Renal Cell Carcinoma Metastasis to the Maxillary Bone: A Case Report and Review of the Literature

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Case report

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Abstract

Background: Metastasis of renal cell carcinoma (RCC) to the oral cavity is rare. Given the poor prognosis of metastatic RCC, treatment choice is difficult. Here, we report a case of RCC metastasis to the maxillary bone, and provide a detailed literature review regarding the patient characteristics, treatments and outcomes of RCC metastasis to the oral cavity.

Case presentation: An 89-year-old Japanese man presented with an 8 × 8-mm granulomatous tumor with palpable pulsation in the left upper gingiva, which had been clinically suspected as an arteriovenous malformation. The patient had undergone left nephrectomy for clear cell carcinoma 7 years prior. Pulmonary metastasis had appeared 3 years later. The patient underwent tumor resection of the maxilla after intravascular embolization, and the tumor was histopathologically diagnosed as a metastasis of clear cell RCC to the maxillary bone. Seventeen months after surgery, he died because of pulmonary metastasis without evidence of recurrence in the oral cavity.

Conclusion: Our literature review reveals that oral metastatic lesions of renal cancer often exhibit rapid enlargement and cause severe symptoms, such as dysphagia and bleeding. Although oral metastasis of RCC has a poor prognosis due to the presence of concurrent disseminated metastases, surgical therapy may be recommended because of its high local control rate and ability to maintain quality of life.

Background

Tumor metastasis to the oral cavity is uncommon, comprising only 1% of all oral malignant tumors [1]. After lung and breast cancers, renal cancer is the third most common tumor that metastasizes to the head and neck [2-4]. Because oral metastasis of renal cell carcinoma (RCC) is a late-stage phenomenon, often accompanied by lung metastasis, its prognosis is very poor [5]. RCC metastases are often regarded as radioresistant tumors, and surgical treatment is recommended. However, given the poor prognosis of metastatic RCC to the oral cavity, careful consideration is necessary regarding whether surgery can improve quality of life for end-stage oncological patients. In this report, we describe a patient with RCC metastasis that developed in the maxillary bone and provide a review of the current literature regarding oral cavity involvement of RCC metastases.

Case presentation

An 89-year-old man noticed swelling of the left maxillary gingiva in November 2016. In December 2016, he was referred to our department because the mass slowly enlarged. His past medical history included clear cell RCC in the left kidney 7 years prior, which had been treated by nephrectomy. Multiple pulmonary metastases of RCC had appeared 3 years after surgery. He had received molecular targeted therapy with sorafenib for 4 years, which suppressed the growth of pulmonary metastases. Intra-oral examination showed an 8 × 8-mm granulomatous tumor with palpable pulsation in the buccal side of the left upper gingiva (Fig. 1A). The lesion enlarged rapidly over 2 weeks (Fig. 1B).

Panoramic radiography revealed resorption of the left maxillary alveolar bone (Fig. 2A). Enhanced computed tomography showed a tumor destroying the left maxillary bone as well as the anterior and lateral walls of the maxillary sinus (Fig. 2B). Magnetic resonance imaging showed a 47 × 31 × 22-mm mass in the left maxillary bone and maxillary sinus, which extended into the oral cavity (Fig. 2C). Computed tomography angiography demonstrated that the mass in the left maxillary bone had strong enhancement and was fed by the infraorbital artery, posterior superior alveolar artery, and sphenopalatine artery (Fig. 2D). The patient was clinically suspected to have an arteriovenous malformation or neoplastic lesion in the left maxilla.

In January 2017, 5 days after intravascular embolization of three feeding arteries, the patient underwent maxillary tumor resection. Pulsation around the tumor was not palpable after embolization. Prior to surgery, a biopsy specimen of the left maxillary gingiva had been subjected to frozen study. The results indicated that metastasis of the previously treated RCC could not be ruled out. Subtotal maxillectomy was performed by an intraoral approach (Fig. 3). Although no tumor recurrence was observed in the oral cavity, the patient died 17 months after surgery because of widespread pulmonary metastases.

Histologically, the neoplastic cells exhibited clear cytoplasm and proliferated in an alveolar pattern with delicate vascular stroma (Fig. 4A). The nuclei of tumor cells were round to polygonal with mild to moderate atypia (Fig. 4B). Periodic acid–Schiff-positive granules were found in some tumor cells (Fig. 4C). Immunohistochemistry staining revealed that the tumor cells were positive for CD10 and pan cytokeratin (AE1/3) (Fig. 4D, E). The tumor was histopathologically diagnosed as a metastasis of clear cell RCC to the maxillary bone.

Discussion

Nearly one in three patients with RCC develops distant metastatic disease. The most common site of distant metastasis is lung (75%), followed by bone (20%) and liver (18%) [6]. Metastasis of RCC to the head and neck region is relatively rare, with a reported incidence of 15% [7]. A literature review revealed 153 patients with renal carcinoma metastasizing to the oral cavity from 1970 to 2020 [5, 7–67] (Table 1). Male patients were more frequently affected (male to female ratio, 3.0:1), with ages ranging between 1 and 89 years (mean age, 61.4 years). The tongue was involved in renal metastases in most patients (62 patients, 39.5%). More than three-quarters of patients with oral metastasis from renal carcinoma also exhibited other metastatic lesions, primarily lung metastases (86 patients, 59.3%) (Table 1). Because of the high rate of lung metastases, the prognosis is reported to be very poor; most patients die within the first year after diagnosis [5][27].

The literature review revealed that the oral metastasis was the first evidence of renal cancer in 58 patients. Ninety-three patients were diagnosed with oral metastatic lesions after primary renal cancer (Table 1). The information was not described for two patients. The duration from the onset of renal cancer to oral metastasis ranged from 2 weeks to 26 years, with an average of 4.8 years.

Oral metastatic lesions of renal cancer are known to undergo extremely rapid enlargement, which results in severe symptoms and a decline in quality of life. Dysphagia was observed in 17 patients [12][20][21][25][30][32][37][38][41][43][45][47][53][56][67] (Table 1). Obstruction of the upper airways due to rapid growth of oral metastasis led to tracheotomy in one patient [41] and death in one patient [38].

In addition, hemorrhage was observed in many patients because renal cancer is characterized by rich blood vessels. Twenty-seven patients exhibited bleeding [8, 10–14, 16, 17, 19, 21–24, 26, 28, 30, 31, 38, 39, 43, 48, 50, 55, 58, 61], which resulted in death in one case [58]. Ten patients reportedly had difficulty with hemostasis during biopsy or surgery [10, 22, 26, 38, 48, 52, 61, 63, 66]. Three patients underwent preoperative vascular embolization or ligation, which did not lead to complications during surgery [15, 19, 26]. Our experience with the present patient also indicated that preoperative vascular embolization is helpful in preventing massive hemorrhage during surgery for pulsatile oral metastasis of RCC.

Due to abundant arterial blood vessels, pulsation was observed in seven patients at the first visit [10, 15, 19, 20, 38]. Three of these patients exhibited pulsation in the maxillary bone [20] (Tables 1 and 2). In our patient, arteriovenous malformation was clinically suspected due to pulsation. Past reports indicated that two patients with mandibular lesions were also clinically diagnosed with vascular malformation, then diagnosed with RCC metastases upon pathological examination [14, 19]. When a pulsatile mass is present in a patient with a history of renal cancer, the possibility of renal cancer metastasis should be considered.

Histologically, an alveolar pattern of large clear cells is suggestive of RCC. Immunohistochemical examination plays a key role in differentiating other types of clear cell carcinoma, such as clear cell-rich salivary gland and clear cell odontogenic carcinoma, from metastatic RCC [39]. CD10 is a good marker to distinguish RCC from other clear cell-type carcinomas. The literature review showed that immunohistochemical staining of CD10 was performed for 31 patients, and positive expression was present in all patients. The positive expression of vimentin, pan cytokeratin (AE1/3), and epithelial membrane antigen are also suggestive of RCC. These were used for immunohistochemical staining of tissue from 27, 26, and 12 patients, respectively. The negative expression of cytokeratin 7 can often rule out salivary gland origin [39]. Immunohistochemical staining of cytokeratin 7 was performed in tissue from 17 patients, and negativity was confirmed in 14 patients.

Regarding treatments, surgery is often recommended due to the ability of metastatic RCC to resist radiotherapy and pharmacotherapy, including chemotherapy, molecularly targeted therapy, or immunotherapy [40]. However, oral metastasis of renal cancer has a poor prognosis, and hemostasis is difficult during surgery. Therefore, it is difficult for clinicians to judge whether surgery can improve quality of life for patients with end-stage cancer. Mazon et al. described a patient with RCC metastasis to the tongue, who initially decided against surgery due to the poor prognosis. However, doctors were later forced to perform surgery because of a rapid increase in the size of the intraoral mass and resistance of the tumor to chemoradiotherapy [46]. Among 153 patients with oral metastasis of renal cancer described in the literature, the treatment and outcome of the oral lesion were described for 78. These data are

summarized in Table 3. Surgery was performed in most patients (53 cases), and the local control rate was greater than 90%. In contrast, the local control rates of radiotherapy, pharmacotherapy, and palliative surgery (debulking and cryosurgery) ranged from 33.3–66.7%. Considering the high ratio of local control and increased quality of life after surgery, surgical therapy before further disease progression can occur may be the first choice for patients with oral metastasis of renal carcinoma.

Conclusions

Oral metastatic lesions of renal cancer often exhibit rapid enlargement and cause severe symptoms, such as dysphagia and bleeding. Although oral metastasis of RCC has a poor prognosis due to the presence of concurrent disseminated metastases, surgical therapy may be recommended because of its high local control rate and ability to maintain quality of life.

Abbreviations

RCC
renal cell carcinoma

Declarations

Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of his clinical details and clinical images was obtained from the family of the present patient. A copy of the consent form is available for review by the Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

All authors were involved in the preparation of this manuscript. NN and HS designed the report, collected and assembled the data, and edited the article. TO, MY and YS collected the patient's clinical data. YO, KK and TI performed the pathological diagnosis. HH provided critical revision and the approval of the article. All authors read and approved the final manuscript.

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Tables

Table 1. Characteristics of patients (N=153)

Gender	
Men	113
Women	38
Not described	2
Age (yr), range (mean)	1-89 (61.4)
Oral metastatic site (%)	
Tongue	62 (39.5)
Mandibular bone	30 (19.1)
Gingiva	29 (18.5)
Palate	11 (7.0)
Maxillary bone	7 (4.5)
Buccal mucosa	6 (3.8)
Lip	5 (3.2)
Floor of mouth	3 (1.9)
Metastatic site other than oral cavity (%)	
Lung	86 (59.3)
Bone	36 (24.8)
Brain	15 (10.3)
Lymph node	15 (10.3)
Liver	11 (7.6)
Adrenal gland	9 (6.2)
Skin	5 (3.4)
Mediastinum	4 (2.8)
Muscle	4 (2.8)
None	34 (23.4)
Timing of diagnosis of oral metastasis	
Before the diagnosis of primary renal carcinoma	58
After the diagnosis of primary renal carcinoma	93
Not described	2
Time*, range (mean)	2w – 26 yr (4.8yr)
Symptom	
Bleeding	27
Dysphagia	18
Pulsation	7

Abbreviation: yr, year; w, week

* The time from the onset of primary renal carcinoma to the metastasis of oral cavity.

Table 2. Summary of the reported cases of RCC metastasis in the maxillary bone

Case	Age	Gender	Pulsation	Treatment	Outcome		Ref.
					Oral metastasis	Prognosis [*]	
1	66	F	-	S	ND	ND	9
2	58	M	+	E	Uncontrolled	Dead, 2m	20
3	73	M	+	E	NS	Dead, 1.5m	20
4	53	F	-	R+E+S	Controlled	Alive, 14m	26
5	60	M	-	S	ND	ND	52
6	54	M	-	CR	ND	Dead, 11m	59
7	89	M	+	E+S	Controlled	Dead, 19m	†

Abbreviation: F, female; M, male; S, surgery; E, embolization; R, radiotherapy; CR, chemoradiotherapy; ND, not described, NS, no symptom with disease,

^{*} Numbers are length of follow-up in months.

† Present case.

Table 3. Therapeutic outcomes of oral metastatic lesion of renal cancer (N=78)

Treatment	Outcome		Control ratio (%)
	Controlled [*]	Uncontrolled	
S	41	2	95.2
S+P/R	12	1	92.3
PS	3	3	50.0
R	4	3	57.1
P	2	4	33.3
P+R	2	1	66.7

Abbreviation: S, surgery; P, pharmacotherapy; R, radiotherapy; P/R, pharmacotherapy and/or radiotherapy; PS, palliative surgery

^{*} “Controlled” indicates no local recurrence after surgery, or regression of tumor after PS/P/R.

Figures

Figure 1

(A) Intraoral photograph of tumor of the left upper gingiva at the first visit, showing granulomatous appearance. (B) Tumor enlarged rapidly in 2 weeks.

Figure 2

(A) Panoramic radiography revealed resorption of left maxillary alveolar bone (arrow). (B) Enhanced computed tomography showed a tumor destroying the left maxillary bone (arrow). (C) Magnetic resonance imaging showed a 47 × 31 × 22-mm mass in the left maxillary bone and maxillary sinus (arrow). (D) Computed tomography angiography showed a mass with strong enhancement (white arrow) fed by the infraorbital artery (a), sphenopalatine artery (b), and posterior superior alveolar artery (c).

Figure 3

(A) Intraoperative photograph after tumor and surrounding bone were removed. (B) Surgical specimen.

Figure 4

Histological findings of RCC metastasis to maxillary bone. Hematoxylin and eosin staining identified clear cell differentiation with delicate vascular stroma (A, ×100) and cellular atypia (B, ×400). Periodic

acid–Schiff staining revealed positive granules in tumor cells (C, ×400). Immunohistochemical staining revealed positivity for AE1/3 (D, ×400) and CD10 (E, ×400).

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