

Metastasis to the Jawbones: A review of 453 cases

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INTRODUCTION

Metastasis to the oral cavity rarely occurs and constitutes 1% of all oral cavity malignancies,^[1] and has mostly been found in the jaws compared to the soft tissues.^[2] Metastasis to the jaw bones mainly occurs in the posterior region of the mandible, ramus, and the condyle, which are rich in red bone marrow. Metastasis to the maxilla is rare and comprises one-fifth of all metastatic tumors to the jawbones.^[3] The male-to-female ratio is almost equal with a ratio of 1:1.1. The mean age of patients is 45 years.^[4] The primary focus in women is usually located in the breasts, reproductive organs, thyroid gland, and kidneys, whereas in men it is in the lungs, prostate, kidneys, bones, large intestine, and suprarenal glands.^[5-7] Metastases to the jaw bones almost originate from infraclavicular regions. The diffusion through Batson's venous system is the principal process of the oral cavity metastasis.^[8] Histologically, the primary foci are usually carcinomas, and among them adenocarcinomas are more common. Adenocarcinoma is usually a metastasis from the breasts in women or from the lungs, alimentary canal, or prostate in men. There are also descriptions of metastases from embryonal tumors, sarcomas, or even disseminated foci of myeloma

ABSTRACT

The purpose of the present article was to review the characteristics of the jawbone metastases to analyze all variables. A relevant English Literature search in PubMed, Scopus, and Google Scholar was performed. All variables such as age, gender, primary and secondary tumor sites were analyzed. There were 453 metastatic cases. The male-to-female ratio was 1.2:1, and the mean age of the patients was 53.4 years. The lung was the most common primary site in men, and breast in women. The most common metastatic site was the mandible, and adenocarcinoma was the most frequent histological diagnosis. Metastases to the jaw bones occur in the advanced stages of a malignancy hence; a careful examination of patients with jaw bone lesions is strongly suggested. Dentists, as well as general physicians, should take into consideration the possible presence of jaw metastases in cases which present atypical symptoms, especially in patients with known malignant disease.

KEYWORDS: *Jawbones, metastasis, mouth*

or lymphogranulomatosis.^[9] Metastasis to the oral cavity is a complication of malignancy and usually develops at the end stage of cancer.^[10] Distant metastasis has a pivotal role in the management of patients.^[11] Oral cavity metastasis increases in the world and is a one of the main causes of morbidity and mortality in cancer patients.^[12] Oral cavity metastasis is also a therapeutic challenge for clinicians. Early detection and treatment of oral cavity metastasis may improve patient's life and prolong survival.^[13-15] The dentists have an important role in the diagnosis and management of cancer patients, especially in those with undiscovered malignancy.^[16] The purpose of the present article was to review the characteristics of the jawbone metastases to analyze all available information. A relevant English Literature search in PubMed, Scopus, and Google Scholar was performed. The keywords "oral cavity," "jawbone," and "metastasis" were searched the in title/abstract of publications limited to 1930–2015. Only the related publications were included. All variables such as age,

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gender, and primary and secondary tumor sites were analyzed. In some reports, especially in case series, most of the variable assessments were incomplete.

RESULTS

In general, there were 453 available cases of jaw bone involvement in the English language literature. A significant predominance of men was detected (245 men; 54.1%, 208 women; 45.9%). The male-to-female ratio was 1.2:1. The mean age of the patients at diagnosis was 53.4 years (range: 4 months to 94 years), with a mean age of 54.81 years for men and 51.81 years for women. The youngest patient was a 4-month-old girl

(metastasis from adrenal glands), and the eldest was a 94-year-old woman (metastasis from breast). Significant details from the literature concerning the cases of jaw bone metastases are summarized in Tables 1 and 2. In addition, Table 3 demonstrates the comparison of the results of this review with those of the previous reviews.

Overall, the breast with 86 cases (19%) was the most common primary site, followed by the lung (66 cases; 14.6%) and thyroid gland (39 cases; 8.6%). The primary site differed between genders. The most common primary sites for men were the lungs (*n* = 49; 20%), followed by liver (*n* = 40; 16.3%) and prostate (*n* = 27; 11%), and

Table 1: A summary of oral metastasis in men

Primary site (No. of patients)	Age range (years)	The time intervals from primary tumor detection to diagnosis of an oral metastasis	Range of time duration of development of a metastatic lesion	The time intervals from diagnosis to death	References
Lung (49)	45-78	1 month-5 years	1 week-3 years	2 weeks-26 months	[5-7,17-41]
Liver (40)	6-78	2 months-7 years	1 week-10 months	1 month-2 years	[7,26,37,39,42-70]
Prostate (27)	32-90	3 weeks-7 years	2 weeks-17 months	1-17 months	[3,5,9,22,28,36,39,40,62,66,71-77]
Kidney (24)	48-78	1 month-13 years	1 week-1 year	2 months-2 years	[5,22,26 28,40,73,78 89]
Unknown (14)	35-77	11 months	1-2 months	5 months-1 year	[5,22,28,36,40,90]
Esophagus (12)	30-69	1 month-7 years	1-4 months	1-6 months	[28,37,39,70,91-98]
Rectum (7)	56-76	2 years-4 years	3 weeks-2 years	1 month-2 years	[5,38,99-101]
Adrenal Gland (6)	1-59	4 months	1 week-5 months	1 month-1 years	[102-107]
Skin (6)	23-68	2-4 years	2 months-2 years	3 months-5 years	[108-112]
Eye (5)	4-8	10 month-7 years	1 week-2 months	3 weeks-19 months	[27,113-116]
Thyroid (5)	58-65	6-28 months	1 month-2 years	2-6 months	[26,34,38,117,118]
Testis (5)	43-81	1-2 years	1 week-4 months	13-17 months	[36,73,119-121]
Breast (5)	43-73	4-9 years	2 months-6 years	4 months-3 years	[62,122-125]
Urinary bladder (4)	48-69	20 months-7 years	2-5 months	1-18 months	[126-129]
Colon (4)	59-75	5-24 months	2-5 months	1-6 months	[5,28,130,131]
Brain (3)	7-16	2-18 months	2 months	6 months	[26,132,133]
Thigh (3)	19-33	6 months-1 year	2 months	7 months-2 years	[3,134,135]
Bronchus (3)	34-51	3 months-1 year	9 months	alive	[73,136,137]
Nasopharynx (2)	69-70	1 year	1-6 months	alive	[27,138]
Femur (2)	11-21	6-18 months	1 month	2 months	[139,140]
Leg (2)	7-69	1-5 years	No data	2 months	[27,62]
Stomach (1)	67	9-10 months	9 months	1 month	[141]
Foot (1)	61	1 week	1 week	6 months	[142]
Forearm (1)	14	1 year	2 months	6 months	[143]
Maxilla (1)	56	1 year	No data	alive	[144]
Tibia (1)	17	1 year	2 month	1 week	[143]
Hemitorax (1)	12	1 year	1 week	6 months	[143]
Thoracic wall (1)	28	10 years	2 months	2 years	[145]
Mediastine (1)	23	3 years	3 months	6 months	[146]
Pancreas (1)	54	No data	No data	alive	[147]
Secum (1)	65	5 months	1 month	2 months	[148]
Sacroiliac (1)	21	5 months	1 month	No data	[36]
Ileum (1)	68	No data	3 weeks	11 months	[149]
Intestine (1)	75	No data	No data	alive	[27]
Gallbladder (1)	78	No data	4 months	2 months	[150]
Shoulder (1)	68	8 months	2 weeks	Alive	[151]

for women was the breast ($n = 81$; 39.1%), followed by thyroid gland ($n = 39$; 18.8%), and lungs ($n = 17$; 8.2%). All cancer types mostly metastasized to the mandible with 334 cases (73.7%), tempromandibular joint (TMJ), and condyle in 37 cases (8.1%). The posterior mandible was involved more commonly than the anterior parts ($n = 130$ vs $n = 20$). Maxilla and palate were involved in 71 cases (15.7%), among which anterior region was involved in 7 cases, and in 11 cases, the metastatic lesion developed bilaterally. In 11 cases (2.4%), both

the mandible and maxilla were involved. The presence of teeth was the most frequent finding. Metastasis to edentulous cases was found in only 7 cases. In 16 cases (3.5%), the oral metastasis developed in a tooth extraction site. The metastatic tumors were distributed equally on the right and left sides. In 61 cases (13.4%), the metastatic lesion was on the contralateral side of the primary tumor. In 68 cases (16.6%), overlying soft tissue was also involved. Swelling, pain, and numbness were the most common clinical features. A radiolucent

Table 2: A summary of oral metastasis in women

Primary site (No. of patients)	Age range	The time intervals from primary tumor detection to diagnosis of an oral metastasis	Range of time duration of development of a metastatic lesion	The time intervals from diagnosis to death	References
Breast (81)	24-94	2 months-25 years	1 week-3 years	1 week-3 years	[3,5,22,26-28,36,38,40,62,66,73,79,89,152-174]
Thyroid (34)	9-83	6 months-15 years	1 week-5 years	1-19 months	[3,5,26,28,36,37,70,175-189]
Lung (17)	49-75	11 months-5 years	3 weeks-3 years	2 weeks-1 year	[5,28,34,36,38,62,190-196]
Kidney (12)	2-84	6 months-316 months	3 weeks-4 months	2 weeks-22 months	[5,28,40,89,197-201]
Unknown (11)	44-83	1-5 months	1-3 months	2 months-2 years	[28,36,40,66,202-204]
Liver (8)	15-76	1-6 years	2 weeks-3 months	10 months-2 years	[39,205-209]
Uterus (7)	19-75	9-28.5 months	1-2 months	3 months-3 years	[37-39,210-213]
Colon (5)	29-70	1-49 months	No data	6-17 months	[28,37,73,214]
Adrenal Gland (5)	4 months-12 years	3-8 years	No data	Alive	[26,39,215,216]
Ovary (4)	29-61	2 years	2-5 months	6 months	[37,217-219]
Endometrium (3)	45-71	1 month	1-2 months	6 months	[26,220,221]
Eye (2)	3-61	1-7 years	1 month	3-5 months	[79,114]
Bronchus (2)	45-60	1-2 years	No data	17 months	[73]
Rectum (2)	79	49 months	2 weeks	1 month	[222,223]
Stomach (2)	51-58	10-12 months	2-3 months	1 year	[224,225]
Cerebellum (2)	8	12-13 months	No data	1-6 months	[28,40]
Shoulder (1)	31	3 years	No data	3 months	[226]
Skin (1)	30	3 years	4 months	6 months	[227]
Rib (1)	12	10 months	No data	2 months	[228]
Follopian tube (1)	44	No data	2 months	Alive	[229]
Esophagus (1)	67	5 years	No data	No data	[62]
Bone (1)	27	No data	No data	6 months	[26]
Brain (1)	60	7 years	5 years	Alive	[230]
Cervix (1)	63	1 year	No data	Alive	[231]
Thigh (1)	16	No data	No data	No data	[3]
Urinary bladder (1)	29	No data	No data	No data	[37]
Limb (1)	36	No data	No data	No data	[36]

Table 3: Comparison of the results with those of previous reviews

Reference No.	Age (years)	Male/female ratio	Most common primary sites	Most common metastatic site (s)	Most common histologic tumor type	Oral metastasis as the first sign
Current Review	53.4	1.2:1	Breast	Mandible	Adenocarcinoma	27.6%
3	43	1:1.5	Thyroid and prostate	Equal involving of mandible and maxilla	Adenocarcinoma	0
26	60.5	4:11	Breast	Mandible	Adenocarcinoma	26.3%
38	64.5	0.6:1	Breast and lung	Mandible	Adenocarcinoma	0
233	52	Equal distribution	Breast and lung	Mandible	Not mentioned	Not mentioned

destructive lesion with ill-defined irregular margins was the most common radiographic feature ($n = 290$). The diagnosis of a metastatic lesion was the first indication of a malignancy in 125 cases (27.6%). Adenocarcinoma was the most frequent histological diagnosis ($n = 119$; 26.3%), followed by hepatocellular carcinoma ($n = 44$; 9.7%), and in lower numbers, ductal carcinoma ($n = 28$; 6.1%), follicular carcinoma ($n = 23$; 5%), and squamous cell carcinoma ($n = 18$; 3.9%) have also been described. Interestingly, there were 5 cases of Ewing's sarcoma, 4 cases of osteosarcoma, and 2 cases of chondrosarcoma. Most reported cases were from the United States of America with a total of 73 cases, followed by Spain and India with 40 and 34 cases, respectively.

DISCUSSION

Metastasis to the oral cavity is a rare event. Three main criteria have been suggested to diagnose a lesion as metastatic.^[1] The histopathological verification of the primary tumor,^[2] the unification of histological type of the metastatic tumor and primary tumor,^[3] the exclusion of the possibility of direct local spread from the primary tumor.^[232] A previous review showed that the number of the jaw bone metastasis was equal for men and women,^[233] however, the current review found a higher prevalence of metastases for males. In this review, the mean age of patients for both males and females were different from previous studies which was 45 years.^[4] In the present series, the most common primary sites for men were the lungs, liver, and prostate, and for women were the breasts, thyroid gland, and lungs. These findings are in disagreement with a previous review which indicated the lungs, prostate, kidneys, and liver as the most common primary sites in men, and the breasts, adrenal glands, genital organs (uterus, cervix, ovaries), and colorectal in women.^[234] In the present review, only 16 cases were from the female genital tract, which is in agreement with a previous report indicating the low incidence of bone metastasis from the female genital tract.^[235] Regarding the involved bone, the mandible was the most commonly affected bone, and condyle and TMJ were the least. Hematopoietically, active bone marrow is an attractive site of metastasis. Moreover, the vascular spaces are sinusoidal in nature, therefore, it is easy for cancer cells to penetrate.^[236] In addition, the bone marrow contains growth factors, which promote tumor cells proliferation and survival.^[237] Metastasis to TMJ is rare and mostly occurs in the final stage of a malignancy, which is associated with generalized skeletal metastases.^[238] Metastases to the condyle mostly originate from the breasts, uterus, rectum, and melanoma.^[239] The exact mechanism of the low incidence of metastatic lesions in the condyle is not well understood, however,

might be due to the deficit of bone marrow and isolated blood supply which is derived from the maxillary artery and temporal artery.^[240] Maxillary involvement comprises nearly one-seventh of all metastatic tumors to the jawbones. This finding is in disagreement of the previous studies indicating involvement of the maxilla in one-fifth of all metastatic lesions to the jawbones.^[3] The early diagnosis of jawbone metastasis is more difficult than those of the soft tissues.^[241] The most common symptoms of jaw metastasis are anaesthesia and paraesthesia over the chin, lower lip, and submental area due to mental nerve involvement, which is called numb chin syndrome or mental nerve neuropathy.^[96,242] Numb chin or mental nerve neuropathy should always raise the possibility of a metastatic disease in the mandible, invasion of the tumor into the bone, and involvement of the inferior dental or mental nerves.^[10] The other common symptoms are pain, swelling, and loosening of teeth.^[243] Current review revealed anesthesia and paraesthesia in 90% of cases.

On the radiographic examination, metastatic lesions mostly appear as a radiolucent area with ill-defined borders. However, metastases from sites such as prostate present as a radiopaque or mixed radiopaque-radiolucent lesion.^[244] Bone metastases from thyroid carcinoma are mostly osteolytic, therefore, osteoblastic metastasis rarely occurs.^[245] In this review, majority of metastasis to the jaws appeared as an ill-defined and radiolucent area on the radiograph examination. In 7 cases, it looked like a mixed radiopaque-radiolucent lesion, in 9 cases it appeared as a radiopaque lesion, and in 1 case it had a ground glass appearance. In addition, there were 4 cases of thyroid cancer, and 5 cases of breast cancer metastasis that presented as a lytic lesion on the radiographic examination. According to a previous study, time interval between diagnosis of the primary tumor and the metastasis is 40 months,^[233] the prognosis of oral metastatic tumor is poor, and the mean survival rate after diagnosis is 6–7 months.^[245] The present review found that time interval between the diagnosis of the primary and metastasis can range from 1 week to 10 years, and the mean survival rate after diagnosis range from one week to 5 years, even though some patients were alive at the time of report. Metastasis to the oral cavity is usually found at the advanced stage of the disease, showing widespread nature of the disease. The site of primary tumor and degree of metastatic spread are the most important factors to predict prognosis and treatment planning.^[246] The metastatic lesion should be treated by radiation, chemotherapy, surgical resection, or a combination of these techniques. Palliative treatment helps in reducing the patient's pain, size of tumor, and also preserves oral function.^[16]

CONCLUSION

In conclusion, the diagnosis of oral metastasis is a challenge to the clinicians. In addition, metastases to the jaw bones are rare and occur in the advanced stages of a malignancy. Although some of the previous reports were not available, this review collected and summarized all available data regarding oral jawbone metastasis. Understanding the characteristics of oral metastasis can help the clinician in early diagnosis. In addition, 27.6% of the cases of a metastatic lesion in the jawbones were the first indication of an undiscovered malignancy; hence, a careful examination of patients with jaw bone lesions is strongly suggested. Histopathological diagnosis of the origin of primary tumor has a crucial role in patient treatment, especially in cases of undiscovered primary malignancy. Dentists, as well as general physicians, should take into consideration the possible presence of jaw metastases in cases that present atypical symptoms, especially in patients with known malignant disease.

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CONFLICTS OF INTEREST

There are no conflicts of interest.

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