

## Research Article

### Oral soft tissue Metastases of distant cancers

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**Abstract:** The oral cavity is not a preferred site for metastasis of distant cancers, accounting for only 1% of all oral cancers. Almost all types of cancers can spread to the oral cavity, and usually are late presentation. Sometimes the oral metastasis may manifest as a benign lesion and may cause challenges in its diagnosis. All patients with oral cavity metastasis diagnosed at King Hussein cancer center (KHCC) during the period between 2007-2012 were studied retrospectively from the medical records and the histopathology database. In the 5 year period studied, 12 cases of oral cavity metastasis were diagnosed. Male to female ratio was 2:1. Most common cancer to metastasize to the oral cavity is lung in males and breast in females. All cases had poor prognosis and were part of a widely metastatic disease. Aim of treatment was palliative in all cases. Oral cavity metastasis remains an uncommon entity that is underreported and not well understood as unfortunately these lesions are not separately reported by cancer registries thus their exact epidemiology cannot be estimated correctly. Metastasis to the oral cavity indicates poor prognosis and usually is part of a widely spread disease.

**Keywords:** oral cavity, cancer, metastasis, malignancy, oral soft tissues.

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#### INTRODUCTION

The oral cavity is not the preferred site for metastasis of distant cancers, and accounts for only 1% of all oral malignancies [1,2]. Most published large series studies have been meta-analyses covering multiple institutions [3]. Metastatic tumors may occur in the soft tissues and jaw bones, nevertheless tumors metastasizing only to oral mucosa are rarer and account for only 0.1% of all oral malignancies [4]. Almost any malignancy can metastasize to the mouth, but some primary tumors have been reported more often than others eg. breast cancer (females) and lung cancer (males)[5].

In most cases, oral cavity metastasis presents after the primary tumor is diagnosed, however sometimes these oral lesions precede the primary tumors and their diagnosis lead to the discovery of the primary.

Due to its rarity, the diagnosis is often challenging and should be considered in the differential diagnosis of inflammatory and reactive lesions which are common in the oral cavity. Oral cavity metastases usually indicate a grave prognosis and are distressing to the patient as they may interfere with feeding and speech and affect their quality of life. In most cases the treatment is palliative, and can include surgery,

chemotherapy, radiotherapy or a combination of these modalities.

The aim of this study was to analyze the oral cavity soft tissue metastases from distant cancers diagnosed at King Hussein Cancer Center (KHCC) in Jordan during the period 2007-2012.

#### PATIENTS AND METHODS

All patients diagnosed with oral metastasis at the oral oncology unit at KHCC during the study period were included. The histo- pathological and medical records of these patients were reviewed retrospectively. Age and sex of patient, initial clinical presentation, histopathology report, oral site, primary tumor, treatment and follow up period of disease were analyzed. We obtained appropriate approval and waiver of consent from the Institutional Review Board at KHCC, before conducting this study.

#### RESULTS

In the five years study period, twelve cases of oral soft tissue metastases were diagnosed. The median age for both males and females was 55 years, there were 8 males and 4 females. Most common pathology was adenocarcinoma. Four cases were in the maxilla, 6 in the mandible, one in both jaws and one in the tongue.

The most common presenting symptom was growing mass. The clinical details of these cases are shown in Table 1.

The time between initial diagnosis and development of oral metastasis ranged from 0-96 months. Follow up period up to 28 months. Treatment was either radiotherapy, chemotherapy or supportive. In all cases the patients died (Table 2).

**Table-1: Clinical Details of Oral Cavity Metastases**

No	Age Years	Sex	Presenting symptoms	Pathology Oral metastasis	Primary tumor
1	29	Female	Bleeding	Metastatic phylloids cancer	Breast
2	65	Male	Painless mass	Metastatic urothelial cancer	Urinary bladder
3	57	Female	Pain	Metastatic adenocarcinoma	Breast
4	58	Male	Pain	Metastatic adenocarcinoma	Lung (NSCLC)
5	54	Male	Painless mass	Plasma cell tumor	Multiple Myeloma
6	61	Male	Painless mass	Metastatic adenocarcinoma	Lung (NSCLC)
7	73	Male	Bleeding	Metastatic adenocarcinoma	Lung (NSCLC)
8	64	Female	Bleeding	Metastatic high grade sarcoma	Uterus
9	33	Male	Painless mass	Metastatic adenocarcinoma	Lung (NSCLC)
10	12	Male	Pain	Recurrent lymphoblastic lymphoma	T-Lymphoblastic lymphoma
11	50	Female	Painless mass	Metastatic adenocarcinoma	Breast
12	10	Male	Painless mass	Ewing sarcoma	Scapula sarcoma

**Table-2: Management Details of Oral Cavity Metastases**

No	Primary tumor	Affected oral site	Time relation between detection of metastases and primary tumor (month)	Treatment	Follow up
1	Breast	Palatal gingiva	Same time as primary	Palliative	Died after 1 month
2	Urinary bladder	Tongue	44 months	Chemotherapy	Died after 3 month
3	Breast	Mandibular gingiva	48 months	Radiotherapy	Died after 8 month
4	Lung (NSCLC)	Mandibular gingiva	12 months	Radiotherapy	Died after 28 month
5	Multiple Myeloma	Mandibular gingiva	4 months	Radiotherapy	Died after 2 month
6	Lung (NSCLC)	Maxillary gingiva	Unknown	Radiotherapy	Died after 2 month
7	Lung (NSCLC)	Maxillary gingival	35 months	Radiotherapy	Died after one month
8	Uterus	Mandibular gingiva	1 month	Palliative	Died after 1 month
9	Lung (NSCLC)	Palatal gingiva	8 month	Chemotherapy	Died after 1 month
10	T-Lymphoblastic lymphoma	Mandibular gingiva	42 months	Chemotherapy	Died after 8 months
11	Breast	Mandibular gingiva	96 months	Chemotherapy	Died after 5 months
12	Scapula	Maxillary and mandible gingiva	1 month	Chemotherapy	Died after 1 month

One case represented the recurrence of malignancy and one was diagnosed at same time as the primary tumor while the remaining cases were diagnosed in patients with multiple organ metastases.

**DISCUSSION**

Cancer is a complex disease and for metastasis to occur tumor cells have to breach a sequence of barriers [6]. Considerable evidence indicates that metastases of various cancers to distant organs is not a random event, but is a regulated, site-specific process [7,8].

Zetter et al [9] described the multiple steps needed for tumor cells to metastasize to different tissues. Metastatic process includes detachment of

cancer cells from original tumor, spread, adhesiveness to a new site and the ability to thrive.

Metastatic tumor spread to the oral cavity is uncommon and several reviews have been published on oral cavity metastasis [3,10,11,12,13]. These studies show that the metastatic tumor may occur in the jaw bones or the oral soft tissues [14]. Many metastatic lesions to the bone are not diagnosed, thus the accurate incidence of bone metastasis is difficult to assess and is probably more common than is noted, for example in the mandible microscopic deposits were found in 16% of autopsied carcinoma cases [15]. In the present study lesions affecting the soft tissues only were included.

There were 12 cases of oral metastasis to the mouth. The age range was from 10-73 years of age, with an overall median age of 55 years. It was reported in a previous study that these cancers mainly affect patients in their fifth to seventh decades [13].

There were 8 males and 4 females with a ratio of 2:1. As reported elsewhere the ratio between male and female was equal [16], but in another study the ratio for bone metastasis was equal while for soft tissue metastasis it was 2:1, which agrees with the results in our study [13].

The most common primary tumors in our series were lung followed by breast and this is due to the fact that lung cancer in men in Jordan is the most common cancer and similarly for breast cancer in females [17].

Although it is expected that the most common tumors to metastasize to the oral cavity such as the lung and breast, this is not always the case, probably this reflects the difference in biological behavior of tumors, aggressiveness and possible preference to oral sites [16]. In other countries prostate cancer is more prevalent in men and pancreatic cancer is more aggressive, still lung cancer is more likely to metastasize to oral cavity as prostate cancer is less aggressive while pancreatic cancer is highly aggressive and patients are more likely to die before oral cavity metastasis occur.

It is believed that the preferred sites for metastases are the haemopoietic marrow areas, therefore they are generally more diagnosed in the premolar and molar areas of the mandible than the maxilla [18]. In our series six cases involved the soft tissue of the mandible, four in the maxilla and one in the tongue. Oral soft tissue metastasis is difficult to understand but inflammation may play a role by entrapping the malignant cells through the rich capillary blood supply of the chronically inflamed gingiva, these capillaries contain fragmented basement membrane through which tumor cells can easily penetrate [19].

Batson [20] proposed the valveless vertebral venous plexus as a mechanism for bypassing filtration through the lungs; an increase in intrathoracic pressure directs blood flow into this system from the caval and azygous venous system and accounts for the increased distribution of axial skeleton and head and neck metastasis [20,21].

In ten cases the primary tumors were diagnosed before the oral metastasis occurred, one patient presented to the clinic as a referral case to investigate and the primary was diagnosed as phylloids tumor of the breast, and in the other patient it was the first sign of relapse of a hematological malignancy. Recently Chorost *et al.* reviewed the approach in

evaluating patients with a cancer of unknown primary and this could be applied also to unknown primary of the oral cavity [22].

In this study all cases had their primary cancer pathologically diagnosed as well as the oral soft tissue metastases with the most common pathology being adenocarcinoma (50%) which was also the same in a previous study [13]. Histopathologically the adenocarcinoma is a neoplastic lesion with glandular elements seen in its malignant growth [23]. It can arise from lung, breast, colon and prostate; most of these cancers can metastasize to the oral cavity. Patients with a previous history of cancer can help in identifying the origin of the metastasis by comparing the two pathologically specimens from both sites.

In its early manifestation, oral soft tissue metastases may resemble hyperplastic or reactive lesions (e.g., pyogenic granuloma, peripheral giant cell granuloma, and fibrous epulis) [24]. In our cases most of them presented as a growing mass, and this is most likely due to their late presentation (Figure 1).

In other oral soft tissue locations, especially in the tongue, the metastatic lesion may manifest as a sub mucosal mass [24]. However this was not the case in our study as the patient presented with exophytic mass (Figure 2).

Few studies reported ulceration as the oral manifestation, in our case series 3 of them presented with ulceration and this could be because of the delay in seeking medical advice concerning their oral lesions. The clinical presentation includes gingival bleeding, pain, or painless swelling.

As the disease advances the metastatic lesions may cause progressive discomfort, super infection, dysphagia, interference with mastication, and disfigurement thus necessitating treatment [5,25].

The average time between the diagnosis of the primary tumor and the development of oral metastases was about 26.5 months. Some oral metastases, however, were reported to appear more than 10 years following the diagnosis of the primary tumor [13], such as the case in one of our patients who presented with oral metastasis after 8 years from initial diagnosis. This must be taken into consideration when patients with cancer history present with oral symptoms that may present a metastatic disease. The follow up period for all patients was up to 28 months and the prognosis was poor for all cases, the median survival was 5 months, in a previous study the average survival was 7 months [13].

The main parameters used to determine the treatment are the type of tumor, general health condition of the patient, localization of the tumor, and life expectancy [26].

Usually patients with metastatic cancer are treated with palliative intent taking into consideration the performance status. Surgical intervention depends on localization of the tumor and can help control symptoms, but has a limited role in these patients as the overall prognosis is poor [3].

Radiotherapy is a well known treatment modality in cancer patients with up to 80% of them undergoing it. Radiotherapy not only reduces the size of the tumor and relieves symptoms; low dose radiotherapy also has anti-inflammatory, anti-secretory, anti-edematous, and analgesic effects [27].

The role of radiotherapy in these patients is symptom-oriented palliation which aims to alleviate symptoms like pain, distress, dysphagia, or unpleasant smells. Side effects are kept to minimum and the underlying disease is usually not influenced [27].

The choice of which radiotherapy regimen depends on several factors including prognosis and indications, in oral cavity metastasis; the prognosis is usually less than 6 months and symptoms include ulcerated or painful mass in the soft tissue. The dosage in these cases is between 3-4 Gy for 5 sessions [27].

In our case series the aim of the treatment was palliative in all cases as they were all cases of widely spread cancers, which included palliative treatment, chemotherapy and radiotherapy.

In our patient cohort 5 of them were treated with palliative radiotherapy with the indicated dose described. All showed good response in controlling symptoms such as the case in one of our patients while others responded partially( Figure 3).

Although metastatic disease is unlikely to be cured, meaningful improvements in survival have been coincident with the introduction of newer systemic therapies [28].

The primary goals of systemic chemotherapy for metastatic disease are prolongation of survival, alleviation of symptoms, and maintenance and improvement in quality of life, despite the toxicity associated with treatment [29]. Median survival for metastatic patients is believed to be improved by the availability of new, more effective agents, including taxanes and trastuzumab [28,30].

Five of our patients were treated with chemotherapy with a median survival of 3.6 months; this short survival maybe explained by the fact that all cases were wide spread metastatic disease.

Management of these cases is usually directed at improving the quality of life of patients [13]. Patients' quality of life has become an important outcome assessment in the head and neck cancer population during the last few decades [31]. Taking into consideration the short anticipated survival in these patients, the quality of life is significantly important, and is associated with social, functional and psychological aspects of patient's life [32], and palliative treatment of these patients is indicated.

In medical literature, mainly unusual cases have been published, which could cause bias in the favor of unusual cases regarding the primary site and oral site. Taking this into consideration, well documented oral cavity metastases must be published to allow proper and unbiased knowledge of their nature.



**Fig-1: growing mass**



**Fig-2: Tongue lesion**



**Fig-3: radiotherapy treatment of metastatic oral cavity lesion**

## CONCLUSION

Oral cavity metastases remain an uncommon entity that is underreported and not well understood as unfortunately these lesions are not separately reported by cancer registries thus their exact epidemiology cannot be estimated correctly. They are a challenging diagnosis both to the clinician and the pathologist, and their clinical presentation maybe misleading. Although the oral cavity is not a common site for metastatic colonization, it is an interesting area that may help in future in understanding better the metastatic process thus more research and more epidemiological studies are needed concerning oral cavity metastases. Most common cancers to metastasize to the oral cavity in the present study are lung and breast cancers, and remain a late presentation and has very poor prognosis.

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