Tumors Metastasizing to the Oral Cavity: A Study of 16 Cases

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Purpose: An analysis was performed of the clinical and epidemiologic characteristics of a group of patients diagnosed with oral metastases of distant primary tumors or unknown primary malignancies.

Material and Methods: The study series consisted of 16 patients with oral metastatic lesions seen in the Department of Stomatology and Maxillofacial Surgery, Valencia University General Hospital (Valencia, Spain) that had been diagnosed in the previous 15 years. A retrospective analysis was made of patient age and gender, clinical characteristics of metastatic lesions, location of the primary tumor, and time elapsed from diagnosis to the death of a patient.

Results: There were 13 male and 3 female patients (mean age, 58.8 years). Ten patients had been diagnosed previously and were being treated for a primary tumor; 2 patients were diagnosed with a primary malignancy in the department; and 4 patients presented with an unidentified primary tumor (metastatic disease diagnosed from biopsy study). The predominant clinical presentation was mixed soft tissue and bone metastases followed by solely soft tissue lesions and solely bone lesions. Some patients showed no apparent oral lesions. Primary malignancies originated mainly from the lung followed by the prostate, gastrointestinal tract, thyroid gland, breast, and liver. Mean survival from diagnosis of oral metastases was 8.25 months.

Conclusion: Oral metastatic lesions are infrequent, can affect male and female patients equally, can manifest at any age, and may constitute the first manifestation of a still unidentified primary malignancy. According to the literature, bone metastases are more common than soft tissue metastases. Nevertheless, in the present series, there was a clear male predominance, and the oral metastases showed a predominance of mixed presentations followed by solely soft tissue lesions and solely bone metastases.
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Oral tumor metastases are very infrequent, representing approximately 1% of all oral tumor lesions.[1] These metastases often affect bone and are less commonly located in the oral soft tissues.[2] The mandible is the most frequent location, particularly the molar region.[1,3] Oral metastases are more common in male than in female individuals and can develop at any age.[4]

Any malignant tumor can metastasize to the oral cavity, although such lesions are most commonly associated with primary lung, kidney, breast, or liver malignancies.[5,6] In 30% of cases, oral metastases are the first manifestation of the disease,[7] although most patients with distant primary tumors have been diagnosed and are receiving treatment at the time oral metastases are detected,[4] which constitute a sign of advanced malignant disease that can modify the prognosis and treatment strategy.

The present report describes a group of patients diagnosed with oral metastases of distant primary tumors or unknown primary malignancies and analyzes their clinical and epidemiologic characteristics.

Material and Methods

The study series consisted of 16 patients with oral metastatic lesions seen in the Department of Stomatology

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and Maxillofacial Surgery, Valencia University General Hospital (Valencia, Spain) that had been diagnosed in the previous 15 years. A retrospective analysis was performed of patient age and gender, clinical characteristics of metastatic lesions, location of the primary tumor, and time elapsed from diagnosis to a patient's death. The study was approved by the local institutional review board.

Results

The 16 patients with oral metastases of distant primary malignancies included 13 male (81.25%) and 3 female (18.75%) patients (mean age, 58.8 yr). Ten patients (62.5%) had been diagnosed previously and were being treated for a primary tumor; 2 patients (12.5%) were diagnosed with a primary malignancy in the department at the time of evaluation of the oral lesions; and 4 patients (25%) presented with an unidentified primary tumor (metastatic disease diagnosed from biopsy study). Mean survival from diagnosis of an oral metastasis was 8.25 months (Table 1).

The most frequent clinical presentation of the oral lesions (8 patients) was mixed soft tissue and bone metastases (with a predominance of soft tissue involvement) followed by solely soft tissue lesions (3 patients) and solely bone lesions (2 patients). Three patients showed no apparent oral lesions.

The soft tissue metastases manifested as hemorrhagic, fast-growing tumor lesions, with an ulcerated appearance in some cases. Patients with osteolytic metastases had paresthesias and pain, whereas physical examination disclosed sensory or motor alterations in the 3 patients without apparent oral lesions.

The 16 identified primary tumors were lung malignancies in 6 patients, prostate cancer in 3 patients, gastrointestinal malignancies in 3 patients, thyroid gland tumor in 1 patient, breast cancer in 1 patient, hepatocarcinoma in 1 patient, and a primary malignancy of unknown origin in 1 patient.

The authors present 1 of these cases, a patient with metastatic cancer of the rectum. The patient's clinical image (Fig 1), computed tomograms (Figs 2, 3), and histopathologic image (Fig 4) are presented.

Discussion

Oral metastases of primary malignancies are infrequent, representing 1% to 3% of all oral cancers. However, because maxillary bone is not routinely examined at necropsy, the true frequency may be higher.[1] Hirshberg et al,[5] in a review of the English-language literature from 1916 through 1996, found the most frequent primary tumor locations to be the lung (25%), kidney (15%), bone (10%), breast (9%), and liver (8%) (Fig 5). Yoshii et al[6] in turn estimated the probability of lung tumor metastasis to the oral cavity to be 10% to 20%. Lim et al,[8] in a study of 41 Korean patients with oral metastatic lesions, found the most common primary tumor location in these patients to be the liver followed by the lungs and thyroid gland. The authors' observations in this respect are consistent with data found in the literature: the most common primary malignancies were in the lung and prostate gland followed by the thyroid gland, breast, and liver.

The biological mechanism underlying metastatic spread is complex and begins with a series of coordinated molecular changes that allow the cells to lose adhesion and adopt the mobility of cancer cells, a process referred to as *epithelial to mesenchymal transition*.[9] This is followed by the expression of epidermal growth factors that facilitate cancer cell invasion and the production of extracellular matrix metalloproteinases that likewise contribute to cancer cell mobility.[9] Tumor progression is fundamentally dependent on the formation of new blood vessels (angiogenesis) and apoptosis.[9]

Metastatic invasion of a given organ at a distance from the primary tumor is not a random phenomenon. Paget[10] was the first to postulate the "seed and soil" hypothesis, whereby a "seed" (tumor cell) preferentially grows in "soil" (organ) offering conditions adequate for growth. This process is mediated by an interaction between specific receptors on the disseminating tumor cell surface and the endothelium of the target organ. In this context, cancer cells that can metastasize to bone are those that can alter the optimum balance between osteoblasts and osteoclasts, such as prostate, breast, or thyroid gland tumors.

Although oral metastases are found in similar proportions in male and female patients, there is a series of gender-linked particularities, such as the fact that oral metastases of lung cancer are more common in men because lung cancer is more frequent in men. Likewise, breast cancer is very rare in men, thereby explaining why practically all breast cancers metastasizing to the oral cavity are diagnosed in women.[4] In the present study, there was a clear predominance of oral metastatic disease in men versus women (proportion, 13:3).

Hirshberg et al[9] reported that gender proportion depends on differentiating bone from soft tissue metastases. Thus, although bone metastases are equally frequent in male and female patients, oral soft tissue metastases predominate 2 to 1 in men versus women. In the present series, a male predominance was recorded for all oral metastases (mixed, bone, and soft tissue).

Oral metastases can develop at any age, although most researchers agree that the greatest prevalence