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Case Report

Metastasis of follicular carcinoma of the thyroid gland to the mandible: A report of a rare case

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ABSTRACT

Malignant tumors are able to grow at sites distant from the primary site of origin. Breast, prostate, renal, thyroid, and lung carcinomas commonly metastasize to bone. Jaw metastasis is rare but may occur more often than generally estimated. Follicular carcinomas of the thyroid gland are tumors of follicular cell differentiation that consist of a microfollicular architecture with follicles lined by cuboidal epithelial cells. It is very difficult to diagnose this type of cancer at the preoperative or intraoperative stage of treatment. Here, we report a case of follicular carcinoma of the thyroid gland who was referred due to a mandibular lesion.

Key Words: Follicular carcinoma, mandible, metastasis, thyroid gland

INTRODUCTION

Metastatic carcinoma is the most common form of cancer involving bone. The most common primary sites for carcinomas that metastasize to bone are the breast, lung, thyroid, prostate, and kidney. The bones that most frequently exhibit metastasis include the vertebrae, ribs, pelvis, and skull. Bone metastasis may be the first manifestation of cancer.[1] Primary and metastatic disease should be included in the differential diagnosis of unexplained musculoskeletal pain in adults.

In an autopsy study of the mandible from patients with various extraoral primary carcinomas, microscopic examinations reveal metastasis in 16% of cases, with most of metastases found to be clinically, radiographically, and grossly undetectable. In general, elderly people are mostly affected and the posterior site of the mandible is more frequently involved.[2] It is interesting that metastases are more common in the mandible than the maxilla because the vascular supply of the mandible depends on a single arterial branch whereas the maxilla is supplied by several branches. However, it may be that the tissue microenvironment of the bone is more responsible for the development of metastasis than the anatomic arterial system. It is not known whether healing extraction sockets and/or subclinical chronic inflammation, which may occur with increased frequency in the jaws and result in

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foci of increased vascularity, affect the occurrence of metastasis.[3]

Thyroid carcinoma is the most frequently diagnosed endocrine carcinoma and the most common cause of death among patients with these tumors. Bone metastases are found in 1%–3% of well-differentiated thyroid carcinomas, occurring more often in follicular carcinoma and in patients more than 40 years of age. Sarcomas arising in soft tissues or other bones metastasize to the jaws very rarely. We describe a case of metastatic follicular carcinoma of the thyroid gland with metastasis to the mandible. A 74-year-old woman presented with a history of right lobe thyroidectomy several years ago (1994), who now is referred with an osteolytic lesion in the lower jaw.

CASE REPORT

A 74-year-old female presented to an oral and maxillofacial surgeon with a chief complaint of pain and paresthesia of the lower lip for unknown duration. There is no past medical and dental significant history. In intraoral examination, mild mandibular swelling in the area of premolar teeth with mild mobility of involved teeth was observed. The surgeon realized an ill-defined radiolucency of the mandible in radiographic findings [Figure 1].

Radiographic differential diagnoses of the osteolytic lesion were composed of infected residual cyst, Langerhans cell histiocytosis, and rolling out of malignancy. An incisional biopsy was performed.

Microscopic examination of the lesion showed a solid mass composed of sheets and strands of large epithelial cells with centric nuclei and eosinophilic-to-clear cytoplasm in syncytial and trabecular pattern demonstrating nuclear atypia and atypical mitotic features which mimic a trabecular and solid pattern of small and large follicle structures. Tumoral cells are surrounded by a sparse hyalinized to hemorrhagic stroma. There were no adenoid structures [Figure 2].

Histopathologic differential diagnoses were undifferentiated carcinoma, metastatic carcinoma, clear cell odontogenic carcinoma, and clear cell carcinoma with salivary gland origin.

We found that the patient had a history of right lobe thyroidectomy several years ago (1994). Differentiated non-invasive and minimally invasive thyroid follicular neoplasms may develop blood-borne metastasis over ten years after diagnosis and should be monitored closely.

Immunohistochemistry (IHC) study results shows that tumor cells were positive for cytokeratin 8 (CK8)/CK18, thyroid transcription factor 1 (TTF-1), paired-box gene 8 (PAX8), progesterone receptors, and pan-cytokeratin (PAN-CK) (some cells). No tumor protein 63 (P63), GATA-3 (GATA3 is a transcription factor encoded by the GATA3 gene in humans), or estrogen receptor immunoreaction was detected. Proliferative activity (Ki67) was not significant [Figure 3].

The diagnosis of metastatic carcinoma with IHC evidence consistent with metastatic follicular carcinoma of the thyroid gland was confirmed. The patient was undergone chemotherapy regimen.

Now after 3 years of treatment, the patient is alive with no significant problem and no evidence of recurrence. She has been receiving iodotherapy for the last couple of years. She gets tested every 3 months to check her immunoglobulins. Antithyroglobulin has remained stable at 20. Moreover, she has had no surgery. She is generally well.

DISCUSSION

Jaw metastases have been reported over a broad age range but most often affect older adults; the mean age is approximately 43–52 years, with no significant gender bias. There is a marked predilection for the mandible, especially the molar region.[4]

Metastatic cancer does not always cause symptoms. When symptoms do occur, what they are like, and how often you have them will depend on the size and location of the metastatic tumors. Clinical signs and symptoms of jaw metastasis may include pain, swelling, tooth mobility, trismus, and paresthesia. In particular, mandibular metastasis with involvement of the mental nerve may produce paresthesia in the lower lip and chin (numb chin syndrome). The rarity of jaw metastases and the nonspecific clinical presentation may lead to a mistaken impression of an inflammatory process.[5] Sometimes, an osseous metastasis is discovered in a nonhealing extraction site from which a tooth was removed because of local pain or significant mobility. In other instances, the patient may be completely asymptomatic, and the lesion is discovered incidentally by radiographic examination.

Occasionally, the diagnosis of jaw metastasis is the first indication that the patient has a primary

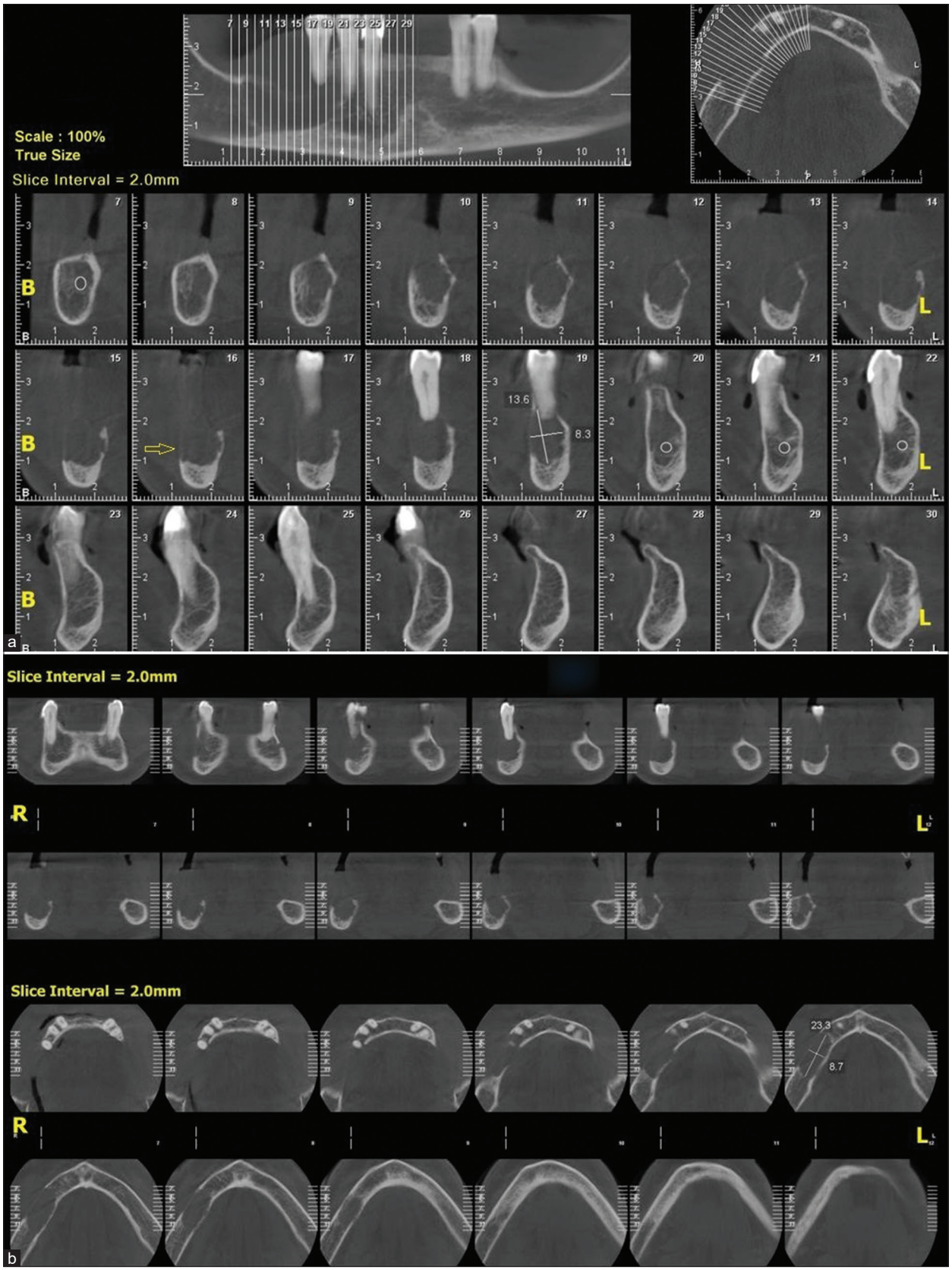

Figure 1: Radiographic findings: (a) There is an ill-defined radiolucent lesion demonstrating perforation of the buccal cortex in some areas (yellow arrow), (b) Coronal and axial view showed extension and lytic structure of the lesion.

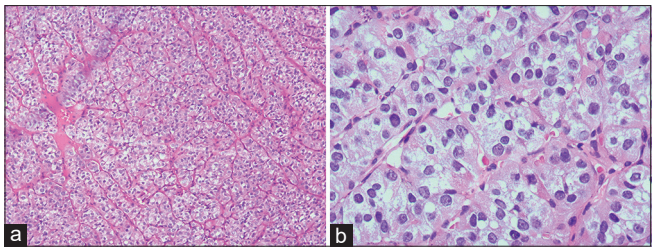

Figure 2: Histopathologic findings: (a) Sheets and strands of large epithelial cells with scant fibrous stroma (×100), (b) Tumoral cells with abundant eosinophilic-to-clear cytoplasm (×400).

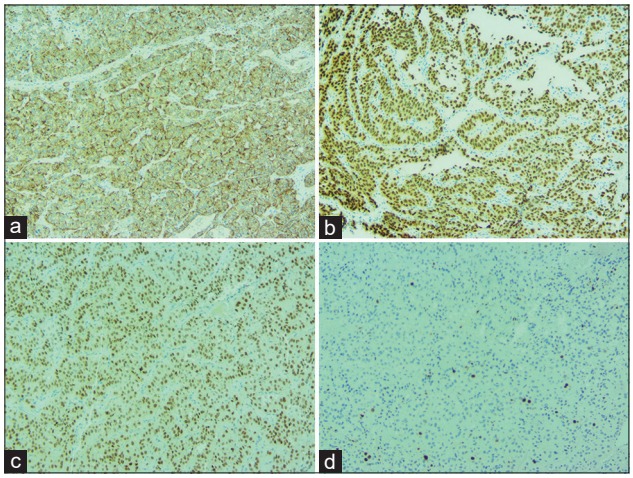

Figure 3: Immunohistochemical findings: (a) Tumoral cells demonstrated positive immunoreaction for cytokeratin 8/cytokeratin 18 (×100), (b) Strange diffuse positive reaction for thyroid transcription factor-1 in tumoral cells (×100), (c) Positive nuclear immunoreaction for PAX8 in tumoral cells (×200), (d) Low proliferative activity has been shown in Ki67 immunostaining (×200).

malignancy at some other anatomic sites.[6] The location of the occult primary tumor may be difficult and may require extensive evaluation.

If plain film radiography is not sufficient for diagnosis, a bone scan may detect occult lesions. Most radiographically evident jaw metastases appear as ill-defined or "moth-eaten" radiolucencies. However, some examples – particularly metastatic prostate and breast carcinomas – may appear radiopaque or mixed radiolucent–radiopaque.[7] Osteolytic (bone-resorbing) and/or osteoblastic (bone-forming) activity may result from various growth factors and other substances produced by tumor cells. Some lesions may mimic periapical inflammatory disease or periodontal disease. Cortical erosion, pathologic fracture, and widening of the periodontal ligament space may be noted as well. Compared to plain radiography, bone scintigraphy is more sensitive for detecting osseous metastasis.[8]

The microscopic appearance of metastatic carcinoma in bone varies. In some instances, the metastasis exhibits well-differentiated features that suggest an origin from a specific site, such as the kidney, colon, or thyroid.[9]

Follicular carcinomas are malignant epithelial tumors that show evidence of follicular cell differentiation but lack the diagnostic nuclear features of papillary thyroid carcinoma (PTC). They account for approximately 15% of malignant thyroid tumors. The relative incidence of follicular carcinoma is higher in iodine-deficient areas.[10] The frequency of this tumor type has decreased in recent years, owing primarily to the recognition of the follicular variant of PTC.[11] Similar to PTCs, previous radiation exposure also increases the risk of follicular carcinoma, although to a lesser extent.[12] We report here a rare case of metastatic follicular carcinoma of the thyroid in a patient with a history of thyroidectomy after 29 years.

In 2013 in Mashhad, Vazifeh Mostaan *et al.* presented a case of FTC that metastasized to the mandible, 12 years after the thyroidectomy. They emphasized that metastases of thyroid tumor to the mandible might occasionally be the sole indication of the initial cancer.[13]

In 2022 in India, Jawanda *et al.* did a review of literature about 44 cases of metastatic FTC to the jaws with 40 cases involving metastasis to the mandible. They stated that early diagnosis is now more crucial than ever to prevent future repercussions due to the increased incidence of oral metastatic tumors in recent years.[14]

In 2023 in India, Nayyar *et al.* described a middle-aged adult with metastatic thyroid carcinoma of the mandible who initially had a little diffuse swelling in the right buccal vestibular area of the jaw. Radiographic and microscopic analysis and IHC findings represented metastatic follicular thyroid cancer.[15]

Patients with follicular carcinoma are, on average, 10 years older than those with PTC. Similar to PTCs, follicular carcinomas are considerably more common in females than in males. Most patients present with a palpable thyroid nodule, which is usually "cold" on scan. Occasionally, patients may present with distant metastasis involving bone or the lung. Follicular carcinomas are subdivided into encapsulated and widely invasive types.[16]

Follicular carcinoma cells are positive for thyroglobulin, TTF-1, PAX8, and low-molecular-weight cytokeratins. The CK7+/CK20-pattern of immunoreactivity in these tumors is similar to that seen in PTCs and nonneoplastic thyroid cells. The expression of the peroxisome proliferator-activated receptor (PPARγ) protein, which can be detected by IHC and correlates well with the presence of PAX8-PPARγ rearrangement, may be of diagnostic value. Follicular carcinomas are usually positive for B-cell leukemia/lymphoma 2 protein and p27 (cyclin-dependent kinase inhibitor), have low expression of cyclin D1 (a protein required for progression through the G1 phase of the cell cycle), and are negative for p53 (tumor suppressor gene). Several studies have shown that IHC for p63 is useful in distinguishing primary adnexal carcinomas from metastatic disease. D2–40 also plays a role in this distinction: primary adnexal neoplasms are often positive for this marker, while metastatic carcinomas are negative. IIt is proven that using p63 alone has limitations, so it is recommended to use panels of markers instead.[17] Our reported case showed positive CK8/18, TTF-1, PAX8, progesterone receptors, and PAN-CK and negative P63, GATA-3 or estrogen receptors, and Ki67 immunoreactions.

More often, however, metastatic carcinomas are poorly differentiated, and the tumor origin is not readily apparent. Poorly differentiated metastatic carcinoma may be difficult to differentiate from lymphoma, melanoma, or anaplastic sarcoma. In such cases, IHC may aid in diagnosis.[18] Definitive diagnosis requires the correlation of laboratory studies with a thorough medical history, complete physical examination, and imaging studies.[19]

Although a solitary metastatic focus may be treated by excision or radiation therapy, jaw metastasis almost always is associated with widely disseminated disease. Management depends on the specific underlying tumor type and often is palliative in nature. Administration of bisphosphonates may help to slow the progression of bone metastases, decrease bone pain, and reduce the risk for pathologic fracture.[20] By definition, osseous metastasis constitutes stage IV disease. Accordingly, the prognosis for metastatic carcinoma to the jaws is poor, and most patients survive <1 year.

CONCLUSION

Metastatic carcinomas mostly involve bone. The accurate diagnosis of metastatic carcinoma is achieved through IHC, histopathological, and radiographic findings. It is very essential to have a high index of suspicion in patients with a known history of malignancy, especially when disease is advanced. It is important to correctly diagnose the histologic type and the primary site of the metastatic lesions to establish the optimal treatment strategy. A collection of clinical data that include radiologic findings and laboratory results is very important for the correct pathologic diagnosis of metastatic tumors. However, early diagnosis has a great effect on the patient's survival, but the prognosis for metastatic carcinoma is very poor.

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 initials 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

The authors of this manuscript declare that they have no conflicts of interest, real or perceived, financial or non-financial in this article.

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