rank as the first five carcinomas metastasizing to the oral cavity in the US, whereas in China those are carcinomas of the lung, thyroid, liver, esophagus and gastric carcinoma (4,6).

The RCC belongs to the group of tumours characterized by unpredictable clinical features and poor disease prognosis (1,2,6). It accounts for 2%-3% of all malignant tumours in adults and 90%-95% of all kidney tumours (6). The RCC is more frequent in males from northern Europe and North America than in Asia and Africa, with overall annual mortality of 100,000 or 2% of deaths from malignancies (7).

Besides humans, RCC distal metastases to oral cavity have also been recorded in domestic animals, cattle and dogs (8).

The RCC is characterized by the absence of early warning symptoms, variegated clinical signs and resistance to radiotherapy and chemotherapy (9). Because of its high metastatic potential, secondary lesions are frequently (25%-30% of patients) present at the time of primary renal carcinoma diagnosis. Following nephrectomy in the early stage of RCC, relapse or metastatic disease develops in 50% of patients. Metastatic disease occurs in 85% of patients in the first three or more years of primary tumour resection (10). Distal metastases from RCC are very common and usually multiple to different body organs. These metastases are mostly localized in the lungs (50%-60%), bones and liver (30%-40%), head and neck (12%-16%) (2,7). About 50% of metastases are found in the thyroid, nose and paranasal sinuses, and pharynx (4,10). Solitary metastases from primary RCC to the head and neck are rare, recorded in only 1% of patients (11).

Distal metastases to oral cavity are very rare and are usually localized in facial bones, mostly mandible, or even less commonly in soft tissues, mostly gingiva (4,6). Distal metastases to the tongue are extremely rare, with a prevalence of 0.17 % (12). Primary tumours of the lung, pleura, bronchi, esophagus, colon and breast, and skin melanoma mostly metastasize to the tongue (12). The diagnostic of a metastatic lesion in the oral region is challenging both in recognition as metastatic lesion and in determination of the site of origin.

The aim of this article was to present a patient with RCC and distal metastases to the tongue and neck lymph nodes as the first manifestations of RCC and to offer a review of the related literature.

PATIENT AND METODS

Patient and study design

A 51-year-old man was admitted to the Ear, Nose and Throat (ENT) Department at General Hospital Slavonski Brod. The patient complained of symptoms of pain in the left side of the pharynx, difficult swallowing, pain radiating to the left ear area, hypersalivation, and edema under the left mandibular angle, persisting for five months. In the same period, he lost 10 kg of body weight. At the time of the admission the patient was giving the impression of medium heavy patient.

Methods

Clinical examination of the patient and nasofiberendoscopy with special attention to the base of the tongue and oropharyngeal cavity was done.

Aspiration biopsy was recommended, and histopathology was done at the Department of the Pathology and Clinical Cytology, General Hospital Slavonski Brod. Diagnostic multi-slice computed tomography (MSCT) of the head and neck, chest and abdomen was done at the Department of the Radiology, General Hospital Slavonski Brod.

After an exhaustive literature search between 1911 and 2017, using Pubmed, Researchgate, Google Scholar, clinical characteristics of 51 patients who were diagnosed with tongue metastasis from RCC were found and evaluated.

RESULTS

Physical findings of lung and heart were normal, blood pressure was 140/85, temperature was 37.2, the abdomen was soft. The patient was a smoker, occasionally taking alcohol drinks.

Table 1. Cases of renal cell cancer metastasizing to the tongue published in available literature during the period of 106 years (1911-2017)

First Author /Year of publication (reference number)	Gender/Age	Other metastasis	Treatment
Kostenko MT / 1911 (17)	M/43	unknown	Unknown
Coenen H / 1914 (17)	F/62	unknown	None
McNattin RF / 1931 (18)	M/58	lung, heart, skin	None
Trica AJ / 1936 (17)	M/57	unknown	Unknown
Scharg AR / 1945 (19)	M/61	lung	Surgery
Del Carmen BV / 1970 (20)	M/77	unknown	Surgery
Satomi Y / 1974 (21)	F/41	lung	None
Friedlander AH / 1978 (22)	M/84	lung	surgery
Fitzgerald RH / l982 (23)	M/63	brain	surgery, radiotherapy
Kitao K / 1986 (24)	M/57	lung	surgery
Matsumoto A / 1987 (25)	F/77	lung	chemotherapy, interferon
Inai T / 1987 (26)	M/42	lung	interferon
Kapoor VK / 1987 (27)	M/70	unknown	surgery
Madison JF / 1988 (28)	M/58	lung, liver	unknown
Ishikawa J / 1991 (29)	F/59	lung, brain	surgery
Okabe Y / 1992 (30)	M/58	lung, brain	surgery
Shibayama T / 1993 (31)	M/41	lung, bone, lymph node	interferon
Ziyada WF / 1994 (32)	M/59	none	surgery, radiotherapy, interferon
Airoldi M / 1995 (33)	M/51	lung	surgery
Aguirre A / 1996 (34)	F/82	brain	surgery
Konya E / 1997 (35)	M/59	para-aortic lymph node	surgery, interferon
Tomita T / 1998 (36)	M/52	lung, brain, skin	radiotherapy
Navarro F / 2000 (37)	M/50	none	surgery
Fukuda M / 2002 (38)	M/74	unknown	unknown
Pritchyk KM / 2002 (39)	M/60	lung	biopsy
Meki A / 2002 (40)	M/63	none	unknown
Goel MC / 2003 (41)	M/62	lung	surgery, interferon, interleukin-2
Lang EE / 2003 (15)	M/45	lung, nose	Surgery
Marioni G / 2004 (42)	F/87	lung, liver, pancreas, thyroid gland	Surgery
Kyan A / 2004 (43)	M/66	lung	surgery, interferon
Torres-Carranza E / 2006 (44)	F/49	lung	Surgery
Huang HC / 2006 (45)	F/76	lung, liver	Surgery
Cochrane TJ. / 2006 (46)	M/41	lung, scalp, brain, bones	surgery, chemotherapy
Regaldo RR / 2007 (47)	M/81	none	Surgery
Longo R / 2008 (48)	M/68	none	None
Will TA / 2008 (49)	M/63	lymph node	None
Azam F / 2008 (16)	M/78	lung, bones	surgery, radiotherapy
Basely M / 2009 (50)	F/46	lymph node	Surgery
Yoshitomy I / 2010 (51)	M/47	none	Surgery
Ogunyemi O / 2010 (52)	M/27	spine, lung, liver	surgery, radiotherapy
Morvan JB / 2011 (53)	F/48	bone, lymph node	Surgery
Wadasadawala T / 2011 (54)	F/48	adrenals, lung, mediastinum, bone	palliative radiotherapy
Ghazali N / 2012 (55)	F/64	none	Surgery
Ganini C / 2012 (56)	M/70	adrenals, lymph node, lung, bone	embolization
Balliram S/ 2012 (57)	M/72	lung	Surgery
Mazeron R/ 2013 (58)	M/66	none	brachytherapy
Ray A/ 2013 (59)	M/65	lung, lymph node, muscle	immunotherapy
Abbaszadeh-Bidokhty/2014 (60)	M/80	none	Surgery
Altuntas/2015 (12)	M/70	lung, mediastinal vertebra	immunotherapy, surgery
Lieder/2017 (61)	M/56	lung, bones, mediastinal	surgery, radiotherapy
Raiss/2017 (2)	M/55	lung, muscle	systemic therapy
Present report	M/51	lung, liver, lymph node	surgery, radiotherapy, chemotherapy

An examination of patient's oral cavity showed free from pathologic lesions. Fiber endoscopy showed mucosal thickening on the left side of the tongue base, extending to the lateral wall of the pharynx and pushing the epiglottis. Mucosa over the tumour appeared normal, without pathologic lesions. The tumour was very painful on palpation with limited tongue mobility. Enlarged submandibular gland with a bundle of lymph nodes in the region II/III was detected on the left side of the neck.

Aspiration biopsy cytology showed monolayered sheets of malignant glandular cells with granular cytoplasm, slightly pleomorphic nuclei and intraneuclear pseudoinclusion and raised suspicion of adenocarcinoma metastasis to lymph nodes. Diagnostic multi-slice computed tomography (MSCT) revealed a tumour of the left kidney, 13x8 cm in size, with a number of secondary metastases to the liver and lungs (Figure 1). Histopathology of the renal tumour confirmed RCC.

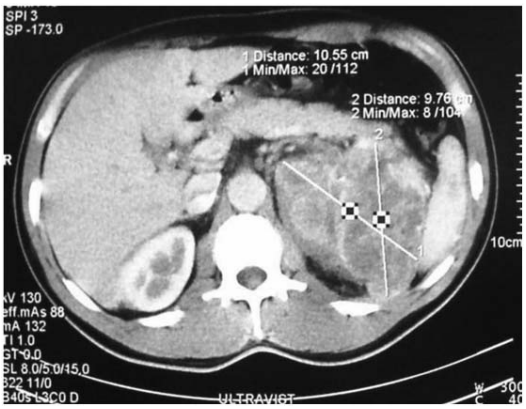

Figure 1. Multi-slice computed tomography (MSCT) of a primary tumour of the left kidney measuring 13x8cm (General Hospital „ Dr. J. Benčević", Slavonski Brod, 2015)

The left kidney was removed together with the tumour, which was non-sharply demarcated, infiltrating the fatty capsule, small pelvis and large blood vessels of the hilum; histopathology confirmed RCC.

Three months after nephrectomy, regression of secondary metastases to the liver occurred. Tongue tumour resection and radical neck dissection were performed. Histology of the tongue base tumour tissue confirmed RCC metastasis. Postoperatively, the patient started radiotherapy of the head and neck region and polychemotherapy. The patient died six months after the diagnosis of RCC metastasis to the tongue and lymph nodes of the neck.

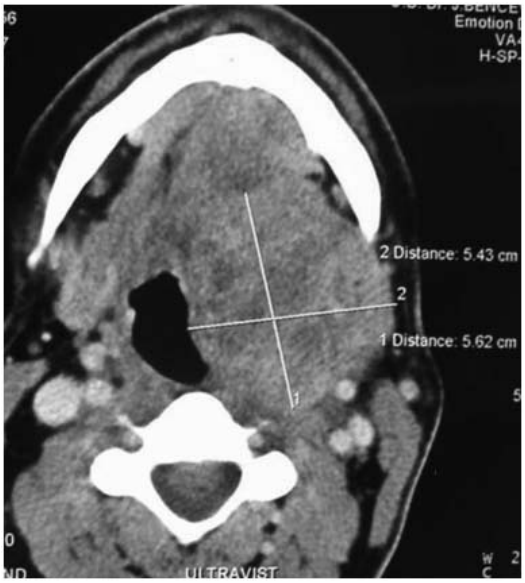

Figure 2. Multi-slice computed tomography (MSCT) of the tongue metastasis measuring 5x5 cm (General Hospital „ Dr. J. Benčević" Slavonski Brod, 2015)

After an exhaustive literature search only 51 cases of RCC metastasizing to the tongue were found, which had been reported since 1911 (Table 1). Forty-three patients were males and eight were females. The mean age of these patients at the time of the diagnosis was 59 years (27-87 years). Tongue metastasis of RCC was found in only eight cases (Table 2). Synchronous disseminated metastases were detected in other organs and the most important metastasis target organs were the lung, brain and liver.

Table 2. Eight cases of tongue metastases of renal cell cancer as the first sign of malignancy

First Author /Year of publication (reference number)	Gender/ Age	Localization on the tongue	Other metastases	Survival time
Kapoor WK / 1987 (27)	M/70	unknown	unknown	unknown
Ziyada WF/ 1994 (32)	M/59	base	None	> 6 months
Aguirre A/ 1996 (34)	F/ 82	apex	Brain	> 3 years
Azam F / 2008 (16)	M/68	lateral edge	lungs, bones	6 months
Yoshitomi I/ 2010 (51)	M/47	dorsum	None	2 years
Balliram S/ 2012 (57)	M/72	dorsum	Lung	3 months
Ray A/ 2013 (59)	M/65	dorsum	lung, lymph node, muscle	Unknown
Present report	M/51	base	lungs, liver, lymph node	6 months

DISCUSSION

This paper presents a rare example of the patient with unknown primary renal carcinoma with minimal symptomatology but great metastatic potential. The RCC may remain clinically occult

and tongue tumour was an initial presentation of the renal carcinoma. Metastatic carcinoma was localized in the posterior third of tongue, the base, patient had nonspecific difficulties in swallowing, occasional moderate pain and enlarged neck lymph nodes. A thorough evaluation to distinguish between primary and metastatic tongue cancer is essential (1,5,6). Primary cancer of the tongue is treated with curative intent and metastatic tumours are managed with palliative intent (3).

Oral cavity does not belong to the site-specific process group for metastatic colonization of different types of carcinoma (13-15). Oral metastatic carcinoma most frequently results from secondary dissemination from other carcinoma involved organs, mostly lungs, whereas direct dissemination of metastases from distal organs involved by primary tumour is unknown (6). The most common localization of metastasizing to the tongue is tongue base, probably due to its rich vascularization (*via* dorsal artery of tongue) and relative immobility of the region (15,16). The tongue mostly shows a clinical picture of a submucous tumour growth. Such a clinical picture and nonspecific radiographic characteristics may often suggest benign inflammatory or benign tumour lesions (10).

Friedman and Osborn reported numerous examples of secondary malignant tumours in the ear, nose and throat region and three cases of metastatic malignant RCC in the tongue by Kostrenko (1911), Coenen (1914) and Trinca (1936) (17). A literature review revealed 51 cases of RCC metastasizing to the tongue during the period of 106 years (2,12,15-61). Two-thirds were males with average age of 59 years, which did not differ significantly from the mean age of patients with carcinoma of other localizations and oral metastases (1,4). In the literature, the prevalence of oral metastases as the first sign of malignancy ranges from 20% to 33% for different primary tumour localizations (2,6). Although RCC accounts for only 3% of the overall prevalence of malignant diseases, its metastatic potential to oral cavity is significantly higher, i.e. 13%, pointing to early dissemination of the tumour disease (4). The magnitude of RCC metastatic potential is best illustrated by cases of distal renal carcinoma metastases that may develop years after primary RCC has been diagnosed and treated (61,62).

The mechanism of distal metastasizing to oral cavity has not yet been fully clarified. In majority of RCC patients, distal disease dissemination is believed to occur *via* arterial and paravertebral venous routes (Batson's plexus) rather than the lymphatic system, where skipping and obviating filtration and dissemination of tumour cells to the lung is possible (16). An analysis of the reported causes revealed that two-thirds of patients had multiple secondary metastases to other organs (lung, brain and liver). We believe that the real number of multiple secondary metastases must have been even greater. In the past, before the advent of computed tomography, magnetic resonance imaging or fluoro-2-deoxy- D-glucose positron emission tomography (FDG) positron emission tomography, these metastases could not be detected.

The treatment of RCC has changed greatly over the past 15 years. Progress in the surgical management of the primary tumour and metastatic disease increased understanding of the molecular biology and genomics of the disease leading to the development of new therapeutic agents (63-66). In the patient presented in this report, the treatment of renal carcinoma metastasis to the head and neck region was directed mainly towards palliation. The excision of tongue metastasis and neck dissection is usually performed for pain control and to manage any potential complications from the space occupying mass in the head and neck region (11). Disease prognosis is very poor and more than 90% of patients die within a year of RCC diagnosis (56,61,66).

We believe that each patient requires individualized approach considering the stage of the tumour disease and associated comorbidities. Therapeutic decisions should maximize patient comfort and minimize morbidity considering the poor long term prognosis at this stage of the disease. Additional studies are needed to develop a more efficient therapy for RCC and its metastases.

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