

REVIEW ARTICLE

METASTATIC TUMOURS TO THE JAWS AND ORAL CAVITY: A BRIEF REVIEW

Srishti Gupta¹, Harkanwal Preet Singh², Piyush Gandhi³

¹BDS Intern, ²Reader, ³Senior Lecturer, Department of Oral Pathology, Dasmesh Institute of Research and Dental Sciences, Faridkot, Punjab, India

ABSTRACT:

Cancer is a disease involving complex multiple sequential irreversible dysregulated processes showing metastasis that results in morbidity and mortality. Metastasis to the oral region are uncommon and account for about 1% of the oral malignant tumors and 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 and in 23% it was the first indication of an undiscovered malignancy at a distant site. So we can say that oral cavity is the mirror of whole body. Oral lesions and manifestations suspect the possibility of metastasis from distant sites and that initiate the necessary investigations. This article has emphasised on various pathogenetic mechanisms related to tumours metastasizing to oral cavity.

Key words: Metastasis, Jaw tumours, Chemotherapy.

Corresponding author: Dr. Srishti Gupta, BDS Intern, Dasmesh Institute of Research and Dental Sciences, Faridkot, Punjab, India

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INTRODUCTION:

Cancer is a complex disease characterized by malignant growth or tumour resulting from an uncontrolled division of cells.¹ After a quarter century of rapid advances, cancer research has generated a rich and complex body of knowledge, revealing cancer to be a disease involving dynamic changes in the genome. The foundation has been set in the discovery of mutations that produce oncogenes with dominant gain of function and tumor suppressor genes with recessive loss of function; both classes of cancer genes have been identified through their alteration in human and animal cancer cells and by their elicitation of cancer phenotypes in experimental models.²

Incidence of the metastatic involvement of oral cavity shown in literature ranges from 1% to 8%. These occur in the soft as well as in the osseous tissue of the upper and lower jaw. Meyer and Shklar (1965) reported, out of 2,400 malignancies in the mouth and jaws, only 25 were accepted as metastatic tumours.⁵ Because of their rarity, metastatic tumours to the oral region are challenging to diagnose. Therefore, they should be considered in the differential diagnosis of inflammatory and reactive lesions that are common to the oral region.³ In some cases, the oral lesion is the first and only symptom of malignant disease of a primary which might be growing silently elsewhere in the body.⁴⁻⁶

PATHOGENESIS

Metastasis involves sequential progression of the primary tumor towards invasion and dispersion/spreading of cancer cells through the lymphatic or blood vessels. Circulating cancer cells survive and settle in the microvasculature of

the target organ and extravasate through the vessel wall. These cancer cells gain access, advance towards evident 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.[6] Cancer cells must possess some characteristics that will allow them to survive in new environment. Thus, a successful metastatic area/focus depends on the ability of cancer cells to sustain suitable distinct microenvironments in the metastatic cascade by the following steps.^{6,7}

- The primary tumor,
- Systemic circulation, and
- The final metastatic destination.

Further, the tumor progression depends on angiogenesis and revascularization, the formation of new blood vessels which is a must for tumor development.⁷ It is a well established fact that the growth and size of tumor is angiogenesis dependent. The development of the tumor vasculature is dependent on a variety of proangiogenic and antiangiogenic, inflammatory, and coagulation factors.^{9,10} Hypoxia in the tumor mass is the critical stimulus for angiogenesis in the growing tumor at initial stages. Hypoxia directs the up-regulation of few transcription factors which regulate proangiogenic signals, mainly the vascular endothelial cell growth factors (VEGFs).⁹⁻¹² The oral region is not a preferred site for metastatic colonization and are usually the result of secondary spread from other metastatic lesions, mainly from the lungs. In such cases, tumor cells bypass the filtration of the lungs and accounts for the increased circulation to axial skeleton leading to head and neck metastasis.

However, the pathogenesis of the metastatic tumors in the jawbones is not clear. Within the skeleton, bones with red marrow are the favored sites for metastatic deposits. In contrast, jawbones have little active marrow, mainly in elderly persons. However, remnants of hematopoietic active marrow can be detected in the posterior areas of the mandible and the hematopoietically active sites attract metastatic tumor cells. The oral soft tissues have a rich network of capillaries which can entrap malignant cells. Chronic inflammation has been linked to various steps involved in tumor genesis, including cellular transformation, promotion, survival, proliferation, invasion, angiogenesis, and metastasis.³⁻⁶ The proliferating capillaries show uneven basement membrane and the tumor cells can penetrate more easily. Hirshberg¹⁰ suggested that inflammation plays an important role in attracting metastatic cells to the gingiva.

CLINICAL PRESENTATION:

Primary carcinomas metastasizing most frequently to the oral region are those of the breast and lung. The clinical presentation of metastatic tumors can be variable, which may lead to erroneous diagnosis or may create diagnostic dilemma. In some cases, the oral lesion is the first and only symptom of malignant disease of a primary which might be growing silently elsewhere in the body.⁴⁻⁶ Oral metastasis is considered a late complication and is commonly associated with multiple organ metastases. Oral metastases can grow rapidly causing pain, difficulty in chewing, dysphagia, disfigurement and intermittent bleeding, leading to poor quality of life. In some cases metastases is discovered after a recent dental extraction at the site. In the jawbones most patients complained of rapidly progressing swelling, pain and paresthesia. The early manifestation of the gingival metastases resembled a hyperplastic or reactive lesion, such as pyogenic granuloma, peripheral giant cell granuloma, or fibrous epulis. In other locations in the oral soft tissues the clinical presentation was that of a submucosal mass. Only in a few cases the lesion appeared as ulceration. In some cases, especially those of metastatic hepatocellular carcinoma, severe post-biopsy hemorrhagic episodes had been reported. A peculiar site for metastasis is the post-extraction site. Analysis of the literature by Hirshberg revealed 56 cases in which tooth extraction preceded the discovery of the metastases. In many of these cases the metastatic tumour was assumed to be present in the area before extraction.^{1,10} Metastatic lesions may mimic odontogenic infections and other disease conditions in the oral cavity in presentation leading to late diagnosis by the unwary clinician.

TUMOURS OF ORAL CAVITY WHICH CAN MIMIC METASTATIC TUMOURS ORAL SOFT TISSUES¹⁻¹⁵:

Oral Soft Tissues:

- Malignant Melanoma

- Pyogenic Granuloma (Lobular Capillary Hemangioma)
- Oral Fibromas and Fibromatoses
- Peripheral Giant Cell Granuloma
- Squamous Cell Carcinoma

JAW BONE (DIFFERENTIAL DIAGNOSIS DEPENDS ON LOCATION)

- Malignant tumors (eg, primary intraosseous carcinoma, other malignant odontogenic tumors)
- Central malignant salivary gland tumors
- Sarcoma (eg, malignant fibrous histiocytoma, fibrosarcoma)

BONY LESION CAN MIMIC BENIGN LESION (SOME CASES)

- Periapical pathology
- Infected odontogenic cyst or tumor
- Osteomyelitis

DIAGNOSIS

- Review the clinical history and 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 histologic features, determine the need for special studies (eg, histochemical staining, immunohistochemical tests, electron microscopy).
- The histologic diagnosis is a keystone in evaluating patients with cancer of unknown primary. Attention should be given to differentiating primary intraoral malignancies from metastatic tumours. Several primary intraoral malignancies, especially those originating from salivary glands, have similar histological features to tumours occurring in distant organs. For example, primary ductal carcinoma of salivary gland origin versus metastatic breast carcinoma; primary intraoral clear cell tumour of salivary gland origin or intraosseous clear cell carcinoma versus metastatic renal cell carcinoma; and primary squamous cell carcinoma versus metastatic squamous cell carcinoma from the lung. In addition, malignant soft tissue tumours may originate intraorally but, because of their relatively uncommon occurrence in the oral region, metastatic origin should be considered. Plan the treatment protocol based on the clinical, pathological, and radiographic informations.

CONCLUSION:

Misdiagnosis of a metastatic lesion as a benign reactive lesion may delay diagnosis and treatment. Metastatic

tumors should always be considered in the differential diagnosis of benign-looking lesions in the oral cavity, especially in patients with a previous history of a malignant disease. Biopsy is mandatory to establish an accurate diagnosis.

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