

## Gnathic Bone Metastasis: A Retrospective Analysis of 20 Patients from A Single Institution

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### ABSTRACT

**Aim:** The aim of this study was to retrospectively analyse 20 cases of metastatic tumors to the jaws seen in a single institution over a period of 7 years.

**Materials and Methods:** A retrospective analysis of 20 patients of metastasis to jaw bones were retrieved from the archives of Department of Pathology, Government Medical College and hospital, Srinagar. Data about patient's age, sex, site of metastatic deposits, clinical history, including the presence of a known primary cancer were collected.

**Results:** The mean age of patients was 42.55 years. Out of 20 patients, 7 cases (35%) were seen females and 13 (65%) were males with F:M ratio 1:1.8. The most common primary site was prostate (30%) followed by breast (25%) and kidney (20%). In males, prostate was the most common primary site whereas in females breast was primary site in the jaw bones. Mandible (15 cases, 75%) was most commonly affected than the maxilla. The most common type of metastatic tumor included adenocarcinoma (n = 14; 70%), followed by renal clear cell carcinoma (n = 4; 20%), and in lower numbers, neuroendocrine carcinoma (n = 2; 10%). The common symptom in these patients was swelling resulting in gross facial asymmetry.

**Conclusion:** Gnathic bone metastases are rare and may affect any age group and both sexes, with higher prevalence in the mandible than maxilla. However it is rare and it may be the first manifestation of unknown primary. 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.

**Key words:** Jaw Tumors, Metastasis, Oral Cavity, Primary Tumors.

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### INTRODUCTION

Cancer is a disease involving complex multiple sequential irreversible dysregulated processes showing metastasis that results in morbidity and mortality. Metastasis is a complex biological course that begins with detachment of tumor cells from the primary tumor, spreading into the distant tissues and/or organs, invading through the lymphovascular structures followed by their survival in the circulation.<sup>1</sup> The estimated incidence of metastasis from primary elsewhere to oral and maxillofacial region ranges from 1 to 3%.<sup>2</sup> Oral metastasis carries a grave prognosis for the patient because it represents advanced disease.<sup>3</sup> The major primary sites presenting oral metastases are the lung, kidney, liver, and prostate for men; breast, female genital organs (FGO), kidney, and colo-rectum for women.<sup>4,5</sup> In the oral soft tissues, the attached gingiva is the most commonly affected site (54%).<sup>5</sup> Metastasis in gnathic bones mainly occurs in the posterior region of the mandible, ramus and the condyle due to abundant vascular and hematopoietic tissue. Metastasis to the maxilla is rare and comprises one-fifth of all metastatic tumors to

the jawbones.<sup>6,7</sup> The male-to-female ratio is almost equal with a ratio of 1:1.1. The mean age of patients being 45 years.<sup>8</sup>

Oral metastasis is considered as a late complication and frequently associated with multiple organ metastases. It can grow rapidly causing pain, difficulty in chewing, dysphagia, disfigurement and intermittent bleeding, leading to poor quality of life.<sup>4</sup> Metastatic foci from distant sites in the abdomen or thorax are thought to be deposited by the blood vascular system, largely through Batson's vertebral and paravertebral plexus of veins, or by tertiary deposits from metastatic lung foci.<sup>3,9,10</sup>

These tumors however, are of great clinical significance, as their appearance may be the first indication of an undiscovered malignancy at a distant primary site, or the first evidence of dissemination of a known tumor from its primary site. In fact, there is a limited number of surveys published in the literature. Thus, the aim of this study was to retrospectively analyse 20 cases of metastatic tumors to the jaw, seen in a single institution over a period of 7 years.

**MATERIALS AND METHODS**

We carried out a retrospective study from 2011 to 2017, comprising of 20 patients with metastatic lesions to the jaws, retrieved from the archives of Department of Pathology Government Medical College and Hospital, Srinagar. Only the cases with distant metastasis involving the jaw bones were considered. All the H and E stained slides available, were reviewed by two pathologists. Only the cases with complete information on the primary site, biopsy, immunohistochemistry and clinico- radiological findings of jaw bone involvement were considered for the study.

Data about patients' age, sex, site of metastatic deposits, clinical history, including the presence of a known primary cancer were collected. The data were tabulated, analyzed and compared with the available literature.

**RESULTS**

Table 1 summarizes the demographic data of 20 cases that metastasized to the jaws with reference to the patient's sex, age, location and primary sites. The mean age of patients at diagnosis was 42.55 years. The youngest patient was 27 years (metastasis from colon) and the eldest was a 72-year-old woman (metastasis from breast).

A significant predominance of men was detected (n=13; 65%) and 7 cases (35%) were seen in women. The female to male ratio was 1:1.8. Overall, the prostate with 6 cases (30%) was the most common primary site, followed by the breast (5 cases; 20%) and Kidney (4 cases; 20%). The most common primary sites for men were the prostate (n = 6; 30%), followed by kidney (n = 4; 20%) and for women, breast (n = 8; 39.1%), 1 case (5%) was seen in colon, and lung in both the genders. (Table 2)

**Table 1: Demographic and clinical data of patients with metastatic tumors to the oral cavity**

S. no	Age	Sex	Procedure	Jaw location	Diagnosis	Primary site
1	28	Male	Biopsy	Mandible	Clear cell ca	Kidney
2	55	Male	Biopsy	Maxilla	Adeno ca	Prostate
3	70	Female	Biopsy	Mandible	Adeno ca	Breast
4	52	Male	Biopsy	Mandible	Clear cell ca	Kidney
5	55	Male	Biopsy	Mandible	NEC	Lung
6	51	Male	Biopsy	Mandible	Adeno ca	Rectum
7	45	Female	Biopsy	Maxilla	Adeno ca	Colon
8	48	Male	Biopsy	Mandible	Clear cell ca	Kidney
9	27	Male	Biopsy	Mandible	Adenoca	Colon
10	52	Male	Biopsy	Mandible	Adeno ca	Prostate
11	50	Female	Biopsy	Mandible	Adeno ca	Breast
12	65	Male	Biopsy	Maxilla	Adeno ca	Prostate
13	52	Female	Biopsy	Maxilla	NEC	Lung
14	43	Female	Biopsy	Mandible	Adeno ca	Breast
15	68	Male	Biopsy	Mandible	Clear cell ca	Kidney
16	55	Male	Biopsy	Mandible	Adeno ca	Prostate
17	65	Male	Biopsy	Maxilla	Adeno ca	Prostate
18	45	Female	Biopsy	Mandible	Adeno ca	Breast
19	58	Male	Biopsy	Mandible	Adeno ca	Prostate
20	72	Female	Biopsy	Mandible	Adeno ca	Breast

**Table 2: Distribution of metastatic tumours to the oral cavity based on gender**

Location	Kidney	Prostate	Colon	Lung	Rectum	Breast
Male	4(20%)	6 (30%)	1(5%)	1(5%)	1(5%)	-
Female	-	-	1(5%)	1(5%)	-	5(20%)

Mandible was the commonest jaw bone involved. 15 cases (75%) had metastasis in the mandible. Metastasis to the maxilla was seen in 5 cases (25%). In the mandible, body region (area between parasymphysis and angle of the mandible) was the commonest site involved by metastasis followed by the angle of mandible. The most common type of metastatic tumors included adenocarcinoma (n = 14; 70%), followed by renal clear cell carcinoma (n = 4; 20%), and in lower numbers, neuroendocrine carcinoma (n = 2; 10%). The commonest finding in these patients was an expansile lesion resulting in gross facial asymmetry. Other Clinical manifestations included pain, paraesthesia, necrosis, perforation of the cortex, ulceration of the mucosa and loose teeth, but some lesions were asymptomatic.

**DISCUSSION**

The oral cavity and the jawbones are occasionally the site for metastasis from primary malignant tumors elsewhere in the body. It is reported that metastatic tumors account for only 1%-3% of all malignant neoplasms presenting in the oral region.<sup>11</sup> Metastasis is a consequence of complex biological cascade that begins with detachment of tumor cells from the primary tumor, spreading into the tissues, invading the lymphovascular structures followed by their survival in the circulation.<sup>12,13</sup>

In our study the mean age of patients at diagnosis was 42.55 years. The youngest patient was 27 years with metastasis from colon and the eldest was a 72-year-old woman with metastasis from breast which was in accordance with previous studies.

Review of literature from all the series consistently showed a significantly greater frequency of jaw metastases in patients over 50 years of age,<sup>14-16</sup> although some studies have shown involvement in young age group.<sup>3,9</sup> A significant male predominance was detected 65% and 35% were seen in women. The female to male ratio was 1:1.8. Our results were consistent with most of the studies, which mentioned similar kind of gender predilection.<sup>13,14</sup>

Mandible was the commonest jaw bone involved in our study. 75% cases had metastasis in the mandible, body region was the commonest site involved followed by the angle of mandible. Metastasis to the maxilla was seen in 25%. A study conducted has shown that the mandible and the maxilla were equally involved by bone metastases, which is different from data in the literature and results in our study also.<sup>6,17</sup> Hirshberg et al studied 390 cases of gnathic bone metastases, of which 316 cases (81%) were located in the mandible, and only 58 cases (14%) were located in the maxilla; involvement of both bones was seen in 21 patients (5.4%). This study was in accordance to our results.<sup>6,13</sup> A study by Antunes and Antunes, have described maxillary involvement in 50% cases which contradicts our results.<sup>6</sup> An explanation for the mandibular predilection may be related to the larger amount of hematopoietic tissue having sinusoidal vascular spaces that provide easy access to tumor cells.<sup>18</sup> Furthermore, the pattern of blood supply to mandible compared to maxilla might be responsible for mandibular predilection.<sup>12</sup> In a study of cases dating from 1992, prostate was the most common primary site (21%) for oral metastases in Ontario population<sup>19</sup> and lung was not the most common primary site to metastasize to the mouth and jaws.<sup>20</sup> This was also consistent with our study in which metastasis from prostate (30%) was the most common primary site, followed by the breast (20%) and kidney (20%).

Piattelli et al in their study of gnathic bone metastases, stated prostate was the primary site in men which was in accordance to our study.<sup>21</sup> Prostate metastasis was followed by metastasis from kidney. In a study conducted by Hirshberg et al the primary site in men was the lung, followed by the prostate, kidney, bone and adrenal glands which was not consistent with our results. Whereas in females the most common site of origin of primary cancer was the breast, followed by the adrenal, colo-rectum, female genital organs and thyroid.<sup>13,22</sup> Similar results were seen in our study, with metastasis from the breast being the most common followed by colon metastasis. D'Silva et al. mentioned that the most common primary site in females is breast followed by the lung.<sup>14</sup> However metastasis from rare sites (esophagus and liver) was not seen in our study.<sup>23,24</sup> Van der Waal et al. stated adenocarcinoma as the main histological type of gnathic bone metastases from a variety of primary tumors, which is in agreement with the data from our sample also and most of them were seen in mandible.<sup>6,15</sup> In our study renal clear cell carcinoma (20%) and neuroendocrine carcinoma were also seen.<sup>25</sup>

Metastases to the oral cavity may be the first indication of an otherwise occult malignancy.<sup>12</sup> This was true in our series also as the patients presented with an expansile lesion resulting in gross facial asymmetry, pain, paraesthesia, necrosis, perforation of the cortex, ulceration of the mucosa and loose teeth, however some lesions were asymptomatic. These clinical presentations with histopathological diagnosis and additional investigations led to the diagnosis of the primary lesions.

## CONCLUSION

Gnathic bone metastases are rare and may affect any age group and both sexes, with higher prevalence in the mandible than maxilla. However it is rare and it may be the first manifestation of unknown primary tumor. Diagnosis can be challenging for both clinician and pathologist. A suspected jaw swelling should be thoroughly evaluated and the possibility of metastasis should be considered in the differential diagnosis. Recent advancement in imaging technologies, molecular-profiling tools and immunohistochemical testing improve the identification of the primary site of origin and have an impact on treatment choices.

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