

Oral Metastasis-A Reason To Expose The Primary Site–A Short Review

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Abstract

Metastasis to the oral region are uncommon & account for about 1% of the oral malignant tumors & it may occur in the oral soft tissue or jaw bones. In 25% of cases, oral metastasis were found to be the first sign of the metastatic spread & in 23% it was the first indication of an undiscovered malignancy at a distant site. Oral lesions & manifestations suspect the possibility of metastasis from distant sites & that initiate the necessary investigations. Most of the tumor of internal organs like liver, kidney or lung may not have severe signs & symptoms in its earliest stage and so oral metastasis will expose the primary tumor site.

INTRODUCTION

Metastatic process involves sequential steps, including progression of the primary tumor towards invasive carcinoma and dispersion of cancer cells through the lymphatic or blood vessels. Circulating cancer cells that survive settle in the microvasculature of the target organ and extravasate through the vessel wall. Infiltrated cells might proceed towards overt metastasis with or without an intervening period of latency. These steps are supported by functions of the cancer cells themselves or of the tumor microenvironment. Cancer cells must possess traits that will allow them to survive in new environments. Thus, a successful colony depends on the ability of cancer cells to appropriate distinct microenvironments at each step in the metastatic cascade; primary tumor, systemic circulation, and the final metastatic destination.^{1,13}

One of the most basic features is cell movement through the extracellular matrix, a process known as epithelial-to-mesenchymal transition. This process is marked by a complex and coordinated set of molecular changes leading to the motile behavior of the invading cancer cells, which involves dynamic cytoskeleton changes, cell matrix interactions, localized proteolysis, actin-myosin contractions and focal contact disassembly.^{1,13}

Metastatic tumors to the oral region are uncommon & account for about 1% of the oral malignant tumors and it may occur in the oral soft tissue or jaw bones. The jaw bones, particularly the mandible, where more frequently

affected than the oral soft tissue. In the oral soft tissue, the attached gingiva was the most commonly affected site.² The major primary sites presenting oral metastasis were lung, kidney, liver and prostate for men where as breast, female genital organs, kidney & colo-rectum for women.²

The pathogenesis of the metastatic process in the jawbones is not clear. In the skeleton, bones with red marrow are the preferred sites for metastatic deposits. Several primary malignancies prefer bone as their metastatic target, especially cancers from the breast, prostate, lungs and kidney. Expression of CXCR chemokine receptor and its ligand are known to be involved in cancer metastasis.¹

In 25% of cases, oral metastasis were found to be the first sign of the metastatic spread & in 23% it was the first indication of an undiscovered malignancy at a distant site.² Here we will discuss some of the presented cases where the oral metastasis expose the primary site of the tumor.

ORAL METASTASIS EXPOSED THE PRIMARY SITE

Senthil et al presented 59 years old male patient with 3 months history of constipation, hesitancy in micturition, dysuria & weight loss. There was no history of vomiting, abdominal pain or bleeding per rectum. Oral examination revealed 1x1 cm nodule in the hard palate adjacent to the right upper second incisor tooth. A CT scan of the abdomen & pelvis showed a large heterogeneously enhancing pelvic mass lesion in relation to the prostate, which is diagnosed as metastasis from retroperitoneal leiomyosarcoma. The same

author also presented a 40 year old man was a chronic smoker with complaints of an exceptional dyspnoea & non-productive cough of 1 month duration, but no history of fever, chest pain or discomfort, hemoptysis, change in voice or dysphagia. On oral examination he had 1x1 cm red, non-ulcerated nodule over the lower gingiva adjacent to the left incisor tooth. All the investigation finally revealed as gingival metastasis from non small cell lung cancer.¹⁴

Dhanrajani et al presented a case of 35 years old soudi female with a soft tissue pedunculated mass in the region of right maxillary alveolus, but it was diagnosed as metastatic lesion of the mid-esophageal carcinoma. The same author also presented the case of six month old baby girl had a soft tissue mass over right maxilla resembling an epulis, but further investigation, they have found a large tumor mass with multiple cystic areas originating from the anterior part of the right kidney.⁷

Faisal Azam et al presented a case of 78 year old man who was a chronic smoker with a six week history of difficulty in swallowing food together with pain in his pharynx. On examination there was a 3x2cm solitary pedunculated lesion on right side of the anterior two thirds of his tongue crossing the midline. The lesion was biopsied & initially reported as a primary sq.cell carcinoma with some clear cell changes. But after CT scan of the neck, chest, & abdomen revealed a 4.7cm sized irregular mass in the left kidney suggestive of renal cell carcinoma.¹⁰ Thomas et al presented the case of a 63 yr-old Caucasian man with an oral cavity lesion that was painful & that had grown substantially over several months. Biopsy resulted in persistent bleeding requiring cautery & manual pressure. The immunoperoxidase testing & further investigation diagnosed as metastatic renal cell carcinoma.¹⁸

Tamiolaki et al presents 4 cases, two originated from the thyroid gland, one was from esophagus & one from the liver. Three metastasis occurred in the mandible & one in the maxilla with the symptoms of facial swelling, pain, oral mucosal ulceration, oral bleeding and nasal obstruction etc.⁶ Yutaka Horie et al presented the two cases of hepatocellular carcinoma metastatic to the oral cavity, one patient had metastasis to the maxilla & finally to the mandible and the other patient, to the mandible. Both cases histologically showed highly-differentiated trabecular hepatocellular carcinoma.²⁰

Among all the above cases oral lesions & manifestations suspect the possibility of metastasis from distant sites and that initiate the necessary investigations to find the primary

site. Most of the tumor of internal organs like liver, kidney or lung may not have severe signs & symptoms in its earliest stage, but metastasis usually will occur in advanced stages. So oral metastasis in all the above cases exposed the primary tumor and initiate the required immediate treatment for the survival of the patient.

DISCUSSION

S.Y.Lim et al analyzed the 41 Korean patients with metastatic oral tumors, among 23 cases were metastasized to the jaw bone & 18 cases metastasized to the oral soft tissue. Eight out of nine lung tumors metastasized to the jaws and the lung being the most common primary site for jaw bone metastasis, followed by the liver & thyroid. For oral soft tissue, the liver was the most common primary site, followed by female genital organs & the thyroid.¹⁶

Autonio azoubel autones et al presented the retrospective study of 10 cases of gnathic bone metastasis and they have found that, gnathic bone metastasis are rare & may affect any age group and both sexes with equal prevalence in the mandible & maxilla. The thyroid gland & the prostate appear to be the most frequent primary sites for distant metastasis to gnathic bones.³

In male patients, the most common primary cancers that metastasize to the oral region are those in the lungs, followed by the kidneys, prostate, bone and skin. In female patients the most common primary cancers that metastasize to the oral region are those in the breasts followed with much lower frequency by those in the female genital organs, colorectum, bone and kidneys¹. Most metastatic tumors to the oral region occur in patients aged 40-70yrs. On average, patients with metastasis to the jawbones are younger than those with metastasis to the oral soft tissues¹.

Most common symptoms associated with oral metastasis in the soft tissues is lump and in the jawbones, swelling, pain and paresthesia of the affected nerve. With the progression of the disease, oral metastatic lesions cause progressive discomfort, pain, bleeding, superinfection, dysphagia, interference with mastication and disfigurement. In some cases, the metastasis is discovered in a recent extraction site, so tooth extraction can serve as a promoting factor in the metastatic process.

The presence of teeth seems to have a crucial effect on the oral site preference of metastasis. In the dentulous patient, about 80% have metastasis in the attached gingiva. In the edentulous patient, metastatic lesions are distributed equally

between the tongue and alveolar mucosa. In the jaw bones, the common location of the metastatic lesion is the mandible; the molar area is the most frequently involved site.

The jawbones have little active marrow, especially in elderly person; however, remnants of hematopoietic active marrow can be detected in the posterior areas of the mandible, especially in cases of focal osteoporotic bone marrow defects. These hematopoietically active sites may attract metastatic tumor cells. In the oral soft tissues, the rich capillary network of chronically inflamed gingiva can entrap malignant cells. The proliferating capillaries have a fragmented basement membrane through which tumor cells can more easily penetrate.

The criteria for considering a malignant lesion to be metastatic are as follows, 1) There must be histologically verified primary 2) The secondary lesion must be histologically the same as primary & 3) the possibility of direct extension from the primary must be excluded.⁷

The following steps constitute the diagnostic algorithm for evaluation of oral metastasis¹; Review the clinical history: Review the available radiographic findings: If a history of a previous tumor exists, obtain the slides and reports for review.

Perform a biopsy of the lesion; evaluate the light microscopic features of the neoplasm. On the basis of the histological feature, determine the need for special studies like Histochemical staining; Immunohistochemical tests, Electron microscopy; In cases which the primary tumor is not found, look for signs & symptoms in an attempt to identify the potential primary. This can be accomplished with a complete history and physical examination.

The standard battery of laboratory tests includes a complete blood cell count, liver function tests, calcium level, urine analysis and serum creatinine value; A chest radiograph and CT scans have proven to be useful in the detection of primary lung tumors and also to identify primary tumors in the pancreas, liver, adrenals, kidney, gallbladder, ovaries and stomach; Sex specific tests include serum prostate-specific antigen assay and transrectal ultrasound for male patients and mammography and cervical papanicolaou test for female patients; Positron electron transmission scanning with fluorodeoxyglucose is rapidly gaining favor in the evaluation of unknown primary cancers, particularly in instances which other image modalities have failed to identify a source.

CONCLUSION

Some time most of the tumors of internal organs like liver, kidney or lung may not have severe signs & symptoms in its earliest stages, so it will be unnoticed. Some of these organs may metastasize to the oral cavity leads to suspect the primary site and to go further investigation and that expose the primary site. But the most of the metastasis will occur in advanced stages and the exposure of the primary site of the tumor finally initiate the immediate treatment to survive the patient.

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