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Dates: Received: 21 December, 2016; Accepted: 03 January, 2017; Published: 04 January, 2017

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Keywords: Mandible; Thyroid; Follicular variant; Metastasis; Follow-up

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Case Report

Rare Late Mandibular Metastasis in Follicular Variant of Papillary Carcinoma Thyroid: 'Resurgence of the Sleeping Tumour'

of papillary carcinoma thyroid. It reiterates the significance of vigilant screening during follow-up visit so as not to miss timely diagnosis.

Case Report

A 58 year old lady reported with a persistent soft, non-tender swelling of 1 month duration over the left side of her face. The swelling was sudden in onset and there was no associated paresthesia reported.

Examination

On extra oral examination, a solitary, oval diffuse swelling was observed over the left side of face measuring 5 x 6 cms over left ramus of the mandible (Figure 1a). It was palpable deep to the masseter extending from the pre-auricular region to the angle of the mandible inferiorly.

Intra-oral examination revealed hypertrophic tissue in the left retro-molar trigone area with no other associated abnormality (Figure 1b). There was no tooth mobility or any evidence of ulcero-proliferative growth seen. The patient gave no history of recent extraction or spontaneous exfoliation of any tooth.

Past medical history

The patient had first reported to our hospital 3 years ago

Introduction

Cancer of the thyroid gland is the most common endocrine malignancy constituting for less than 1% of all reported human cancers¹. The propensity of occurrence of thyroid carcinomas is two to four times more in females as compared to males with a median age at diagnosis being 45–50 years [1,2]. Papillary thyroid carcinoma (PTC) is the most common histological type of thyroid cancer and accounts for more than 80 % of thyroid malignancies. Classical PTC (cPTC) is the most common (80%) sub-type of papillary thyroid carcinoma followed by follicular variant (FVPTC) which is found in 9–22.5% of patients [3].

FVPTC was first described by Crile and Hazard in 1953 as alveolar variant of PTC. It was subsequently confirmed by Lindsay, Chen and Rosai as an independent entity with typical nuclear features and follicular growth pattern. FVPTC further has histological variants namely, completely encapsulated form, well circumscribed form, and infiltrative form, the last being the most aggressive [2,4]. The encapsulated variant is relatively more prevalent than the other sub-type and is non-aggressive in nature. In order to distinguish it from the invasive variant, histologically, it has been renamed as 'noninvasive follicular thyroid neoplasm with papillary-like nuclear features'.

Invasive follicular variant of PTC presents several diagnostic and management challenges [5]. Late metastasis to the mandible is extremely rare and could be the only sign of a silent underlying neoplasm. Such lesions may resemble odontogenic lesions and should be carefully differentiated from them. This case report is a description of rare late mandibular metastases in a previously diagnosed case of invasive follicular variant

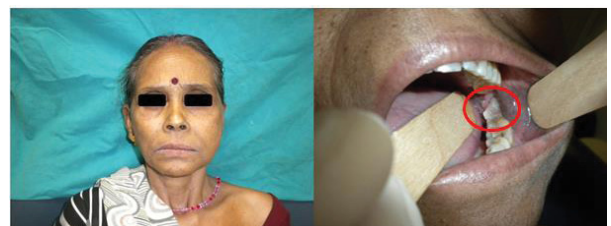


Figure 1: (a) Oval extra oral swelling seen on the left side of face. (b) White exophytic tissue seen intra orally in the left retromolar trigone area.

with complaints of lower back pain and scalp swelling of 1 year duration. On examination, a 5 cm x 4 cm sized discrete soft swelling was palpable in occipito-parietal region and 1 cm x 1 cm sized nodule was palpable in left lobe of thyroid. Hopkins evaluation was normal with mobility seen in both vocal cords. Ultrasonographic examination (USG neck) demonstrated two ill-defined, heterogeneous lesions measuring 2.8 cm x 1.4 cm and 1.4 cm x 1.4 cm with raised vascularity and coarse linear calcification, in the isthmus and left lobe of the thyroid, respectively. In addition, bilateral level Ib and II nodes were visualized that essentially appeared as reactive. Both the lesions raised a suspicion of an underlying neoplasia. Magnetic resonance imaging (MRI) demonstrated altered signal intensity with expansion involving C3, D2, D3, D9, L2 and L4 vertebrae.

An ultrasound guided fine needle aspiration cytology (USG-FNAC) was conducted, which revealed cytopathologic features of papillary carcinoma thyroid, involving the left thyroid. Histopathologic review of the lytic lesion in the occipital bone and sacrum showed atypical follicular epithelial cells arranged in a predominantly, follicular and solid pattern with interspersed colloid, consistent with the diagnosis of metastatic follicular variant of papillary thyroid carcinoma (FVPTC).

Comprehensive clinical, radiological and cytopathologic examinations established the carcinoma as cT2 N0 M1 stage (stage IVc). Total thyroidectomy with left central compartment sampling was conducted. Frozen section examination revealed a single reactive central compartment lymph node.

Subsequently, on gross examination, a grey-white, encapsulated tumour measuring 2 cm x 1.8 cm x 1.7 cm was noted in the upper pole of left lobe of the thyroid. In addition, the isthmus showed a lesion measuring 3 cm x 2.5 cm x 1 cm with bone formation in the centre of the lesion. Histopathologic examination revealed predominantly follicular and focally, solid arrangement of tumor cells, exhibiting nuclear margination, intranuclear grooves and focal, intranuclear inclusions. In addition, focal areas of oncocytic differentiation were also seen. Capsular invasion and lymphovascular emboli were noted. Diagnosis of FVPTC was offered. The central compartment lymph nodes were microscopically free of tumour deposits (Figure 2).

Further, the patient was administered 260 mCi of radioactive iodine I131. Multiple bony metastases in sacral and lumbar region were managed with palliative external beam radiotherapy (EBRT) of 20 Grays (Gy) equally distributed in 5 fractions. The patient attended the hospital for a 6-month follow up in April 2014 with no fresh complaints. Good loco-regional control was achieved. However, she was lost to further follow-ups and did not report to the hospital.

Investigations

An Orthopantograph (OPG) examination showed extensive diffuse multilocular radiolucency with ill-defined borders over the left ramus extending upto the condyle superiorly, anterior margin of ramus anteriorly and angle of the mandible inferiorly (Figure 3). The lesion showed mixed areas of dense

radiolucency interspersed with areas of radio-opacity. These findings were consistent with a differential diagnosis of an odontogenic carcinoma and/or, metastatic disease.

A contrast-enhanced Computed Tomography (CECT) scan demonstrated a destructive expansile lesion over the left ramus of the mandible extending to the condyle and coronoid process. (Figure 4).

Diagnosis

The positive findings of the CECT scan along with clinical findings negative for an inflammatory lesion and a history of invasive FVPTC helped in arriving at the diagnosis of metastatic disease of the mandibular ramus.

Management

Due to the extensive nature of bony destruction which had already occurred including involvement of left parieto-occipital region of scalp, surgical resection of the lesion was not advised. Since the patient did not complain of significant pain associated with the lesion, palliative radiotherapy of 30 Gy equally divided in 10 fractions was administered to the disease site.

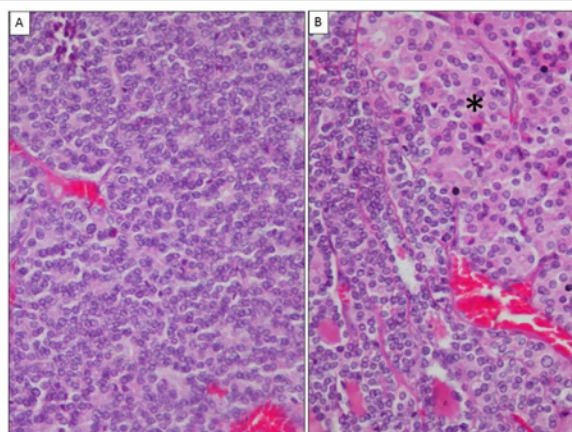


Figure 2: Histopathologic findings. Microscopic examination of the thyroidectomy specimen revealing cells arranged in a prominent microfollicular pattern, exhibiting nuclear overlapping, margination of chromatin, intranuclear grooves and focal inclusions, indicative of follicular variant of papillary carcinoma. Hematoxylin and Eosin (H and E) x 200. B. Focal area showing hurthle cell change (asterisk) with cells containing abundant eosinophilic cytoplasm, but revealing other features FVPC. H and E x 400.



Figure 3: Orthopantograph (OPG) showing extensive diffuse multilocular radiolucency with ill-defined borders involving the left ramus, coronoid and condyle.



Figure 4: Contrast-enhanced CT scan (CECT scan) demonstrating a destructive expansile lesion over the left ramus, coronoid and condyle.

to conventional papillary thyroid carcinoma (c-PTC), as well distant metastasis via the bloodstream similar to follicular thyroid carcinoma (FTC) [5].

Only about 20% of patients with differentiated thyroid carcinomas show a metastatic evolution. In 50–80% of cases, there are multiple bone metastases. According to different studies, bone metastases are more common in patients with follicular carcinomas (15.2–33.7%) than in those with papillary carcinomas (0.6–6.9%). Sternum, ribs, and spine are the most frequent sites of osseous metastases in such differentiated thyroid carcinomas [9].

A literature review done by Nikitakis et al. [10], in 2012 revealed only 37 published cases collectively, of all forms of thyroid cancer metastasizing to the oral cavity [11–40]. Metastases to the maxilla and/or, mandible are extremely rare in histologically invasive FVPTC with literature reports of only a few cases. Pal et al. [41], Bhadage et al. [42], Bingol et al. [6], and others [7,43], have reported metastasis to the body and angle of mandible manifesting in invasive form of FVPTC. However ramus metastasis is extremely rare and has been described in the literature by Saha et al. [8], and Noolkar et al. [44]. A solitary case of maxillary metastases has been cited by Bhansali et al. [45].

In the presented case, the patient was diagnosed with invasive FVPTC with sacral metastases in the first instance. In accordance with the Tata Memorial Hospital guidelines for evidence-based management vol. XI A 2012 [46], total thyroidectomy followed by 260 mCi of I131, radioactive ablation was carried out. Palliative EBRT of 20 Gy equally distributed in 5 fractions was given to locally manage sacral metastases.

Distant metastases to the ramus of mandible were detected after 2.5 years of completion of the primary treatment. Moreover, the patient was pain-free and had reported to the department with a complaint of seemingly ‘harmless’ swelling. On further investigations it was confirmed as a metastatic lesion involving the ramus of the mandible for which 30 Gy of palliative EBRT equally distributed in 10 fractions was advised. However, in a patient affected by metastases to the mandibular body region, Bingol et al. [6], performed hemi-mandibulectomy followed by reconstruction with costo-chondral rib graft as a definitive procedure.

Conclusion

Metastasis from invasive FVPTC to mandible is a rare occurrence and should be kept in mind with the other differential diagnoses of tumors in the facial region. Despite the relatively indolent behavior of encapsulated follicular thyroid neoplasm, the 5-year survival rate in patients detected with bony metastases in invasive FVPTC is reported to be 79.4% with 10-year survival rate being 52.9% [47].

Hence, there is need for a long term, strict vigilant follow up of a patient diagnosed with invasive FVPTC as evident with our experience. Metastatic FVPTC is of greater significance, since at times its appearance may be the only symptom of an undiscovered underlying malignancy and metastatic lesions may be the first or only clinical manifestation.

Discussion

Metastatic lesions are the first clinical sign of many unknown primary tumors. Metastatic tumors to the oral and maxillofacial region are rare and account for approximately 1% of all malignant oral tumors. Malignancies can metastasize to the jaw bones either through blood vessels or lymphatics, with the hematogenous route being most common one. In females, tumours arising from breasts, adrenal, colorectum, cervix and ovary and thyroid more commonly metastasize to maxilla and/or, mandible. On the contrary, in males, lung followed by the prostate, kidney, bone, and adrenal show distant metastases to jaw bones. Thyroid carcinoma with isolated mandible metastasis accounts for 3.85% of all jaw metastasis. A review of literature suggests that jaw metastases is more frequent than to oral mucosa in the ratio of 2.5:1. [6].

Mandible is more commonly affected than maxilla with the premolar-molar region being the most frequent site of metastasis. There is a high propensity of metastases to the body of the mandible as compared to ramus due to the presence of hematopoietic bone marrow and thus greater entrapment of metastatic cells as a result of sluggish blood flow [6–8].

Metastatic carcinomas affecting either maxilla or mandible should always be considered in the differential diagnosis of a long-standing, painless facial swelling in old individuals. Such carcinomas are difficult to be distinguished from inflammatory and reactive lesions of oral and maxillofacial region [6]. Extra care should be taken so as not to miss any such metastatic lesion affecting ramus since it is covered by the parotid gland [5].

In this presented case, mandibular ramus was affected and OPG showed extensive area of radiolucency with ill-defined borders over the left ramus extending upto the condyle superiorly, anterior border of ramus anteriorly and angle of the mandible inferiorly. These findings were confirmed in a CECT scan and were thus, consistent with a differential diagnosis of an odontogenic carcinoma and/or, metastatic disease.

Invasive FVPTC presents several diagnostic and management challenges to the clinician. It has hybrid metastatic capacities with lymph node metastasis via the lymphatic system similar

Acknowledgements

The patient has given her consent to the use of clinical photographs for educational purposes.

The authors wish to declare no conflict of interest in the work submitted.

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