



Oropharyngeal Metastasis from Papillary Thyroid Carcinoma: A Rare Event

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Abstract

Metastatic oral malignancy accounts for 1% of all oral cancers. Primary tumor sites are lung, kidney, liver, breast, female genital organs and colo-rectum. Metastasis from thyroid carcinoma to the oropharynx is very rare. Papillary thyroid carcinoma (PTC) favors lymphatic spread. Hematogenous spread rarely occurs to the lung, bones and brain. We report a rare case of a 36 year old female in whom metastatic lesion from papillary thyroid cancer presented 13 years after treatment of the primary, as an oropharyngeal mass clinically mimicking a second malignancy. CT scan revealed a mass lesion arising from posterior wall of oropharynx, partially extending over posterior wall of hypopharynx at the metastatic site, with a large primary in the left lobe of thyroid involving larynx. Histology showed a papillary adenocarcinoma which expressed CK7, thyroid transcription factor 1 (TTF1) and thyroglobulin. The review details metastasis in the oro-pharynx, metastatic sites of thyroid malignancies, more specifically differentiated thyroid carcinomas and their prognostic significance. Issues in histopathology, diagnosis of the lesion including distinguishing it from a primary PTC in a thyroglossal cyst or a lingual thyroid, differential diagnosis of other papillary lesions, interesting collision tumours are discussed. Furthermore the mechanism of lymphatic spread to oropharynx and the radiological diagnosis of metastasis and treatment strategies have been outlined.

Keywords: Oropharynx; Metastasis; Papillary thyroid carcinoma

Introduction

Metastatic oral malignancy accounts for 1% of all oral cancers [1]. Primary sites of metastasis are lung, kidney, liver, breast, female genital organs and colo-rectum [2-3]. Metastasis from thyroid malignancies to this area is very rare. Papillary thyroid carcinoma favors lymphatic spread [4]. Hematogenous spread rarely occurs to the lung, bones and brain [5]. We report a rare case where metastasis from papillary thyroid carcinoma presented as an oropharyngeal mass, partially extending over wall of hypopharynx.

Case Presentation

A 36 year old woman presented to her general medical practitioner with a five week long history of difficulty in solid food uptake and hoarseness of voice. She was referred to the Surgical Oncology department of King George's Medical University. On initial examination a pharyngeal exophytic growth was identified on laryngoscopy and a provisional diagnosis of a primary oropharyngeal epithelial malignancy was considered. A biopsy of the lesion was done and sent to our referral laboratory at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow for histopathological evaluation. Microscopic assessment of H&E stained sections showed a tumor predominantly arranged in a papillary architecture. Tumor cells showed high nucleo-cytoplasmic ratio, round to oval nuclei, vesicular chromatin, inconspicuous nucleoli and moderate of eosinophilic cytoplasm (Figure 1A). A differential diagnosis of a primary papillary adenocarcinoma or a metastatic lesion was considered. Initial immunohistochemistry (IHC) for the unknown primary was done for relatively commoner metastatic sites including lung, gastrointestinal tract, breast, female genital organs and kidney. A primary immunohistochemistry panel comprising of CK-7, CK-20, p40, p16, CDX-2, TTF-1 and WT-1 was applied. In view of a strong positive expression of TTF-1 (Figure 1B) and CK-7 (Figure 1C) with negative p40, p16, CK-20, CDX-2 and WT1 a possibility of a primary papillary adenocarcinoma of the lung and papillary thyroid carcinoma were considered. Thyroglobin showed cytoplasmic expression in all cells clinching the diagnosis of a papillary thyroid carcinoma (Figure 1D). On retrospect the patient gave a history of thyroid surgery 13 years back. No documented proof of type of surgery and histopathological diagnosis was available and the patient

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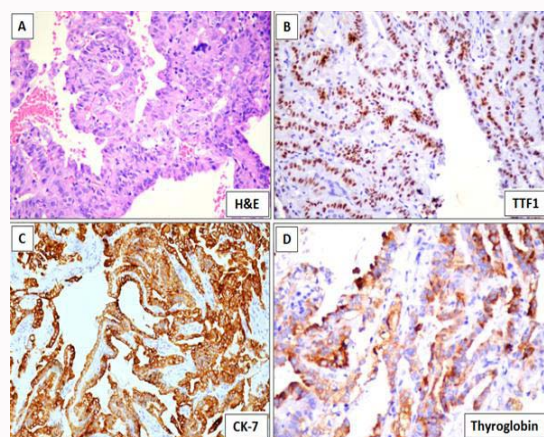


Figure 1: Histological and Immunohistochemical features of index case. A) Tumor cells are arranged in a papillary architecture. B-D) Strong expression of TTF-1, CK-7 and Thyroglobulin.

was not able to provide any details. An axial contrast enhanced CT scan revealed a mass lesion arising from posterior wall of oropharynx, partially extending over posterior wall of hypopharynx at the metastatic site (Figure 2a). CT slice at the level of thyroid cartilage showed involvement of left lateral and posterior aspect of larynx by thyroid mass (Figure 2b). A separate hypo-enhancing mass arising from the left lobe of thyroid was also identified. Final diagnosis of a metastatic papillary thyroid carcinoma was rendered. Patient was given palliative therapy addressing the issue of dysphagia and breathlessness and a tracheostomy was done.

Discussion

The oral cavity is an uncommon site for metastatic disease. Metastatic disease, when present, involves jaw bones primarily the mandible followed by maxilla [6]. Soft tissue and mucosal metastasis is rare. Major primary sites in males are usually the lung, kidney, liver, and prostate while in women oral metastases may come from the breast, female genital organs, kidney, and colo-rectum [7]. A recent study by Thiele et al. [8] have reported incidence of distant metastasis at 2.39% of all malignancies in the oral and cranio-maxillofacial area, which is twice as high as previous published data.

The tissue involved in the oral cavity varies with the primary site and in men metastases from the lung go to the mandible and maxilla followed by oral mucosa (22% and 31.3%, respectively) whereas the prostate adenocarcinoma metastasizes to jawbones (11%) and kidney to the oral soft tissues (14%). In women, breast primaries affect jawbones and soft tissues (41% and 24.3%, respectively), followed by adrenal and female genital organs in the jawbones (7.7% and 14.8% respectively) [6]. The primary site considered initially in

the current case was also lung in view of the papillary morphology and immunoreactivity for TTF1. The classical nuclear morphology of papillary thyroid carcinoma in terms of clear nucleoplasm, intranuclear inclusions and grooves was not evident in our case at the metastatic site. However positive thyroglobulin in the second line of immunostaining confirmed the primary as a PTC.

PTC usually shows lymphatic invasion and frequently metastasizes to regional lymph nodes, although distant metastases are considerably less frequent [4]. Thyroid carcinoma metastasis to the jaws is rare with only a limited number of cases previously reported in the literature. Nikitakis in 2011 reported a case of mandibular metastasis from PTC and summarized a review of 36 previously reported cases of metastases from malignant thyroid neoplasms including 33 to the jaw bones and three to the mucosa which included one to the dorsal tongue and lower lip, right maxillary gingiva and anterior mandibular gingival [9-10]. PTC accounted for 8 (22.2%) cases. Single cases of metastasis from Hurthle cell, medullary, and poorly differentiated carcinoma have been reported. In their review, the vast majority of oral metastases from thyroid cancer were located in the mandible (32/37; 86.5%). Further in a fair number of cases of metastatic thyroid cancer to the oral cavity reviewed, there was also involvement of adjacent structures such as the parotid, infratemporal fossa, and masticator space and sinus. In our case also an extensive spread of the primary thyroid mass to left lateral and posterior aspect of larynx was evident in CT scan.

Recently Siddique et al. [11] reported a PTC with sarcomatoid transformation metastasizing to the gingival mucosa. Nawale et al. [12] reported 12 cases of metastatic neoplasms to the jaw bones and observed 4/12 to be cases as PTC. However, none of their cases had mucosal involvement. Summarizing, oral soft tissue metastasis from PTC appear to have been reported in 6 cases only and these were located mostly in the gingiva.

Parapharyngeal region metastasis from PTC thyroid is also rare. Parapharyngeal lesions are often nonspecific or asymptomatic when the tumor does not exceed 3.0cm in size. Cases with larger lesions frequently complain of a mass in the neck or oropharynx that causes dysphagia [13], as was present in our case. Most parapharyngeal metastases are unilateral; whereas some rare cases are bilateral. Integrated ^{131}I -SPECT/CT is a useful tool for the screening patients with differentiated thyroid carcinoma, especially early lesions [14]. Parapharyngeal metastasis usually present as cystic lesions in the parapharyngeal region and retropharyngeal space, sometimes cystic metastasis in lymphnodes or masquerading as a deep lobe parotid mass. A transoral approach has been used to approach these lesions both for FNAC and surgical resection but they may rarely involve the as oro-pharyngeal mucosa. Our case presented with an exophytic mass in the oropharynx which was visualized on laryngoscopy.

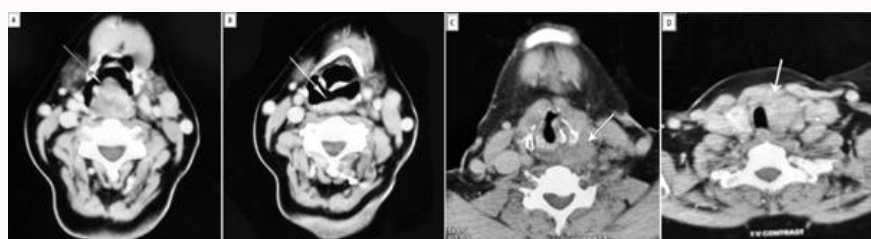


Figure 2: A) Axial contrast enhanced CT scan reveals a mass lesion (arrow) arising from posterior wall of oropharynx. B) Inferiorly, mass is partially extending over posterior wall of hypopharynx. C) Section at the level of thyroid cartilage shows involvement of left lateral and posterior aspect of larynx by thyroid mass. D) Hypo-enhancing mass arising from the left lobe of thyroid.

Subsequent CT evaluation showed the lesion involving the posterior wall of oropharynx, partially extending over posterior wall of hypopharynx. Calcification has also been reported at metastatic sites. Other proximal sites of metastasis include the larynx and pharynx [15].

Differentiated Thyroid Cancer (DTC) is usually indolent with good prognosis and long-term survival. However, DTC distant metastasis is often a grave event and accounts for most of its disease-specific mortality. Metastasis in DTC occur in only 2.2% cases and independent factors associated with distant metastases include male gender, older age, single status, black and other non white races, follicular and Hurthle cell histology, large tumor size, and positive regional lymph nodes [16]. The major sites of distant metastases are the lung and bone. Metastases to the brain, breast, liver, kidney, muscle, parapharyngeal, parotid, adrenal, ovaries and skin are rare. Recognizing rare metastases from DTC has a significant impact on the clinical decision making and prognosis of patients. ¹³¹I single photon emission computed tomography/computed tomography (¹³¹I-SPECT/CT) can provide both metabolic and anatomic information about metastatic lesions. Care should be taken to determine whether ¹³¹I uptake found at an unexpected site is DTC metastasis or false-positive uptake [17]. Prognostic factors in DTC include tumor size, multifocal or bilateral occurrence, angioinvasion, and extra capsular growth, presence of cervical lymph node metastases, distant metastases and early local relapse.

Primary thyroid malignancies may also arise in the oropharynx from thyroglossal duct remnants and in thyroglossal cyst. Occurrence of primary carcinoma is reported to be present in 1% cases in thyroglossal cyst of which 94% are histologically papillary thyroid carcinoma [18]. Hoffman et al. [19] observed PTC in a thyroglossal cyst along with a small thyroid carcinoma and three positive lymph nodes. These authors argue the case of whether the cystic carcinoma is primary or a metastasis from thyroid carcinoma in their case report. It is interesting to note that the location of oral foramen caecum of the thyroglossal duct is anatomically in a proximal relation to the vallecula. A possibility of a primary from thyroglossal duct remnants in the oral cavity was considered in our case initially, however the presence of a large mass in the left lobe of the thyroid along with extensive involvement of adjacent tissues and lymphnodes in CT scan supported a primary in thyroid with metastatic lesion in the oropharynx. In rarer instances primary thyroid malignancy may arise in an ectopic lingual thyroid.

Clinical suspicion of a second primary tumour possibly Oral Squamous Cell Carcinoma (OSCC) with a past history of a thyroid carcinoma was considered in our case and the biopsy was sent as an oropharyngeal carcinoma. Multiple synchronous head and neck cancers are known to occur [20]. Collision metastases have also been reported in the cervical lymphnodes from PTC and OSCC simultaneously [21]. Collision tumors pose a diagnostic as well as therapeutic challenge. Squamous elements may occur in the process of a dedifferentiation of papillary thyroid carcinoma and may appear at metastatic site rather than the primary site and the diagnosis of a collision metastasis should be given with caution [21]. In the current case a well differentiated papillary lesion lined by a single layer of neoplastic columnar epithelium with focal clustering and solid areas was evident at the metastatic site.

Papillary pattern in metastatic lesions is encountered frequently in primaries from lung, renal papillary carcinoma, papillary thyroid

carcinoma, papillary GI lesions, ovaries, urothelial neoplasms. Differential diagnosis can be resolved using a panel of IHC including CK 7, 20, TTF1, Napsin, CDX2, Thyroglobulin, WT1, ER, uroplakin. Well differentiated morphology, a strong cytoplasmic thyroglobulin and nuclear TTF-1 expression confirmed metastatic PTC in our case. The modality of spread of tumor to the posterior wall of the oropharynx in the current case could have been through lymphatic route or through hematogenous spread. Minute dissection of 22 neck-halves (11 adult cadavers) was undertaken by Saito et al. [22] to determine the location and topographical relationships of the lymphatics of the pharynx. Saito et al. [22] reported that Lymphatic drainage from the hypopharynx was multidirectional with the pathways being classified as follows: ascending pathway to the lateral pharyngeal and lateral retropharyngeal nodes, lateral pathway to the internal jugular chain, and descending pathway connecting to the uppermost vessels ascending from the recurrent laryngeal nerve chain. The treatment of oral metastases of thyroid carcinoma has varied extensively from palliative to various combinations of surgical resection, radioactive iodine treatment, radiotherapy, and/or chemotherapy. It has been recommended that surgical resection of the metastatic tumor in conjunction with total thyroidectomy, followed by radioactive iodine treatment and/or external-beam radiation may afford better survival. Nonetheless, the treatment decision depends on various factors, including the operability of the metastatic lesions and the presence of a solitary metastatic focus versus multiple metastasis. In widespread metastatic disease, treatment is usually palliative. In our case, patient had partial thyroidectomy 13 years back and now palliative tracheostomy has been done. In conclusion, metastatic deposit of PTC presenting as oropharyngeal mass has rarely been described. Such a presentation can pose a diagnostic challenge to pathologists in identifying the lesion as metastatic and locating the primary cancer. IHC expression of TTF1 in tumor cell nuclei and thyroglobulin in the cytoplasm confirms origin of tumor.

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