

Lingual metastasis as an initial presentation of renal cell carcinoma

**Izumi Yoshitomi,¹ Goro Kawasaki,¹ Akio Mizuno,¹ Masaharu Nishikido,²
Tomayoshi Hayashi,³ Shuichi Fujita,⁴ Tohru Ikeda⁴**

¹Department of Oral and Maxillofacial Surgery, Unit of Translational Medicine, Sciences, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

²Department of Nephro-Urology, Unit of Translational Medicine, Sciences, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

³Department of Pathology, Nagasaki University Hospital

⁴Department of Oral Pathology and Bone Metabolism, Unit of Basic Medical Sciences, Course of Medical and Dental Sciences, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan

Abstract

Distant metastasis of malignant neoplasm to the oral soft tissue is extremely rare. We report a case of renal cell carcinoma (RCC) metastasizing to the tongue. A 47-year-old man visited our hospital with chief complaint of a lump on the middle third of the dorsum of his tongue, and the lesion fell off from the tongue. Although histopathological diagnosis of the mass was granuloma teleangiectaticum, similar nodule reappeared in the same area 2 weeks later. The second lesion was composed of granuloma teleangiectaticum and aggregation of neoplastic clear cells in ductal arrangement. The clear cells were immunohistochemically positive for EMA and CD10.

The abdominal CT scan revealed a 5.5 cm mass in the left kidney, suggesting RCC. Thus the lingual lesion was consistent with metastatic RCC. There has been no recurrence for 2 years after the radical nephrectomy and local excision of the tongue.

Keywords: Renal cell carcinoma, Lingual metastasis, CD10

Introduction

Renal cell carcinoma (RCC) is the third most frequent neoplasm to metastasize to the head and neck area, following breast and lung carcinomas[1]. The nose and paranasal sinuses are most commonly affected, followed by the oral cavity. RCC metastatic lesions to the tongue are extremely rare[2]. In the present study, we describe a case of renal cell carcinoma metastasis to the tongue, which was the first evidence of a primary tumor in the left kidney.

Case presentation

A 47-year-old male patient was referred to the Department of Oral and Maxillofacial Surgery, Nagasaki University Hospital, Nagasaki, Japan, because of a lump on the middle third of the dorsum of his tongue. The patient had been aware of the lump for approximately 2 months before visiting our hospital, and the lesion fell off from the tongue on the morning at the first visiting us. A clinical intraoral examination showed a reddish smooth lesion measuring approximately 5 x 5 mm on the anterior dorsum of the tongue (Fig. 1). The lump that had fallen off was lightly red in color and was an elastic, soft, and smooth mass (Fig. 2). The patient had no history of malignant disease, drinking alcohol, or smoking. The clinical diagnosis included pyogenic granuloma and a benign tumor of the tongue. At the initial visit, the dropped lump was

submitted for pathological examination. A microscopic examination revealed dilated blood vessels lined with plump endothelial cells and neutrophil infiltration under an ulcerated surface (Figs. 3). A diagnosis of granuloma teleangiectaticum was made. Two weeks later, a similar nodule reappeared on the same part of the tongue (Fig. 4). The histology of an excisional biopsy consisted of granuloma teleangiectaticum including aggregation of clear cells in the base of the polypoid protrusion. The round or cuboidal clear cells have mild atypical nuclei and scattered mitoses. Ductal formation and narrow stroma with rich blood vessels were also noticed (Fig. 5A and 5B). For the differential diagnosis between salivary malignant tumor and metastatic RCC, we performed immunohistochemical examination and ordered an MRI of the head and neck and a CT scan of the chest and abdomen. Immunohistochemically, the tumor cells were positive for CD10 as well as epithelial markers including EMA and cytokeratin AE1/AE3 (Fig. 5C and 5D). CD10 is regarded as good RCC marker to distinguish from other clear cell type carcinomas[3-5]. The abdominal CT scan revealed a 5.5 cm mass in the left kidney, suggesting RCC, and a mass in the right adrenal gland (Fig. 6). Furthermore, a chest CT scan revealed metastasis of the right adrenal gland, pleura, and bilateral multiple metastatic lesions in the lungs. Based on these findings, the lingual lesion was confirmed to be metastasis of RCC. The patient underwent laparoscopic left radical nephrectomy. At the same time, we performed an additional excision of the lingual lesion. The removed kidney contained yellowish-white nodular neoplasm reached the renal hilus accompanied with hemorrhage and necrosis (Fig. 7). Histologically, the neoplastic nodules were well demarcated and composed of tubular and trabecular patterns. Cystic lumens and delicate blood vessels were contained. The tumor cells have a rounded or polygonal shape, abundant clear cytoplasm and mildly atypical nuclei

(Figs. 8). Although the kidney lesion was histopathologically diagnosed as clear cell renal cell carcinoma, there were no tumor cells in the tongue. The patient's surgical treatment was followed by interferon- α , however the metastatic foci increased. Therefore, the patient was treated with targeted therapy by Sunitinib and by Sorafenib later. The patient was followed for 2 years after the radical nephrectomy and local excision of the tongue, and had no evidence of recurrence in either the abdomen or tongue.

Discussion

Metastatic tumors to the tongue are extremely rare. Zegarelli et al. reported an incidence of 0.2% of 6,881 autopsy cases of various malignant diseases [2]. In addition, Friedlander reported that only 1% of all malignancies arising in the oral cavity are metastatic foci and of these, only 5% appear on the tongue [6].

RCC represents 3% of all adult malignancies, and it is the third most frequent neoplasm to metastasize to the head and neck region, following breast and lung carcinoma [1]. Sgouras reported the most common sites of metastasis were the lung (76%), regional lymph nodes (66%), bone (42%), and liver (41%) [7]. Approximately 15% of all patients affected with RCC have metastasis in the head and neck region. have metastasis in the head and neck region, usually associated with lesions in other sites [8]. In the order of metastatic rate in the head and neck region, RCC affects the paranasal sinuses, larynx, jaws, temporal bone, thyroid gland, and parotid gland. However, metastatic RCCs to the tongue are extremely rare.

We reviewed 29 cases of RCC metastasizing to tongue since 1973, including the present case (Table 1). In most cases, the lesions appeared after detection of the primary tumor, but 5 cases appeared as an initial presentation of RCC (Table 2).

Possible routes of the metastasis to the tongue include the systemic, venous, and lymphatic circulation [9]. Most metastasis are located on the base of the tongue, most likely due to its rich vascular supply (the dorsal lingual artery), or to the immobility of this area compared with other areas of the tongue [10]. RCCs invade the local vascular network of the kidney and spread through the systemic circulation. If there are no signs of pulmonary disease, metastatic spread can be explained through Batson's venous plexus or via the thoracic duct [11]. Batson's venous plexus extends from the skull to the sacrum. This valveless system offers little resistance to the spread of tumor emboli, especially during Valsalva maneuvers when there is an increase of intra-abdominal pressure, allowing the bypass of the pulmonary filters [12].

The treatment of RCC metastasizing to the oral cavity usually includes local excision to provide palliation of the symptom and to give patient comfort. A surgical excision has been performed to control pain and prevent bleeding and infection [13]. Marioni et al. indicated that radiotherapy is questionable as a primary treatment [14]. On the other hand, Azam et al. and Simo et al. have suggested the effectiveness of radiotherapy in the treatment of metastatic disease to achieve local control and for palliative management [11, 15]. Chemotherapeutic agents such as vinblastine have been proved ineffective in the treatment of advanced RCC, with a response rate lower than 10%. Cytokine-based immunotherapy (interleukin-2 and interferon- α) were the only therapeutic option for advanced RCC patients several years ago. Shibayama et al.

reported a complete response in a base of the tongue metastasis after interferon- α therapy [16]. However, the effect of this treatment is generally less than 20%[17]. Recently target therapies are dramatically changing the landscape of advanced kidney cancer. Newer agents such as sunitinib and sorafenib, which are multiple tyrosine kinase inhibitors with proven antiangiogenic activity, have been approved for the treatment of RCCs. In the present case, the primary site was completely excised and the patient was administered adjuvant immunotherapy with interferon- α . However the patient's treatment was changed to targeted therapy with sunitinib and sorafenib because of progressive disease. Will et al. reported that most patients die within 1 year after the detection of head and neck metastasis [18]. Campbell et al. reported the overall 5- and 10-year survival rates of patients with metastatic RCC are 5-30% and 0-5%, respectively[19]. Therefore, treatments that reduce morbidity and secure comfort are essential to improve the poor long-term prognoses.

Acknowledgments

We thank the staff of the Department of Radiology and Cancer Biology, Nagasaki University Graduate School of Biomedical Sciences.

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Fig.1



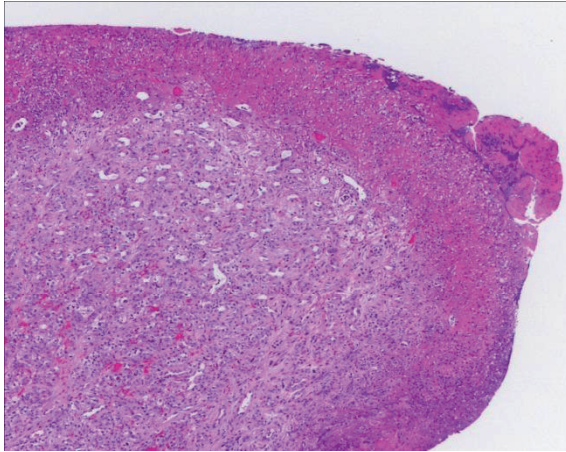
Fig.1 Clinical appearance of the lingual lesion at the time of initial examination

Fig.2

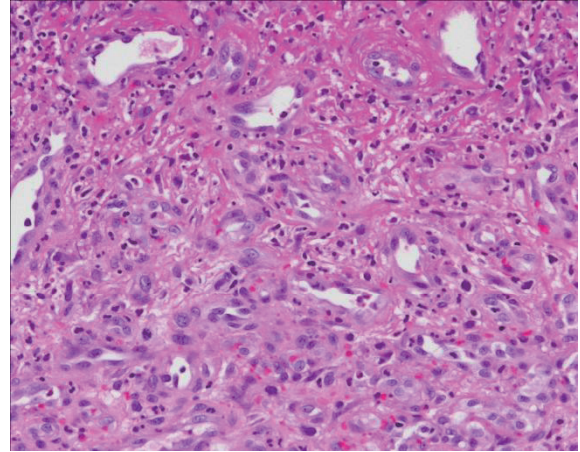


Fig.2 The mass fell out of the tongue looked lightly red granulation tissue with smooth surface. Epithelial covering lacked.

Fig.3



A



B

Fig.3 Histology of the mass dropped out of the tongue.

(A) Fibrin was deposited on the ulcerated surface. Many blood capillaries were noticed under the ulcer. (B) Endothelial cell proliferation with vascular formation was seen in inner portion. Neutrophils infiltrated around the dilated blood vessels.

Fig.4



Fig.4 Clinical appearance of the lingual lesion at the time of second examination

Fig.5

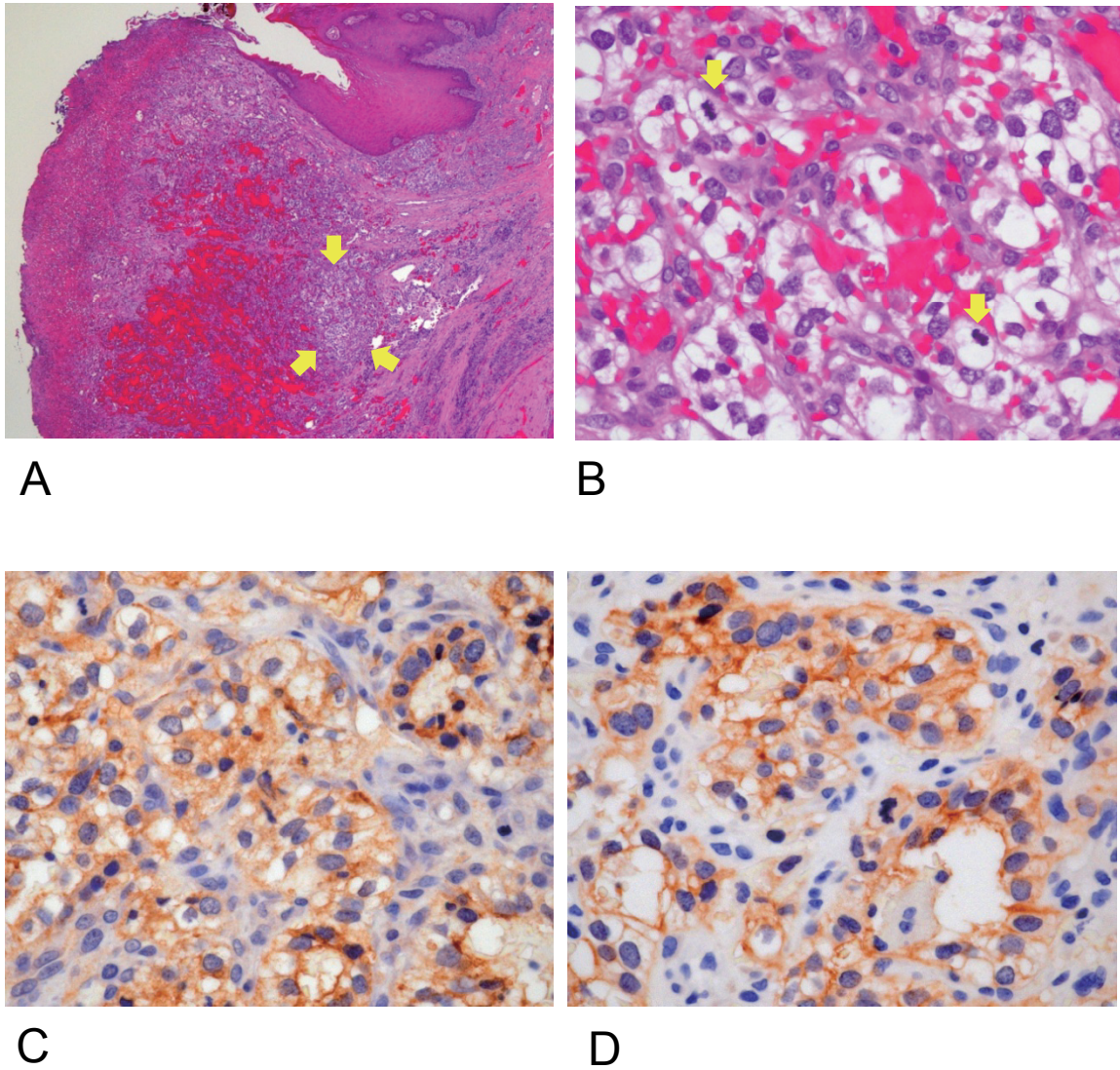


Fig.5 Histology of excisional biopsy specimen.

(A) Polypoid mass had ulcerated surface deposited with fibrin. Hemorrhage and aggregation of clear cells (arrows) were seen. (B) High-power view of the aggregation of clear cells. Trabecular or ductal structures were found with erythrocytes. Mitotic figures were scattered. Immunohistochemically, the clear tumor cells were positive for EMA (C) and CD10 (D).

Fig.6



Fig.6 CT scan showing primary tumour of left kidney

Fig.7

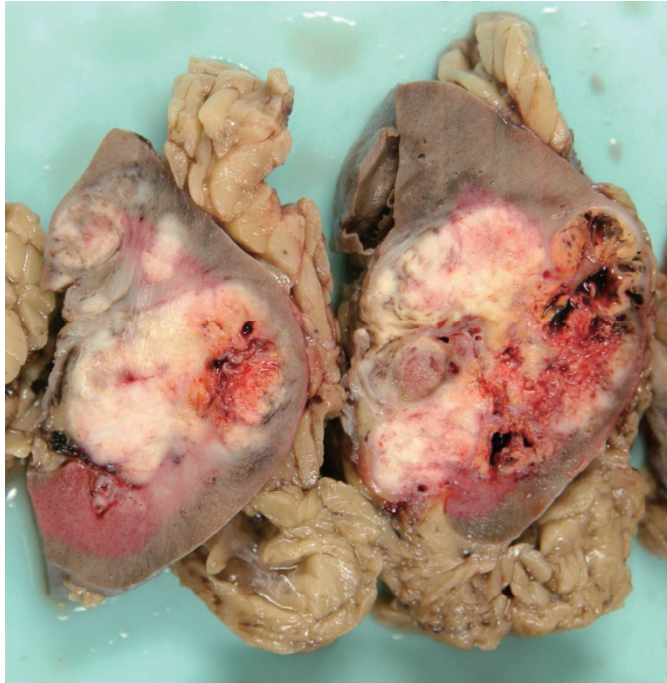
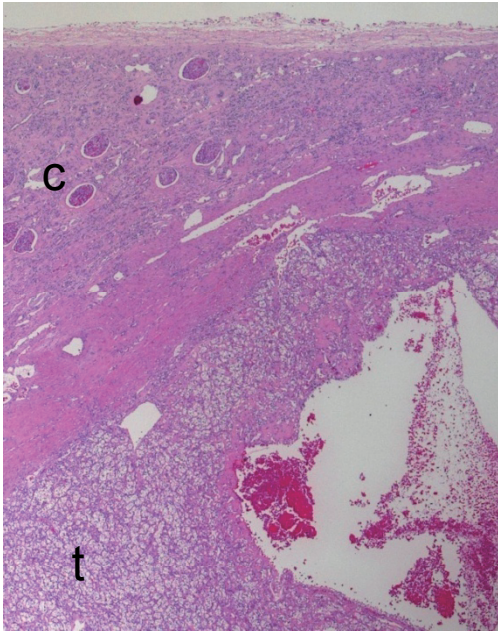
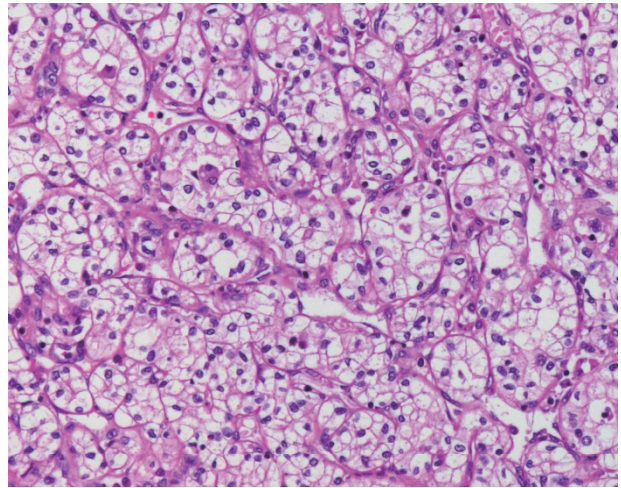


Fig.7 Cut surface of removed kidney. Some yellowish-white nodules occupied from the cortex to the hilus. Hemorrhage, necrosis and cystic change were found.

Fig.8



A



B

Fig.8 Histology of the primary renal carcinoma.

(A) The tumor was well demarcated (c: renal cortex, t: tumor nodule). The tumor show hemorrhagic degeneration. (B) Round to cuboidal tumor cells with clear cytoplasm were arranged in trabecular pattern with sinusoid-like blood vessels.

Table.1 Previously Published Cases of Metastatic Renal cell carcinoma to the tongue

	Age	Sex	Site	Other metastases	year	Author.
1	41	F	Surface	Lung	1974	Satomi et al.
2	84	M	Tip	Lung	1979	Friedlander et al.
3	63	M	Dorsum	Brain	1982	Fitzgerald et al.
4	37	M	Base	None	1986	Kitao et al.
5	42	M	Base	Lung	1987	Inai et al.
6	77	F	Surface	Lung	1987	Matsumoto et al.
7	70	M	Not mentioned	Not mentioned	1987	Kapoor et al.
8	63	M	Ventral surface	Lung, Liver	1988	Madison et al.
9	59	F		Lung, Bone	1991	Ishikawa et al.
10	58	M	Base	Lung, Brain	1992	Okabe et al.
11	41	M	Base	Lung, Bone, lymph nodes	1993	Shibayama et al.
12	59	M	Right base	None	1994	Ziyada et al.
13	51	M		Lung	1995	Airoldi et al.
14	82	F	Tip	Brain	1996	Aguirre et al.
15	59	M		Para-aortic, lymph nodes	1997	Konya et al.
16	50	M	Border	Lung, Brain, Skin	1998	Tomita et al.
17	62	M	Lateral	Lung	2000	Navarro et al.
18	60	M	Base and Anterior	Lungs	2002	Pritchyk et al.
19	62	M	Surface	Lung	2003	Goel et al.
20	45	M	Tip	Nose, Lungs	2003	Emer et al.
21	87	F	Dorsum	Lung, Liver, thyroid, pancreas	2004	Marioni et al.
22	66	M	Base	Lungs	2004	Kyan et al.
23	73	M	Border	Lungs, Bone,Choroidea	2005	Tachi et al.
24	49	F	Dorsum	Lungs	2006	Torres-Carranza et al.
25	76	F	Base	Lungs, Liver	2006	Cochrane et al.
26	82	M	Border	Lungs,Brain	2007	Tanaka et al.
27	78	M	Lateral	Lungs, Bone	2008	Azam, F. et al.
28	46	F	Left base	Humerus	2009	Basely et al.
29	47	M	Dorsum	Adrenal gland, Pleura, Lungs	2010	Present case

Table.2 Tongue metastasis as the initial presentation of RCC

No	Age	Sex	Site	Size	Management of tongue metastasis	Year	Authors
1	70	M	Not mentioned	Not mentioned	Not mentioned	1987	Kapoor et al.
2	59	M	Base	2*1cm	local excision	1994	Ziyada et al.
3	82	F	Tip	2*2cm	wide resection	1996	Aguirre et al.
4	78	M	Lateral	3*2cm	Debulking surgery +Radiotherapy 60Gy	2008	Azam et al.
5	47	M	Dorsul	5mm	wide resection	2010	Present case