CASE REPORT

Composite poorly differentiated mucoepidermoid carcinoma of the thyroid and follicular variant of papillary thyroid carcinoma. Report of a case and review of the literature

Nimeshi S. Jayakody1,*, Morad Faoury1, Lisa R. Fraser1, Sanjay Jogai2, and Nimesh N. Patel1

1Department of Otolaryngology—Head and Neck Surgery, University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton, UK and 2Department of Cellular Pathology, University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton SO16 6YD, UK

*Correspondence address. University Hospital Southampton NHS Foundation Trust, Tremona Road, Southampton SO16 6YD, UK. Tel: +44-23-8120-6511; E-mail: Nimeshi.jayakody@uhs.nhs.uk

Abstract

Mucoepidermoid variant of thyroid carcinoma is a rare and complex disease. Securing a diagnosis and formulating an evidence-based treatment plan is challenging. A case report of a patient with the dual pathology of a composite mucoepidermoid carcinoma of the thyroid and a follicular variant of papillary thyroid carcinoma with malignant metastasis is presented in this article. We discuss the challenges in diagnosis, prognostic factors and management of this rare presentation by reviewing current literature.

INTRODUCTION

Mucoepidermoid carcinoma (MEC) is known to commonly arise in salivary glands but is also seen to occur in organs such as the lung, oesophagus, breast, pancreas and the thyroid [1]. Primary MEC of the thyroid is a rare tumour that is known to have a low-grade histological appearance [1, 2]. The histogenesis of this rare carcinoma has been in debate. MEC in thyroid gland has been theorized to originate from the remnants of the ultimobranchial body, intrathyroidal remnants of the salivary glands, the follicular epithelium, C cells, parathyroid and thyroglossal duct [1–3]. MEC is known to present with other variants of thyroid cancer such as papillary thyroid carcinoma [3].

CASE REPORT

A 71-year-old man was referred by his General practitioner to a district general hospital head and neck clinic with breathlessness and haemoptysis. On initial presentation the patient did not describe any changes in voice, dysphagia, odynophagia, weight loss with a prior smoking history. His past medical history revealed that 6 years previously, he had been fully investigated for a left vocal cord palsy of presumed idiopathic aetiology and had undergone medialisation of injection thyroplasty. Physical examination did not reveal any enlarged cervical lymphadenopathy of the neck. At fibre-optic nasal endoscopy he was noted to have a subglottic mass and
therefore he was referred to a tertiary centre to be cared for under the head and neck multidisciplinary team. Computed tomography (CT) imaging depicted a paratracheal mass within the left trachea-oesophageal groove. Several enlarged lymph nodes were found in the antero-superior mediastinum and left paratracheal space as well as individual lymph nodes in the retrocaval, pretracheal and subcarinal regions. Ultrasound demonstrated several colloid nodules in the thyroid with abnormal heterogenous areas and focal areas of calcification. A positron emission tomography computed tomography (PET/CT) scan further identified lung and bony metastatic deposits. At microlaryngoscopy under general anaesthesia a subglottic mass was biopsied. The initial biopsy results showed stratified squamous epithelium that was hyperplastic and spongiotic with scattered and highly atypical cells with nuclear polymorphism and abundant eosinophilic cytoplasm. Immunohistochemistry of these tissue samples showed positivity for Cytokeratin7 (CK7) and Periodic Acid Schiff Alcian (PAS-alc) blue and negativity for Cytokeratin20 (CK20) and Thyroid transcription factor 1 (TTF1). Due to lack of evidence of thyroid markers on these tissues, an initial diagnosis of ‘mucoid’ tumour of the trachea was made. Based on this evidence, the tumour was staged at T4N2M1.

Clinical management of the patient involved microdebridement of the tumour under general anaesthesia and a palliative dose of radiotherapy (20 Gray in five doses) which failed to improve the patient’s airway obstruction. The patient underwent a surgical tracheostomy at which multiple further pathological samples were taken. These showed evidence of papillary thyroid carcinoma with a follicular growth pattern which was shown to blend imperceptibly with another component of tumour wherein the cells are present in irregular discohesive infiltrating growth pattern. The nuclei of these cells were found to be hyperchromatic with moderate cytoplasm, whilst several of the cells showed intracytoplasmic lumen and eosinophilic inclusions. Immunohistochemistry showed positivity for TTF1 and thyroglobulin in the papillary component of
the carcinoma whilst the poorly differentiated area showed negativity for TTF1 and weak positivity for thyroglobulin. This led to the diagnosis of a follicular variant of papillary thyroid carcinoma with composite MEC of the thyroid. Due to the extensive nature of the disease, the patient was managed with palliative intent and died 2 months later (Figs 1–3).

**DISCUSSION**

Occurrence of MEC in the thyroid as a primary tumour occurs in <0.5% of thyroid tumours [3]. Although there have been reports of ~50 cases of primary mucoepidermoid carcinoma in literature, in a literature search involving EMBASE, MEDLINE and OVID 22 cases of mucoepidermoid occurring with concurrent papillary thyroid cancer were noted. But the presence of MEC with the 'follicular variant' of papillary cancer is even rarer with only two cases which has been described before [4, 5].

The origin of this type of cancer has been debated with several theories suggested (Fig. 4). Two microscopic variants of this carcinoma have been identified according to the histological content of the tumour tissue: mucoepidermoid (MEC) and sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) [3, 6]. The histological appearance of MEC has been defined by the presence of squamous and glandular differentiation within an un inflamed gland [3]. Conversely, SMECE is categorized by the presence of sclerosis and a concomitant eosinophilic infiltrate with a past history of thyroiditis most commonly Hashimoto’s [3]. Immunohistochemistry studies of MEC have shown changes to the cell adhesion complexes such as the new expression of P-cadherin in MEC compared to papillary carcinoma has given rise to theory that MEC is possibly a metaplastic phase of papillary carcinoma [3, 4, 5, 6]. The diffuse sclerosing variant of papillary thyroid cancer has been associated with the SMECE [6, 10].

| Suggested origin | Evidence |
|------------------|----------|
| Solid cell nests (SCN), considered to be remnant of the ultimobranchial apparatus | Histologically, the presence of epidermoid cells, follicular/tubular structures and mucinous cells which are PAS positive has been considered as evidence for the origin to be SCN whilst immunohistochemical studies of MEC have shown similarity between ultimobranchial apparatus and MEC [3]. |
| Follicular origin | Gene expression of TTF1, TTF2, Pax8 and thyroid peroxidase have been shown to be present in MEC providing evidence for the theory of follicular origin [10]. |
| Metaplastic stage of papillary cancer | Immunohistochemical evidence of reduction in the presence of thyroglobulin and increased production of Carcinoembryonic antigen (CEA) in MEC compared to papillary carcinoma has given rise to theory that MEC is possibly a metaplastic phase of papillary carcinoma [3, 4, 5, 6]. The diffuse sclerosing variant of papillary thyroid cancer has been associated with the SMECE [6, 10]. |

**Figure 4:** Table with suggested origins of the mucoepidermoid cancer arising from the thyroid.
shown to give good clinical outcomes [6]. But direct invasion into neck viscera has been shown to be a poor prognostic factor and in such cases treatment with surgery and radiotherapy have been unsuccessful in halting advancement of the disease [6, 8, 9]. Early histopathological diagnosis prior to spread by direct invasion is therefore advantageous in prognosis and treatment options [6, 8].

Dual pathology in thyroid cancer is a rare histopathological entity and provides a diagnostic challenge particularly when the patient presents atypically. The tumour had poor prognostic features at diagnosis and was treated with palliative intent. An agreed management protocol remains to be developed for dual thyroid cancer pathology.

CONFLICT OF INTEREST STATEMENT

None declared.

FUNDING

None.

REFERENCES

1. Prichard RS, Lee JC, Gill AJ, Sywak MS, Fingleton L, Robinson BG, et al. Mucoepidermoid carcinoma of the thyroid: a report of three cases and postulated histogenesis. Thyroid 2012;22:205–9.
2. Rhatigan RM, Roque JL, Bucher RL. Mucoepidermoid carcinoma of the thyroid gland. Cancer 1977;39:210–4.
3. Cameselle-Teijeiro J, Febles-Perez C, Sobrinho-Simoes M. Papillary and mucoepidermoid carcinoma of the thyroid with anaplastic transformation: a case report with histologic and immunohistochemical findings that support a provocative histogenetic hypothesis. Pathol Res Pract 1995;191:1214–21.
4. Miranda RN, Myint MA, Gnepp DR. Composite follicular variant of papillary carcinoma and mucoepidermoid carcinoma of the thyroid. Report of a case and review of the literature. Am J Surg Pathol 1995;19:1209–15.
5. Jung YH, Kang MS. Composite follicular variant of papillary carcinoma and mucoepidermoid carcinoma of thyroid gland: a case report. J Korean Med Sci 2010;25:1683–7.
6. Baloch ZW, Solomon AC, LiVolsi VA. Primary mucoepidermoid carcinoma and sclerosing mucoepidermoid carcinoma with eosinophilia of the thyroid gland: a report of nine cases. Mod Pathol 2000;13:802.
7. Rocha AS, Soares P, Machado J, Máximo V, Fonseca E, Franssila K, et al. Mucoepidermoid carcinoma of the thyroid: a tumour histotype characterised by P-cadherin neoexpression and marked abnormalities of E-cadherin/catenins complex. Virchows Arch 2002;440:498–504.
8. Franssila KO, Harach HR, Wasenius VM. Mucoepidermoid carcinoma of the thyroid. Histopathology 1984;8:847–60.
9. Nath V, Parks GE, Baliga M, Hartle EO, Geisinger KR, Shenoy V. Mucoepidermoid carcinoma of the thyroid with concomitant papillary carcinoma: comparison of findings on fine-needle aspiration biopsy and histology. Endocr Pathol 2014;25:427–32.
10. Minagawa A, Itaka M, Suzuki M, Yasuda S, Kameyama K, Shimada S, et al. A case of primary mucoepidermoid carcinoma of the thyroid: molecular evidence of its origin. Clin Endocrinol (Oxf) 2002;57:551–6.