

Metastatic Tumors to the Oral Cavity: A Clinical Study of 18 Cases

Bruno C. Jham · Andrew R. Salama ·
Shawn A. McClure · Robert A. Ord

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Abstract The aim of this study was to describe the clinical features of 18 cases of metastatic tumors to the oral cavity. The files of patients seen between 1992 and 2009 with oral (soft tissue and jawbones) metastatic lesions were reviewed. Clinical features, including gender, age, site of the primary tumor, site of metastatic tumor and treatment were evaluated. Patients were 11 males and 7 females, with mean age of 64.6 years. In males, most primary tumors originated in the lungs. In females, the lung and breast were the most common sites of the primary tumors. The mandible was the main site for the development of the metastatic lesions and the most common histologic type was adenocarcinoma. Treatment modalities included

radiotherapy, chemotherapy and surgical resection. Metastatic lesions should be considered in the differential diagnosis of oral lesions, particularly when a previous history of cancer is present.

Keywords Cancer · Metastasis · Oral cavity · Clinical study

Introduction

Cancer is a complex disease in which cells develop aberrant proliferation and survival. A common cause of morbidity and mortality in the cancer context is metastatic disease. The metastatic process is a complex biological process that involves detachment from the surrounding cells, regulation of cell motility, invasion, survival, proliferation and evasion of the immune system [1]. It is estimated that about 1% of all oral cancers are metastases of primary tumors elsewhere in the body [2].

Metastatic tumors to the oral cavity are rare. When affecting the oral cavity, tumors may occur in the oral soft tissues or in the jawbones. Due to its rarity, the diagnosis of metastatic lesions is challenging for both the clinician and pathologist. Nonetheless, metastatic disease should be considered in the differential diagnosis of more common inflammatory and reactive lesions, particularly when the patient presents with a history of a previous malignancy [1].

Most of the information available on oral metastatic disease is found in single case reports, with only a limited number of large series being found in the literature [2–6]. Thus, the aim of this study was to describe the clinical features of 18 cases of metastatic tumors to the oral cavity, seen in a single institution over a period of 17 years.

B. C. Jham (✉)

Department of Microbiology, Immunology, Parasitology and Pathology, Institute of Tropical Pathology and Public Health, Federal University of Goiás, Rua 235 s/n, Setor Universitário, Goiânia, GO 74605-505, Brazil
e-mail: brunocjham@yahoo.com.br

A. R. Salama

Department of Dentistry and Oral & Maxillofacial Surgery, Boston Medical Center, Boston University, 100 East Newton Street, Boston, MA 02118, USA

S. A. McClure

Department of Oral and Maxillofacial Surgery, Nova Southeastern University, College of Dental Medicine, 3200 South University Drive, Fort Lauderdale, FL 33328, USA

R. A. Ord

Department of Oral and Maxillofacial Surgery, University of Maryland Dental School, Marlene and Stuart Greenebaum Cancer Center, University of Maryland Medical Center, 650 West Baltimore Street, Baltimore, MD 21201, USA

Patients and Methods

In this retrospective study, the files of 18 patients seen between 1992 and 2009 with metastatic lesions to the oral cavity were retrieved from the archives of our Oral and Maxillofacial Surgery Department. Patients with primary tumors in the oral and maxillofacial region and metastases in the same region were not included. Clinical features, including gender, age at diagnosis, site of the primary tumor, site of metastatic tumor and treatment of metastatic lesion, were evaluated.

Results

Patients were 11 males and 7 females, with mean age of 64.6 years (range 45–87). The majority of patients presented with swelling and pain of the affected area. In males, 36% (4/11) of the primary tumors originated in the lungs. In females, the lung and breast were the sites of the primary tumors in 42% (3/7) of the cases, each. The average time between diagnosis of the primary tumor and the metastatic tumor was 5.3 years (range 3 months–12 years). In six cases (33%), the metastatic tumor led to the diagnosis of a primary lesion elsewhere. The most common histologic type was adenocarcinoma (33%; 6/18), followed by neuroendocrine carcinoma and non-small cell cancers of the lung (16%; 3/18, each). Other primary tumors included leiomyosarcoma and squamous cell carcinoma. Most metastatic cases were treated with radiotherapy and/or surgery. Chemotherapy was also occasionally employed. Demographic information of the patients and clinical data of the lesions are summarized in Table 1.

Discussion

It is estimated that 1 to 8% of all oral malignancies and 1% of all jaw tumors represent metastatic cancer [7]. A recent study found that distant metastasis account for 2.39% of all malignancies in the oral and cranio-maxillofacial area, which is twice as high as previous reports; however, the authors could not identify specific reasons for such an increase [5].

Metastatic tumors to the oral region are seen in patients between the fifth and seventh decade, with a mean age of 54 years [7, 8]. In our series, 61% of the patients were males and 39% females. The mean age was 64.6 years, similar in both groups (66.2 years in males and 62 years in females), in agreement with other studies [5]. Hirschberg et al. [1] observed the mean age for males was 51.1 years and for females 47.1 years. Likewise, van der Waal et al. [2] found

the overall median age was lower in women than in men (53 and 66 years of age, respectively). However, the lower mean age for females was likely due to a small sample size, rather than a true epidemiological difference [2].

The clinical presentation of the metastatic lesions differs between the various oral sites. In the jawbones, most patients complain of rapidly progressing swelling, pain and paresthesia. The early manifestation of the gingival metastases resembles a hyperplastic or reactive lesion [1]. In their study, D'Silva et al. [9] found that pain, paresthesia and swelling were the most common symptoms. In our series, swelling was the most common complaint, but paresthesia was not very frequent; this probably occurred because we included both soft and hard tissue metastatic lesions, whereas the other authors investigated only jaw metastasis. Importantly, paresthesia may be the first symptom of metastasis in 30% of patients and mental nerve paresthesia, known as “numb chin syndrome,” should raise clinical suspicion of malignancy. The phenomenon, which is a late event in the course of disease, probably occurs due to compression or invasion of the mental nerve by the tumor, base of skull involvement, or leptomeningeal spread [10]. Besides swelling and paresthesia, our patients also presented with pain, temporo-mandibular joint issues and dental-related (loose teeth, non-healing extraction sites) problems. Our results indicate metastatic lesions may present with a variety of symptoms, highlighting that dentists and other health professionals should maintain a high level of suspicion when examining and treating their patients.

The most common reported primary sites for oral metastases are the lung, kidney, liver and prostate for men; and breast, genital organs, kidney, and colorectum for females. These cancers are also the most prevalent in the general population [8]. Likewise, in our series, the lungs were the most common primary sites for males, corresponding to 36% of the cases. In females, the lungs and breast were responsible for 42% of primary tumors, each. Similarly, van der Waal et al. [2] found that the most common primary sites for oral metastatic disease were lung and breasts. It has been postulated that metastatic lesions involve more commonly the jaws (65–75%) than the oral soft tissues (25–35%) [11]. Similarly, in our series, 72% of the cases spread to the bones. Furthermore, a recent meta-analysis showed more published cases of jawbone metastases than oral soft tissue malignancies [1]. However, it should be noted that metastatic lesions in the oral soft tissues are easily recognized, in contrast to the jawbone, where a metastatic deposit may not be evident especially in a wide spread disease, in which the patient may succumb within several months [1].

An additional important feature of metastasis is that certain tumors preferentially spread to specific sites. For

Table 1 Demographic information of the patients and clinical data of the lesions

Case	Gender	Age	Primary Site	Signs/symptoms	Pathology	Metastasis site	Treatment of metastatic lesion
1	F	48	Breast	Swelling	Neuroendocrine carcinoma	Mandible, maxilla	Chemotherapy
2	F	67	Esophagus	Facial swelling	Adenocarcinoma	Mandible	Surgery
3	F	51	Breast	TMJD symptoms, trismus	Lobular carcinoma	Condyle	Surgery
4	F	75	Breast	Facial pain, NCS, facial nerve palsy	Adenocarcinoma	Mandible	Radiotherapy
5	F	66	Lung	NCS, mandibular swelling	Neuroendocrine carcinoma	Mandible	Radiotherapy
6	F	54	Lung	NCS	Neuroendocrine carcinoma	Mandible	Radiotherapy
7	F	73	Lung	Loose tooth	Squamous cell carcinoma	Mandible	Radiotherapy
8	M	53	Colon	Gingival swelling	Adenocarcinoma	Gingiva	Surgery, chemotherapy
9	M	84	Lung	Gingival swelling and bleeding	Adenocarcinoma	Gingiva	Surgery
10	M	69	Leg	Pathologic fracture, pain, paresthesia	Leiomyosarcoma	Mandible	Surgery
11	M	60	Breast	Pain, TMJD symptoms	Dedifferentiated cancer	Condyle	Surgery
12	M	60	Leg	Gingival swelling	Leiomyosarcoma	Mandible	Surgery
13	M	58	Lung	Gingival swelling	Non small cell carcinoma	Gingiva	Radiotherapy
14	M	70	Lung	Gingival swelling	Non small cell carcinoma	Gingiva, palate	Chemotherapy
15	M	82	Prostate	Pain, swelling, TMJD symptoms	Adenocarcinoma	Mandible	Surgery
16	M	61	Lung	Gingival swelling	Non small cell carcinoma	Gingiva	Radiotherapy
17	M	45	Liver	Facial pain, swelling, pathologic fracture	Cholangiocarcinoma	Condyle	Radiotherapy
18	M	87	Prostate	Pain, swelling, TMJD symptoms	Adenocarcinoma	Condyle	Radiotherapy

TMJD temporo-mandibular joint disorder, *NCS* numb chin syndrome

instance, 11% of the jaw metastases in men originate from the prostate, compared with 1.5% of soft tissues metastases. In women, 40% of jawbone metastases originate from the breast, compared with 25% of the soft tissues lesions. Other examples include metastatic lesions from the adrenal, thyroid, and eye, which metastasize to the jaws more commonly [1]. Such information is important during clinical work-up to determine which areas are at higher risk of developing metastatic lesions, in patients with a previous history of cancer. In our series, all breast cancer cases spread to the mandible, whereas 57% (4/7) of the lung primaries spread to bones.

Within the jaws, the most common location for bony metastasis is the mandible (80%), with the great majority occurring in the molar (55%) and premolar regions (38%) [5]. Our findings are in agreement with the literature, with most cases seen in the mandible. The condyle is said to be affected in about 3.5% of the cases [7], while in our series condylar metastasis represented 22% (4/18) of the cases.

An explanation for this mandibular predilection may be related to the larger amount of hematopoietic tissue in the mandible, compared to the maxilla. Further, the vascular spaces in hematopoietic tissue are sinusoidal, allegedly allowing more easily penetration by tumor cells. In 5% of the cases, both the maxilla and mandible are affected [11], such as in one patient of our series.

In the oral soft tissues, the attached gingiva is the most common site for the metastatic colonization (57%), followed by the tongue (27%), tonsil (8%), palate, (4%), lip (3%), buccal mucosa (1%) and floor of mouth (<1%) [12]. A recent study analyzed 39 patients with gingival metastasis and found these lesions represented 67% of all soft tissue metastasis [6]. The reason for this distribution is not known, but inflammation may play a role in the attraction of metastatic cells towards the gingiva [12]. Indeed, chronic inflammation has been linked to various steps involved in tumorigenesis, including cellular transformation, promotion, survival, proliferation, invasion,

angiogenesis, and metastasis. The rich capillary network of the chronically inflamed gingival tissue may also entrap malignant cells [13]. Further, the microenvironment present in the chronically inflamed gums, rich in cytokines and chemokines, may favor the progression of the metastatic cells [14, 15]. An intriguing finding is that gingival metastases have a predilection for the maxilla, whereas bone metastases tend to affect the mandible. However, the pathogenesis for such preference remains unclear [6].

Because of its rarity, the diagnosis of a metastatic lesion in oral cavity is challenging, both to the clinician and to the pathologist. In patients with a known malignant disease, the clinical presentation may favor the pre-operative diagnosis of metastasis. However, metastases to the oral cavity are in 20–35% of cases the first indication of an otherwise occult malignancy [2, 5]. Similarly, in our series, the metastatic lesion led to the diagnosis of the primary tumor in 33% of the cases. In some instances the primary tumor may remain occult, despite additional investigations [5].

Conflict of interest The authors declare that they have no conflict of interest.

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