# Metastases to oro-maxillo-facial region from distant sites: are they so rare?

## A single centre 8-years experience

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Valentina Terenzi, Andrea Cassoni, Oriana Rajabtork Zadeh, Ingrid Raponi, Marco Della Monaca, Davina Bartoli, Andrea Battisti, Valentino Valentini

*Maxillo-Facial Surgery, "Sapienza" University of Rome, Rome, Italy*



**Metastases to oro-maxillo-facial front distant sites: are they so rare? A single centre 8 years experience**

AIM: *The goal of our study is investigate the frequency of metastasis to oro-maxillo-facial region to understand if they are really so rare.*
MATERIAL OF STUDY: *In this eight year's retrospective study (2004-2012) we collected 15 cases of metastasis localized in the maxilla-facial region from distant primary tumor.*
RESULTS: *Our results show breast and kidney as the most frequent primary site (40% and 20% respectively), adenocarcinoma as most common histological type (60%). Bone involvement has found to be much frequent than the soft tissue one (53.3%). The mandible (5/15 cases) is more affected than the maxilla, and most common interested subsites are molar and retromolar region. In our study we found only one case of unknown primary tumor, it was a mandibular bone metastasis from a renal clear cell carcinoma.*
CONCLUSION: *Finally, according to our results and considering the increase of survival in cancer disease, even if metastases to oro- maxilla- facial region from distant sites are not frequent, it is important to suspect secondary lesions both in patients that was referred a tumor in their medical history and in those that present a head and neck lesion.*

KEY WORDS: Head and neck metastasis, Metastatic adenocarcinoma, Oral metastasis.

## Introduction

Metastases to the maxillofacial region account about 1% of all malignancies arising in the head and neck region, thus resulting extremely rare [1,2]. Potentially all tumors can metastatize to this site, but in clinical practice most common primaries are localized in the lung and breast [1], and in most cases bone tissue is involved with an hard tissue/soft tissue metastasis ratio of 2:1 [3,4]. In most cases the primary tumor is just known, and patients have developed metastasis in other sites [5]. With the increase of survival in cancer this low incidence is likely to raise, so it is mandatory to consider these lesions among differential diagnosis in maxillofacial malignancies in order to give to patients the best treatment.
We present a 8-years single centre experience reporting epidemiological data.

## Materials and Methods

All data about patients presenting with a malignant lesion of the maxillofacial region from 2004 to 2012 have been retrospectively reviewed. In all cases diagnosis was done after histological examination. Neck nodal metastases, lymphatic tumors and those cases in which the primary tumor was localized in the maxilla-facial area were excluded; melanoma metastases were considered only if primary tumor was distant to head and neck area. Data about sex, age, histological type, oro-maxillofacial localization, follow-up and treatment have been extrapolated.

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*Correspondence to: Oriana Rajabtork Zadeh, Via Orvieto 25, 00182 Rome, Italy (e-mail: oriana.rajab@gmail.com)*

## Results

Of the 1357 patients presenting with malignancies of the maxillofacial area, 15 cases (10 females and 5 males) of metastasis from distant site responding to inclusion criteria have been found. In no cases primary tumor was unknown. Results are summarized in table I. In all cases medical history of a previous distant malignant tumor was referred.

Medium age was 67.7 years (range: 51-87). Most common primary site was the breast (6/15, 40% of cases), followed by kidney (3/15, 20% of cases) and gastroenteric adenocarcinoma (2/15 cases, 13.4% of cases). Most common histological type was adenocarcinoma (9/15, 60% of cases), followed by clear cell renal carcinoma (3/15, 20% of cases). Only considering oral metastasis, bone involvement have been found to be much frequent than the soft tissue one (5/6, 83.3% of cases), and in all patients lesions were located in the mandible. Considering all cases, two other bone metastases have been found in the orbit: in all three cases of orbital involvement the primary was located in the breast. Four cases (26,6%) of parotid gland localization (in one case associated with subcutaneous lesion) were found, but the most common site remained the mandible (33.3%).

In 5/15 cases (33,3%) other distant metastases were present. Most common symptom at presentation was progressive swelling (7/15, 46,6% of cases), followed by V2/V3 impairment (5/15, 33,3% of cases). In all 3 cases of orbital metastases esophtalmus was present, and in one cases visual loss was observed.

In one case of metastasis by a renal clear cell carcinoma the mandibular lesion was present about 1 year before of the detection of the primary, but a previous biopsy performed at another center was not diagnostic.



TABLE I

| Sex | Age | Primary tumor | Metastasis site metastasis | Other distant | FU (after primary tumor diagnosis) | Symptoms | Treatment |
|---|---|---|---|---|---|---|---|
| F | 51 | Breast carcinoma | Mandible | Yes | 193 m | V3 impairment, pathological fracture | CHT |
| F | 63 | Uterine LMS1 | Upper gum | Yes | 14 m | Swelling, hemorrage | Resection |
| M | 73 | Renal clear cell cercinoma | Parotid gland | No | 29 m | Swelling | Resection |
| F | 62 | Breast carcinoma | Orbit (osseous) | No | 105 m | V2 impairment, esophtlmos, vision loss | CHT and RT |
| M | 74 | Colon adenocarcinoma | Mandible | Yes | 17 m | Swelling | Resection |
| F | 71 | Renal clear cell carcinoma | Mandible | Yes | 1 m | Swelling, V3 impairment | Resection |
| F | 61 | Breast carcinoma | Mandible | No | 132 m | Occasional finding (OPT) | CHT |
| F | 62 | Leg skin melanoma | Cervical nodes/subcutaneous tissue | No | 160 m | FU | Resection |
| F | 58 | Breast carcinoma | Parotid gland | No | 201 m | Swelling | CHT |
| F | 72 | Breast carcinoma | Orbit (osseous) | No | 98 m | V2 impairment, esophtlmos | CHT |
| F | 66 | Breast carcinoma | Parotid gland | No | 198 m | Swelling | Resection |
| M | 83 | Adrenal neuroendocrine carcinoma | Parotid gland/ subcutaneous tissue | No | 20 m | Swelling | Resection |
| M | 74 | Renal clear cell carcinoma | Mandible | Yes | 24 m | Swelling, V3 impairment | CHT |
| F | 59 | Breast carcinoma | Orbit (soft tissue) | No | 120 m | Esophtalmos | CHT |
| M | 87 | Gastric adenoicarcinoma | Masticatory space | No | 5 m | Trismus | Palliative care |

Mean time of metastasis diagnosis after primary detection was 87,7 months (range 1-201). In 7/15 cases (46.6%) surgical resection of the metastasis was performed.

## Discussion

Even if rare, maxillofacial lesions with the aspect of primary tumors may be the consequence of haematogenous dissemination from other sites. In those cases (about 1% of all head and neck malignancies) a significant difference in the primary cancers' constituent in the maxillofacial metastasis between United States and China has been observed. In particular, in US the most frequent sites include breast, kidney, prostate and melanoma of the skin, while in China lung, thyroid, liver, esophagus and stomach were encountered more commonly: it depends from the different prevalence of these tumors in the two countries [4]. Neverthess, according to western literature, the most frequent primary site was the lung for males and the breast for females [4,5,7]. In our experience we found that breast was the most frequent primary site, followed by clear cell renal carcinoma, but no cases of lung or prostate primary tumor were observed. In about 30% of cases maxillofacial metastases are discovered before the primary tumor is diagnosed [4]. In our experience, only in one case of metastasis by a renal clear cell carcinoma the mandibular lesion was present about 1 year before of the detection of the primary, but a previous biopsy performed at another center was not diagnostic. Most common histological type is the adenocarcinoma, followed by the clear cell renal carcinoma, and we found the same results in our experience [4].

Hypothetically, all types of malignancies can metastatize to maxillofacial region: the portal haematogenous route is the most represented, but tumor cells can reach the oro-maxillofacial region also through the valveless vertebral venous plexus, explaining the fact that in some cases no contemporary lung metastases are found [4,8].

It has been found that some types of tumors preferentially metastatize to specific oro-maxillofacial subsites, such as ones originating from prostate and the breast to the jaw [9,10]. The mandible is more affected than the maxilla, and most common interested subsites are molar and retromolar region [4, 10,11]: this is probably due to the presence of rich haematopoietic tissue with sinusoidal space that can facilitate tumor cells penetration [10].

Only considering soft oral tissue, the gengiva is interested in most cases (57-67% of cases), since chronic inflammation probably attracts metastatic cells towards this site, and the rich capillary network can subsequently entraps them [10,12]. The fact that in Chinese population gingival metastases are more frequent than those in the jaws validates this theory, since in this country the prevalence of gengivitis is higher [4,13]. Interestingly, in those cases maxilla is more interested than mandible [14].

Clinical findings at diagnosis are not specific; these lesions most commonly manifest as a localized, proliferative mass, and most common symptoms include pain and numbness of the lower lip, less frequently bleeding, ulceration, loosening of the tooth, trismus, cervical lymphadenopathy, dysphagia and facial palsy [4]. Some Authors found that most common sign at presentation was a painless swelling [15]. In case of oral metastasis, most common signs have been found to be swelling and paresthesia; the so called "numb chin syndrome", is a late event in the course of the disease caused by compression or direct invasion of the mandibular nerve, skull base involvement or leptomeningeal spread [10,16]. Clinical apparence is not discriminating, since these lesions can be confused with epulis, pyogenic granuloma, giant cell granuloma and other similar benign lesions. Radiological findings are not specific too, and lesions can be misdiagnosed with odontogenic cystic lesions, periodontal disease or ameloblastoma [4]. It is for this reason that it is important to focus attention to medical history and to the presence of associated symptoms, even if oral-maxillofacial metastases represent the first manifestation of an occult disease in a significant percentage of cases (22-33%) [1,4]. Neverthless, in our experience we did not find this eventuality. In most cases oral metastasis are found in patients aged from 50 to 70 years [10].

In our experience, mean time of metastasis diagnosis after primary detection was 87.7 months (range 1-201): this is due to the fact that breast cancer metastasis were in all cases a late finding. Only considering patients affected by breast cancer, mean time of metastasis diagnosis was 119 months. It is called clinical tumor dormancy, defined as "..the "disease- free" period between treatment of the initial cancer and recurrence.."[15]. This phenomenon is very common in breast cancer, since recurrence can take place after decades of apparent disease-free survival, but also in case of non- Hodgkin's lymphoma, renal carcinoma and melanoma; it is believed to be due to the fact that metastatic cancer cells may remain dormant until some mechanism triggers them to proliferate and progress to clinically relevant metastases [15]. Neverthess, in our series mean time of renal carcinoma metastasis discovery was only 12,6 months.

On these basis, we point attention to the fact that it is very important to suspect a repetitive lesion in a patient previously affected by breast carcinoma, even if out of follow-up.

Diagnosis can be made only after histological examination, and, if it is possible, comparison with the primary tumor has to be performed. Treatment depends on various factors, such as histological type, presence of other distant metastases, patient conditions and associated symptoms. Most authors recommend a purely palliative treatment and radiotherapy has been described to be the most common treatment [5,17]; in our series surgical resection of the metastasis was performed in 46,6% of cases, according to other data [11], and was in order to

improve quality of life if other distant lesions were present, or, as in case of single metastasis, to improve disease-free survival. In remaining cases, chemotherapy was the most common treatment.
In conclusion, oro-maxillo-facial metastases from distant sites are quite rare; nevertheless, due the progress in cancer treatment that has led to an increase in survival, it is mandatory to identify these lesions in order to guarantee an adequate quality of life. In addiction, due to the improvement of curative and supportive therapies, we think that it can be expected that the incidence of oral-maxillo-facial metastases from distant sites is intended to increase.

## Riassunto

Le metastasi nel distretto maxillo- facciale sono rare e rappresentano circa l'1% di tutte le neoplasie cervicofacciali. Nella maggioranza dei casi il tumore primitivo è già noto e risulta essere localizzato più frequentemente al polmone e alla mammella ma in circa il 30% dei casi le lesioni secondarie vengono individuate prima che sia stato diagnosticato il tumore primitivo. Abbiamo condotto uno studio retrospettivo raccogliendo 15 casi di metastasi a distanza a localizzazione cervico- facciale nel periodo compreso tra il 2004 e il 2012. I nostri risultati dimostrano che la mammella e il rene sono le sedi primarie più frequenti (40% e 20% rispettivamente) , il tipo istologico più rappresentato è l'adenocarcinoma (60%). L'interessamento dei tessuti duri è risultato essere più frequente rispetto ai tessuti molli (53,3%). La mandibola (5/15 casi) è risultato essere il segmento osseo più frequentemente affetto e la regione molare e retromolare mandibolari sono le sottosedi più spesso interessate. Abbiamo identificato un solo caso di metastasi da tumore primitivo occulto: si è trattato di una localizzazione secondaria a carico del mascellare inferiore a partire da un tumore renale a cellule chiare . In conclusione sulla base dei risultati ottenuti e considerando l'aumento dell'aspettativa di vita nei pazienti oncologici, nonostante le metastasi localizzate nel distretto oro-maxillo- facciale siano rare, è importante sospettare ,o quantomeno non escludere aprioristicamente, lesioni secondarie sia nei pazienti con anamnesi positiva per patologia neoplastica, sia nei i pazienti che presentano una lesione cervico facciale.

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