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Mucin-secreting papillary adenocarcinoma of the hyoid bone: a unique case

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Abstract
We present a unique case of a mucin-secreting papillary adenocarcinoma of intestinal type which has invaded and completely destroyed the hyoid bone and metastasized to the cervical lymph nodes bilaterally. The tumour is believed to have originated from a malignant thyroglossal duct remnant, and was managed with surgery and radiotherapy. We describe the case and discuss the literature regarding hyoid bone tumours.

Key words: Adenocarcinoma; Papillary; Thyroglossal Duct; Hyoid Bone; Lymph Nodes; Neck

Case report

A 76-year-old man presented with a firm, painless midline mass in his neck that developed over the course of seven months. This was 10 cm in diameter and superior to the larynx; it moved on swallowing. Panendoscopy revealed a vallecular bulge. Examination was otherwise normal and thyroid function tests were unremarkable.

An axial computed tomography (CT) scan of the neck demonstrated a mass at the level of the hyoid (Figure 1). A CT scan of the lungs and abdomen was normal, as was an abdominal ultrasound scan and a gastric biopsy. An isotopic bone scan confirmed high uptake within the hyoid but found no evidence of disease elsewhere.

An ultrasound-guided core biopsy identified the neck mass as a mucin-secreting papillary adenocarcinoma. This tumour was completely excised to include the hyoid bone and a bilateral modified radical neck dissection of the lymph nodes. The adenocarcinoma measured 40 mm in diameter, with both solid and cystic components (Figure 2).

Figure 3 illustrates the histology of the excised tumour. Fragments of papillary tumour with delicate fibrovascular cores were covered by pleomorphic epithelium; in some areas the architecture was

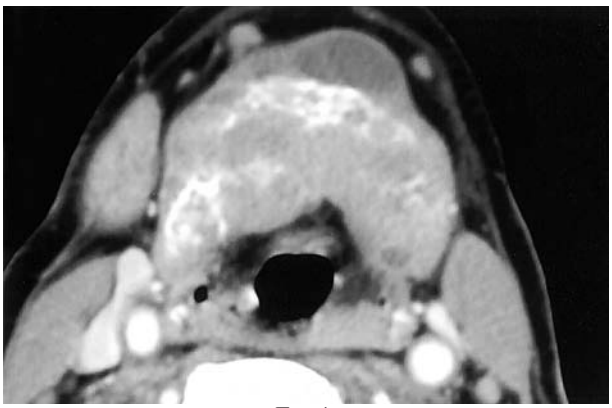

Fig. 1

An axial CT scan of the neck at the level of the hyoid bone (with intravenous contrast) illustrating a grossly expanded hyoid bone with multiple lytic lesions. Associated soft tissue swelling is present. Cervical lymph nodes are not visible.

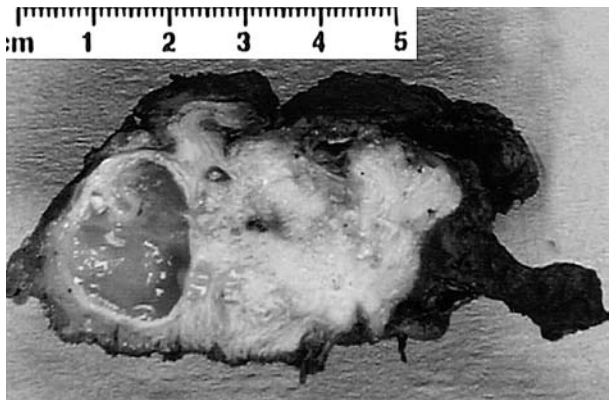

Fig. 2

A cross-sectional photograph demonstrating the gross structure of the tumour. There is a solid white mass and a cyst measuring 25 × 18 mm containing clear fluid.

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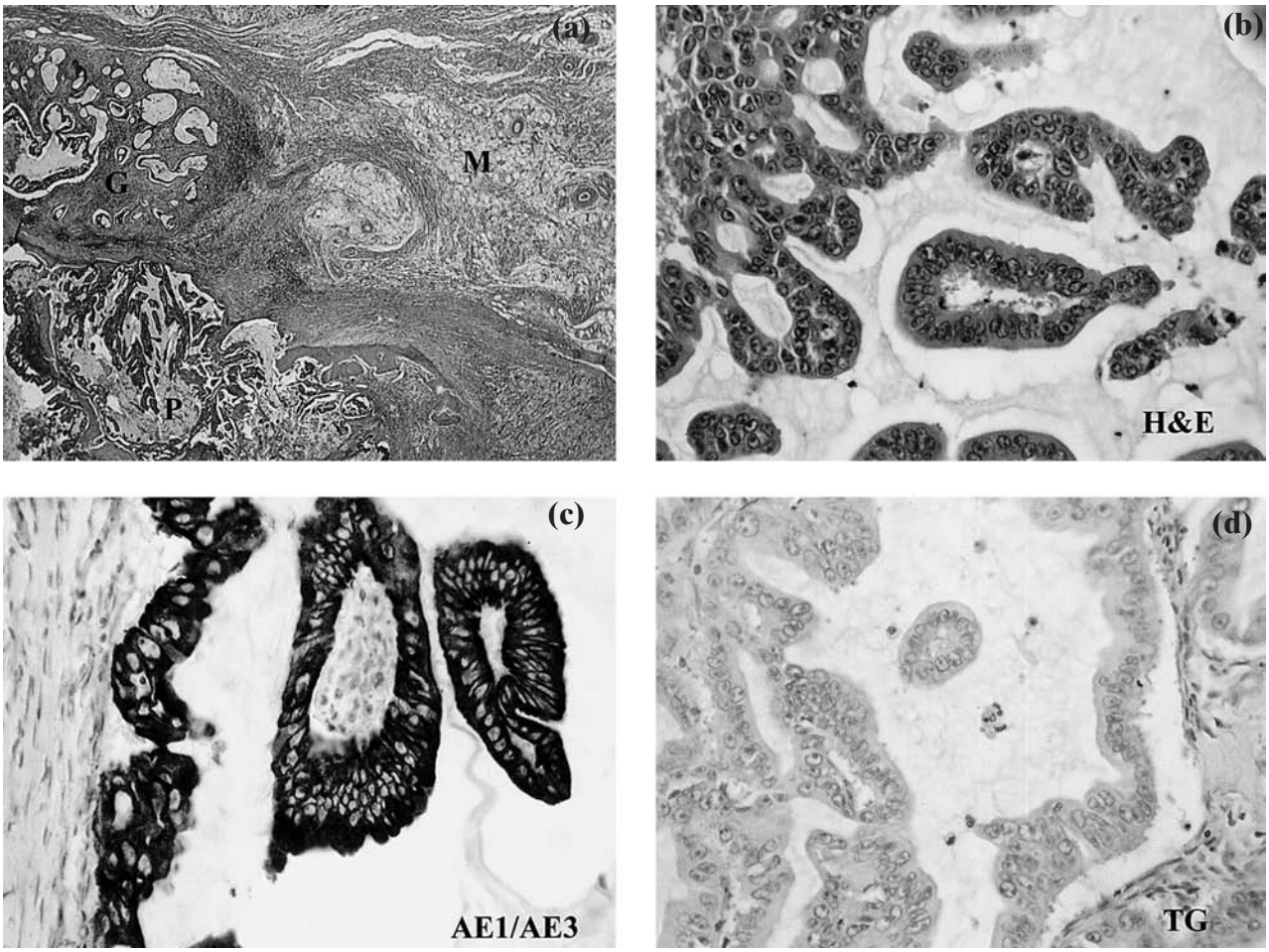

FIG. 3

The photomicrographs show the histology of the excised tumour. (a) Low power of the tumour showing areas of adenocarcinoma with a papillary architecture (P), glandular architecture (G) and abundant mucin production (M). H&E x40. (b) High power view of tumour showing papillary architecture similar to that seen in the core biopsy x400. (c) Immunohistochemistry for epithelial marker AE1, AE3 showing strong positivity of the surface epithelial cells. (d) Papillary tumour showing immunohistochemistry thyroglobulin (TG) showing no positivity. Both at $\times 400$.

glandular and in other areas papillary. The tumour formed cystic spaces filled with mucin and there was evidence of cyst rupture with spaces lined by foamy macrophages and chronic inflammation. The tumour infiltrated the skeletal muscle superiorly. Fragments of the hyoid bone were identified within the tumour but no benign elements of thyroglossal remnant were identified.

Immunohistochemistry tests confirmed an epithelial tumour (AE1/AE3, CAM 5.2 and CEA positive) which had no neuroendocrine differentiation (chromogranin negative), a low proliferation fraction, (less than 5 per cent Ki67 positivity) and some evidence of P53 positivity (less than 5 per cent of nuclei). The tumour was negative for prostatic markers (PSA and prostatic acid phosphatase). Immunohistochemistry for thyroglobulin was performed on the core biopsy and the excised tumour, both of which were negative (Figure 3d).

The appearances were of a moderately differentiated mucin-secreting adenocarcinoma with glandular and papillary architecture.

In the right neck dissection 20 lymph nodes were found, of which five showed metastatic tumour with the largest metastasis 10 mm in diameter. There was no extranodal extension of the tumour. In the left neck dissection 21 lymph nodes were retrieved, of which 10 showed metastatic tumour with the largest positive node measuring 19 mm.

Subsequently the patient received a six-week course of external beam radiotherapy; he remains symptom-free eight months post-operatively.

Discussion

The presentation, radiological and histological findings in this case support our view that the tumour originated locally. The euthyroid status and immunohistochemical marker profile, along with the absence of primary tumours elsewhere, suggested that the tumour arose in the thyroglossal duct.

We conducted a literature search using MEDLINE from 1966 to November 2003 to identify previous cases of papillary adenocarcinoma involving the hyoid bone, cervical lymph nodes or thyroglossal duct remnant. Search terms used were

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TABLE I

TUMOUR TYPES ASSOCIATED WITH DIFFERENT TISSUES IN THE THYROGLOSSAL DUCT

Tissue type associated with thyroglossal duct	Tumour type	Previously described?	Comments
Thyroid tissue	Papillary adenocarcinoma	Most frequently[1]	Forms vast majority of TDR tumours
	Follicular adenocarcinoma	Occasionally[6]	
	Mixed papillary-follicular	Occasionally[7]	
	Anaplastic	Very rarely[8]	
	Undifferentiated	Once[9]	Resembling medullary carcinoma with amyloid stroma
Thyroglossal duct epithelium (non-thyroid origin)			
Squamous tissue	Squamous cell carcinoma	Rarely[9]	Is a rare cause of dermoid cyst development
Glandular tissue	Non-papillary	Gastric and intestinal adenoma	Ciliated columnar, simple columnar, types described[2,3] stratified squamous cuboidal and epithelia were also associated with gastric epithelium
	Papillary adenocarcinoma	Unclear from literature	Many case reports do not make distinction between papillary carcinoma of the thyroid and intestinal adenocarcinoma
	Mucus-secreting papillary adenocarcinoma of intestinal type	Once	This case
Unconfirmed source	Cribriform adenocarcinoma of the tongue	Rarely[10]	Hypothesized to develop from thyroglossal duct anlage
Mixed thyroid, glandular, squamous and lymphoid tissues	Teratoma	Very rarely[5]	Differentiated follicular thyroid tissue, respiratory, transitional and squamous tissues, salivary glands, solid epithelial tissue and lymphoid tissue

'hyoid bone' which was combined with 'adenocarcinoma, papillary', 'head and neck neoplasms' or 'neoplasm metastasis'. Additionally, 'adenocarcinoma, papillary' was combined with 'lymphatic metastasis' or 'head and neck neoplasms' to identify cases where bilateral cervical metastasis of the tumour had occurred. Numerous reports of papillary adenocarcinoma were identified but all were apparently of thyroid origin, arising in the thyroglossal duct remnant. No case reports of tumours with similar histopathology were found within the literature.

The thyroglossal duct is an endodermal structure that enables the embryonic passage of the thyroid to its resting adult position. It is normally lined by squamous epithelium, although transitional, cuboidal and respiratory epithelial types are also described.[1] Although ordinarily the duct involutes during embryogenesis, in approximately 7 per cent of the population incomplete obliteration causes cyst formation within the duct; less than 1 per cent of these cysts become malignant.[1]

The presence of mucus-secreting epithelium in the thyroglossal duct remnant which arises as a diverticulum from the primitive fore-gut in the fifth week of embryogenesis, has been well described by Iswariah and Froome.[2] Chandrasoma and Janssen described a thyroglossal cyst containing both thyroid tissue and gastric mucosa.[3] These authors highlighted the rarity of this phenomenon, explaining why malignancy arising in such mucus-secreting epithelium has not been previously described.

In a series of carefully sectioned thyroglossal ducts, up to 62 per cent were observed to contain ectopic thyroid tissue, which had seeded the duct during development;[4] this tissue is generally considered to be of equal malignant potential to the normal thyroid gland. The classification of the histological features of these tumours is often unclear from the individual case reports and the distinction between papillary cancers that developed from ectopic thyroid tissue and thyroglossal duct epithelium is generally poorly made. The use of nomenclature such as 'epithelioma' (used to describe a solid, apparently undifferentiated, low-grade epithelial carcinoma) compounds this confusion.[5] Table I clarifies the histogenesis by listing epithelia described in thyroglossal duct remnants with

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TABLE II

A COMPARISON BETWEEN THE CRIBRIFORM ADENOCARCINOMA OF THE TONGUE (CAT) AND PAPILLARY ADENOCARCINOMA OF INTESTINAL TYPE

This case	Cribriform adenocarcinoma of the tongue
Encapsulated	Not encapsulated
Papillary and glandular structure	Lobular structure
Solid tumour with mucin-filled cystic spaces	Solid and microcystic architecture
Vesicular tumour nuclei with eosinophilic cytoplasm (Figure 3b)	Pale staining tumour nuclei with ground glass appearance
Abundant mucin production, staining strongly with Alcian Blue, PAS and muci-carmine	Mucin-filled lumina staining strongly with Alcian Blue (pH 2.5), poorly with PAS and muci-carmine
No evidence of myoepithelial differentiation (S100, smooth muscle actin and HHF35 negative)	Myoepithelial component (S100, smooth muscle actin and HHF35 positive)

tumours that have been reported to arise from them.

One review of 115 thyroglossal duct remnant tumours (of all types of tissue) found that 82 per cent were papillary adenocarcinomas; 7 per cent were mixed papillary-follicular carcinomas; 5 per cent were squamous cell carcinomas; and the remainder were follicular and adenocarcinomas of all types, including malignant stroma, epidermoid carcinoma or anaplastic.[1]

Cribriform adenocarcinoma of the tongue (CAT) is another rare, low-grade midline adenocarcinoma of the neck which superficially resembles the solid and follicular variants of the papillary carcinoma of the thyroid.[10] It arises at the base of the tongue and it is speculated to be derived from the thyroglossal duct remnant. As with this case, however, it overgrows any previously existing benign remnants making it impossible to prove the site of origin. The distinction between this case and CAT is made in Table II.

Other abnormal endodermal tissues have also been reported within the thyroglossal cysts, including teratoma containing mixed endodermal and thyroid tissues.[5]

The occurrence of hyoid bone tumours is extremely rare, and we know of no examples where the papillary adenocarcinoma has invaded and destroyed the hyoid bone and metastasized to the cervical lymph nodes. Timon *et al.* describe a hyoid bone and cervical lymph nodes which were infiltrated by a poorly differentiated squamous cell tumour,[11] but whereas the source of this was unknown we propose the probable source of our case as non-thyroid tissue within the thyroglossal duct remnant. However, the unlikely possibility of tumour development from embryological derivatives of the pharyngeal pouches always remains.

Primary tumours of the hyoid previously described in the literature have included chondrosarcomas[12] and giant cell tumours.[13] The hyoid has never been proven as a primary source of squamous carcinoma[10] but bony metastases of head and neck squamous cell carcinomas have been reported as infiltrating the hyoid in 1.6 per cent of laryngeal specimens with pathological evidence of squamous cell carcinoma.[14] In these cases, the invasion of the hyoid was undetectable clinically and was due to the direct spread to the ossified cartilage.

The most widely held explanation for the extremely low incidence of hyoid tumours is that the thyroepiglottic ligament and/or thyrohyoid membrane forms a physical barrier that preserves a tumour-free space between the tumour and the hyoid bone.[14]

In summary, the histopathological features of this tumour and its capacity to invade the cervical lymph nodes and destroy the hyoid bone make it unique. That it was a mucin-secreting papillary adenocarcinoma of intestinal type makes it distinct from either the papillary carcinoma of the thyroid or CAT.

- **Tumours that invade and destroy the hyoid bone are rare but include squamous cell carcinomas, chondrosarcomas and giant cell tumours**
- **It is known that the majority of thyroglossal duct remnant tumours originate within ectopic thyroid tissue**
- **In the case reported here a mucin-secreting papillary adenocarcinoma of intestinal type, which was thought to have originated from a malignant element within the remnant of the thyroglossal duct, invaded the hyoid bone and metastasized to the cervical lymph nodes**
- **This report summarizes the range of tissues contained within the thyroglossal duct remnant and the tumours that have been reported to have arisen from them**

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