Mandibular metastasis of follicular thyroid carcinoma: A case report along with the concise review of literature

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Abstract

Metastasis is one of the most common consequences of malignant tumors, and it is one of the leading causes of morbidity and mortality. Metastatic cancers to oral cavity are extremely rare. Moreover, the true incidence has yet to be determined. Despite their rarity, they are important clinically, since they can be the first and the only evidence of spread in many situations. Breast, kidney, lung, prostate and gastrointestinal tract are the most common sources of metastases in the oral cavity. Thyroid carcinoma is the most prevalent type of endocrine cancer, yet it rarely spreads to the oral cavity. After papillary thyroid carcinoma, follicular thyroid carcinoma is the second-most frequent kind of thyroid cancer. Jawbones are more commonly affected than soft tissues. Literature research revealed that till date, 44 cases of metastatic follicular thyroid cancer to the jawbones have been documented with mandibular preponderance (40 cases). With the rising occurrence of oral metastatic tumors in recent years, it has become increasingly important to diagnose them early to avoid future consequences. We present here an unusual case of metastatic follicular thyroid cancer in the mandible of an elderly adult along with a comprehensive review of the literature.

Keywords: Carcinoma, follicular, mandible, metastatic, thyroid

INTRODUCTION

Cancer is a complicated disease in which several basic processes are disrupted, including cell proliferation, death and cell migration.[1] Metastasis is the transfer of malignant tumor cells from their main site of genesis to distant areas, resulting in their colonization.[2] It causes morbidity and eventually death.[3] Metastatic tumors in the oral cavity are extremely rare, accounting for only 1%–2% of all cancers.[4] The breast, lung, kidney, prostate and gastrointestinal tract (GIT) are the most common main sites, and it affects both men and women.[5] Thyroid cancer is the most prevalent type of cancer in the overall endocrine system, and follicular thyroid carcinoma (FTC) is the second-most common type.[6] It generally spreads to the lungs and bones, and rarely to the oral cavity.[7] The jaw bone is more commonly implicated in the oral cavity than the oral mucosa.[8] And the mandible is affected more frequently than the maxilla.[9] Literature search reveals that 40 cases of metastatic FTC to the mandible have been recorded till date [Table 1]. We present another unusual case of metastatic follicular thyroid cancer (FTC) to the mandible in an elderly male

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Table 1: Cases of follicular thyroid carcinoma metastasizing to jaw bone reported till date in the literature

| Author (year) | Site | Age (in yrs)/sex | Clinical presentation | Time to metastasis | Treatment |
|---------------|------|------------------|----------------------|--------------------|-----------|
| Jawanda, et al. (2017) | Right mandible | 77/female | Pain, swelling | 6 years | Hemimandibulectomy, parotidectomy |
| McDaniels, et al. (1971) | Right mandible | 48/female | Pain, swelling | 3 years | Hemimandibulectomy |
| Adger, et al. (1972) | Left mandible | 33/female | Pain, swelling | 4 years | Segmental mandibulectomy |
| Al-Ani (1973) | Left mandible | 74/male | Slowly enlarging vascular lesion | 2 years | Hemimandibulectomy |
| Perich, et al. (1983) | Right mandible | 50/male | Mimicking AV malformation | 5 years | Radiotherapy |
| Tov, et al. (1999) | Left mandible | 64/female | Painful oral swelling | 5 years | Radiation therapy |
| Klahn and McCord (1999) | Right mandible | 50/female | Left hard palate pain | 6 years | Resection |
| Hefer (1998) | Right mandible | 59/male | Malignant adenocarcinoma | 7 years | Resection |
| Vural and Hamza (1999) | Right mandible | 61/male | Right mandible | 8 years | Resection |
| Ripp, et al. (1977) | Right mandible | 62/male | Parotid swelling | 9 years | Resection |
| Nishimura and Bratton (1982) | Right mandible | 55/male | Right mandible | 10 years | Resection |
| Osguthorpe and Bratton (1982) | Right mandible | 59/male | Right mandible | 11 years | Resection |
| Maitre (1982) | Right mandible | 66/male | Right mandible | 12 years | Resection |
| Parichatikanond, et al. (1984) | Right mandible | 63/female | Pain, swelling | 13 years | Resection |
| Tovi, et al. (1984) | Right mandible | 62/female | Pain, swelling | 14 years | Resection |
| Jawa et al. (2001) | Right mandible | 64/male | Pain, swelling | 15 years | Resection |
| Naveen (2003) | Right mandible | 66/male | Pain, swelling | 16 years | Resection |
| Todi, et al. (2003) | Right mandible | 67/male | Pain, swelling | 17 years | Resection |
| Araki (2008) | Right mandible | 68/female | Pain, swelling | 18 years | Resection |
| Kumar et al. (2010) | Right mandible | 69/male | Pain, swelling | 19 years | Resection |
| Kumar et al. (2009) | Right mandible | 70/male | Pain, swelling | 20 years | Resection |
| Leboda et al. (2010) | Right mandible | 71/male | Pain, swelling | 21 years | Resection |
| Prasad et al. (2012) | Right mandible | 72/male | Pain, swelling | 22 years | Resection |
| Kim et al. (2013) | Right mandible | 73/male | Pain, swelling | 23 years | Resection |
| Kim et al. (2019) | Right mandible | 74/male | Pain, swelling | 24 years | Resection |
| Venugopal et al. (2019) | Right mandible | 75/male | Pain, swelling | 25 years | Resection |
| Vazifeh Mostaan, et al. (2013) | Right mandible | 76/male | Pain, swelling | 26 years | Resection |
| Vheelikar et al. (2013) | Right mandible | 77/male | Pain, swelling | 27 years | Resection |
| Narain and Batra (2011) | Right mandible | 78/male | Pain, swelling | 28 years | Resection |
| Lavanya et al. (2014) | Right mandible | 79/male | Pain, swelling | 29 years | Resection |
| Zandi et al. (2014) | Right mandible | 80/male | Pain, swelling | 30 years | Resection |
| Kori et al. (2015) | Right mandible | 81/male | Pain, swelling | 31 years | Resection |
| Khalid et al. (2015) | Right mandible | 82/male | Pain, swelling | 32 years | Resection |
| Al-Sheddi MA, et al. (2015) | Right mandible | 83/male | Pain, swelling | 33 years | Resection |
| Author (year)       | Age (in yrs.)/sex | Site                        | Clinical presentation                                                                 | Time to metastasis   | Treatment                                              | Survival and follow up                      |
|--------------------|-------------------|-----------------------------|-------------------------------------------------------------------------------------|----------------------|--------------------------------------------------------|---------------------------------------------|
| Kori et al. (2015) | 40/female         | Left mandible, ramus, maxilla | Painless anterior neck swelling for 35 years and swelling over left lower jaw for 2 years, associated with pain | First manifestation  | Radioactive iodine therapy                            | NA                                          |
| Hartnie et al. (2015) | 41/female       | Right mandible              | Painless swelling of the right lower jaw                                             | First manifestation  | Segmental mandibulectomy, Radiotherapy                | NED (6 months)                             |
| Krishnamurthy et al. (2016) | 52/male         | Left mandible               | Rapidly increasing painful swelling of the left lower jaw, loose teeth, ulceration   | First manifestation  | Hemi mandibulectomy, radioactive iodine therapy       | NED (14 months)                            |
| Saha et al. (2016) | 70/female         | Right mandible              | Painful swelling on right side of the jaw along with the history of shortness of breath for last 1 month | First manifestation  | Thyroidectomy, radiotherapy                          | NED till date                              |
| Loureiro et al. (2017) | 54/female        | Left mandible               | Painless swelling in the left jaw                                                    | First manifestation  | NA                                                     | DOD                                         |
| Varadarajan et al. (2017) | 73/female       | Left mandible               | Numbness and swelling of left mandible                                              | First manifestation  | Segmental mandibulectomy radioactive iodine therapy   | NED (18 months)                            |
| Dave PK et al. (2018) | 71/male          | Left mandible               | Swelling on left jaw, loose teeth                                                    | First manifestation  | NA                                                     | NA                                          |
| Sathyanarayan et al. (2019) | 68/female      | Left mandible, ramus, angel | Painful swelling on the left side of the face                                        | First manifestation  | Hemi mandibulectomy, Bridging of defect with miniplate therapy, postoperative radiotherapy | NA                                          |
| Jeon YT et al. (2019) | 67/female         | Right mandible              | Facial and gingival swelling on right side                                            | First manifestation  | Hemi mandibulectomy, total thyroidectomy              | NED till date                              |
| Present case (2020) | 55/male           | Right mandible              | Painless swelling on the right lower jaw in relation to 44–47                         | First manifestation  | Referred to oncologist                                | Follow up continued                        |

AV: Arteriovenous, NA: Not available, FTC: Follicular thyroid carcinoma, NED: No evidence of death, NR: Not reported, DOD: Died of disease
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CASE REPORT

A 55-year-old male patient reported with swelling on the right side of the body of the mandible for the past 4–5 months associated with no pain and no obvious cervical lymphadenopathy. Intra-oral examination showed the presence of swelling in the right mandibular region [Figure 1a]. The patient had given no relevant medical history. Serum thyroglobulin’s (Tg) levels were markedly elevated with the value of 1423.00 ng/ml (normal value-1.6–60 ng/ml) while serum T3, T4 and TSH levels were within the normal range.

Radiographic images revealed an osteolytic lesion in the mandibular right 44 to 47 region, which was round to oval and uncorticated along with thinning of the lower border on the same side with intervening radiopaque septae in the radiolucency [Figure 2a]. Computerized tomography (CT) scan showed an expansile destructive bony lesion involving the body of the mandible in the region of 44 till 47. The tumor caused expansion and perforation of both buccal and lingual cortical plates resulting in bulging of the tumor mass [Figure 2b]. CT scan also showed one enlarged level 1b lymph node.

Based on clinical and radiological findings, provisional diagnosis of Ameloblastoma and Central Giant Cell Granuloma (CGCG) was made.

Incisional biopsy [Figure 1b] was performed and tissue was sent for histopathological examination. Hematoxylin and eosin (H and E) stained histopathological section revealed the presence of well-developed duct-like structures and numerous round to oval follicles lined by a single layer of cuboidal to low columnar epithelial cells. The lumen of follicles contained eosinophilic colloid-like material [Figure 3a]. Follicles and colloid-like material also showed positivity with periodic acid Shiff (PAS) staining [Figure 3b]. Tumor cells in areas formed macrofollicular patterns along with microfollicles [Figure 4a and b]. The trabecular and solid patterns of follicles were also present in few areas with tumor cells exhibiting mild pleomorphism and hyperchromatism [Figure 5a and b]. Stromal hyalinization was also seen [Figure 6a and b]. Based on histopathological findings, diagnosis of metastatic FTC to mandible was made. Immunohistochemical analysis (IHC) revealed that the tumor cells were immunopositive for Tg, thyroid transcription factor-1 (TTF-1) and paired box gene 8 (Pax8) and immunonegative for S100 protein and Calretinin [Figure 7]. The patient was referred to an oncologist for further management. Before publishing this paper, the patient’s consent was obtained.

A comprehensive review of the English literature was performed using PubMed, Medline, Embase and Scopus databases. Papers describing FTC as a metastatic lesion in the jawbones were selected including terms: “thyroid,” “cancer,” “thyroid carcinoma,” “thyroid cancer,” “Follicular,” “Follicular thyroid carcinoma,” “metastasis,” “malignancy” with “oral cavity,” “maxilla,” and “mandible.”. Reports involving metastasis to the soft tissues and other facial structures were excluded. Data were extracted and compiled in a table. Data points obtained from the literature review included authors names and year of publication, age of patients, gender, primary histological diagnosis, site of metastasis, clinical

Figure 1: (a) Clinical photograph showing swelling in the posterior right-side lingual vestibule. (b) Photograph of gross incisional tissue

Figure 2: (a) Panoramic radiograph of patient showing a lytic lesion. (b) Computed tomography scan of the patient showing a lytic lesion with resorption of buccal and lingual cortical plates of the right-side posterior mandible
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DISCUSSION

Metastatic cancers to oral cavity are extremely rare and the true incidence is unknown. According to the literature, these lesions account for only 1% of all oral cancers. They are frequently neglected in diagnosis due to their rarity for the following reasons:

A. They are similar to squamous cell carcinoma, the most frequent malignant tumor of the jaw.
B. The lesions are positioned in the center of the bone.
C. Except in the most advanced stages, the patient has little subjective symptoms.

However, it is possible that the seeming rarity is due in part to a failure to diagnose metastatic malignancies in the jaws. Furthermore, because the jaws are not frequently inspected at autopsy, some abnormalities may be missed. As a result, the true incidence of metastatic cancers in the jaws may be higher.

These tumors, on the other hand, maybe of important clinical significance since, as in many cases, their presence may be the only symptom of an undiagnosed underlying malignancy or the first evidence of the recognized tumor’s dissemination from its originating site.

Most of the cases, reported in the literature had oral metastasis as the first symptom of the disease. Anil et al. in 1999 documented a case with evidence of metastasis after 8 years, Rohilla et al. in 2011 provided a case with evidence of metastasis after 2 years, Narain and Batra in 2011 and Kotina et al. in 2013 described a case with evidence of metastasis after 15 years. Vazifehmostaan et al. in 2013 described a case in which metastasis took 12 years. After 1 year of thyroidectomy, evidence of metastases was found, according to Sathyanarayanan et al. in 2019.

Breast, lung, kidney, prostate and GIT are the most common primary sites. And the prevalence is different for both men and women. Breast cancer is the most prevalent cause of metastatic oral cancer in women, whereas lung cancer, followed by prostate cancer, is the most common cause in men. The most common site of metastasis to the oral soft tissues is the lung, while the most common site of metastatic cancers to the jawbones is the breast.

Though thyroid cancer is the most frequent in the endocrine system, it rarely spreads to the oral cavity. Papillary, follicular, medullary and anaplastic thyroid carcinomas are its four histological variations. While papillary and follicular variations are widely defined, readily curable, and
usually have a favorable prognosis, FTC is more aggressive than papillary variant due to a mutation in the p21 Ras oncogene. Distant metastases have been detected in 10%–15% of FTC patients. After the lungs, bone metastasis is the second most prevalent place. The most common route of transmission is hematogenous, however, lymphatic spread is also preferable.

Although the molecular basis for distant metastasis of thyroid cancer is unknown, current research suggests that embryonic processes involved in cell movements, such as epithelial to mesenchymal transition and collective cell motility, may be reactivated.

The jaw bone is more commonly affected by these metastatic cancers than the oral mucosa. The Mandible is more commonly affected than the maxilla in the jaw bone, with the body of the mandible, particularly the premolar-molar region, being the most commonly affected region. This is due to the presence of rich red marrow and increased trapping of metastatic cells due to sluggish blood flow regulation in this region. In addition, this marrow contains growth factors that may help some metastatic cancers colonize. However, compared to other skeletal bones in the body, the jaw bone has a lower overall incidence of metastasis, which is likely due to the gradual replacement of red marrow by yellow or fatty marrow.

In our assessment of the literature, we found 44 cases with FTC metastasizing to the jaw bone. Out of them, 40 cases included the mandible, while just four cases involved the maxilla [Table 1]. It was discovered that the metastasis had primarily spread to one side of the jaw. Kim et al. in 2013 described one case in which the mandible was involved bilaterally. The site of involvement in our case is also the mandible, which supports the same findings as shown in the numerous cases previously published, as shown in Table 1. FTC affects people in their forties and fifties, with a female predominance and a female: male ratio of 3.3:1. There have been extremely few occurrences of FTC involving males in the published data. Out of 44 cases, 34 involved females and only 10 involved males [Table 1] and the average age of incidence was 58 years. This gender disparity could be attributable to the fact that males and females have distinct hormones. Infertility, irregular menstrual cycles, miscarriage, multiple pregnancies or live births, lactation suppressants, oral contraceptives and other non-contraceptives, and estrogens are all linked to an increased risk of thyroid cancer in women.

An unusual case of metastatic follicular carcinoma of the thyroid in an elderly man patient is presented in our case. Pain, swelling, loosening of teeth, and paresthesia are all common clinical signs in patients who are generally asymptomatic. This tumor appears as a solitary nodule, a multinodular goiter or cervical lymphadenopathy at first.

Mandibular metastasis can mimic other inflammatory conditions including periodontitis, periapical lesions or osteomyelitis, thus clinicians should be aware of these lesions. A primary oral soft-tissue malignancy with osseous invasion, as well as a second primary malignant mandibular bone lesion, should be examined with the appropriate medical history.

Draper et al. in 1979 and Krishnamurthy et al. in 2016 both documented ulceration in their patients. A patient with a progressively growing vascular lesion was documented by Osguthorpe et al. in 1982. In 1984, Tovi et al. described a lesion that looked like an AV malformation. The growth, which resembled an odontogenic tumor, was described

Figure 6: (a) Photomicrograph showing stromal hyalinization (H&E stain, ×100) (b) (H&E stain, ×400)

Figure 7: Immunopositivity for thyroglobulin, thyroid transcription factor-1 and Pax 8 and tumor cells are immunonegative for S100 and calretinin (×400)
Metastatic FTCs are critical because they might be the only distant metastases. A 10-year survival rate of 27% has been observed for bone metastases of differentiated thyroid cancer. After 5 years, Brennan et al. reported a serum Tg level of 480 ng/ml in 2013. Thyroid crisis kills a small percentage of patients, as shown in Table 1. A poor prognosis is linked to the existence of distant metastases. A 10-year survival rate of 27% has been observed for bone metastases of differentiated thyroid cancer. After 5 years, Brennan et al. found that 40% of patients with distant follicular metastases survived. Although oral cavity metastatic tumors are uncommon, early diagnosis of the metastatic disease improves overall survival and treatment outcomes.

CONCLUSION

Metastatic FTCs are critical because they might be the only indication of an undiagnosed underlying malignancy at a distant site, with metastatic lesions being the first or only clinical manifestation. The diagnosis of a metastatic lesion...
in the oral region is difficult, both for the physician and the pathologist, due to its rarity. Recognizing that a lesion is metastatic and determining the site of metastatic spread is difficult. This case report adds to the growing list of rare examples of distant metastases of FTC to the mandible, emphasizing the importance of clinician attentiveness and knowledge while dealing with such situations.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial(s) will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

Abbreviations used
CGCG: Central Giant Cell Granuloma, CT: Computerized tomography, FTC: Follicular thyroid carcinoma, GIT: gastrointestinal tract, H-E: Hematoxylin and Eosin, IHC: Immunohistochemical analysis, PAS: Periodic acid shiff, Pax: Paired box gene, Tg: thyroglobulin, TTF-1: Thyroid transcription factor.

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