Case report

Intrathyroid thymic carcinoma/carcinoma showing thymus-like elements
(CASTLE): An extremely rare presentation of thyroid malignancy

S. Abeygunawardhane*, S. Kanagasabapathy, M. Jayawickrama

Department of Histopathology, National Hospital of Sri Lanka

Submitted on 12.06.2023. Accepted for publication on 27.11.2023.

Abstract

Intrathyroid thymic carcinoma, also known as carcinoma showing thymus-like elements/CASTLE, is an uncommon malignancy that arises in the thyroid gland. This tumour shares both morphological and immunohistochemical characteristics with thymic carcinomas. Preoperative diagnosis can be challenging as the clinical and histological features may mimic other high-grade thyroid malignancies. Differentiating CASTLE from other thyroid lesions is important as it has a better prognosis.

A 46-year-old man presented with progressive dysphagia, difficulty in breathing and cough for eight months. The ultrasound scan (USS) revealed a hypoechoic lesion in the right lobe of the thyroid. The cytology specimen obtained through non-US-guided fine needle aspiration (FNA) was reported as Thy5/Bethesda VI, consistent with papillary thyroid carcinoma and a total thyroidectomy was performed. Macroscopic examination revealed a white, non-encapsulated tumour in the right lobe of the thyroid, measuring 45x40x25 mm, with gross extrathyroidal extension. Microscopically, this lesion predominantly showed a squamous morphology with admixed lymphocytes. The tumour cells tested positive for CD5, CD117, CK5/6, CK19 and synaptophysin, and were negative for TTF1 and calcitonin, confirming its classification as CASTLE.

This case brings attention to the difficulties encountered in diagnosing uncommon lesions in both cytology and histology and emphasizes the crucial contribution of immunohistochemistry in navigating through such complex scenarios.

Keywords: CASTLE, thyroid malignancies, ectopic thymic

Introduction

Intrathyroid thymic carcinoma is a rare thyroid carcinoma and accounts for 0.1-0.15% of all thyroid malignancies (1). Most commonly, this condition affects middle-aged individuals and occurs with almost equal ratio in both males and females. (2). Most reported cases were from Asia, including 0.083% of primary thyroid malignancies in Japan and 0.15% in China(2).

Miyauchi et al. first described this entity in 1985 as an “Intra-thyroidal epithelial thymoma” (3). In 1991, Chan and Rosai classified this tumour as "ectopic
hamartomatous thymoma, ectopic cervical thymoma, spindle epithelial tumour with thymus-like differentiation (SETTLE) and carcinoma showing thymus-like differentiation (CASTLE)” (3). The origin of this tumour is likely from ectopic thymic tissue, remnants of the thymopharyngeal duct or branchial pouch remnants (3). SETTLE and CASTLE are on the malignant end of the spectrum (3). Histologically, CASTLE shows similarities to thymic carcinomas, especially squamous cell and lymphoepithelioma-like subtypes (3).

Most cases were found within the thyroid gland with the majority being reported in the lower poles (2). The reported symptoms include neck tumours and hoarseness, which may be caused by recurrent paralysis of the laryngeal nerve (2).

Cytology findings in CASTLE are largely nonspecific. According to one study carried out on CASTLE cytology, the commonest cytological diagnosis given was “malignant tumour or poorly-differentiated carcinoma”. Cohesive sheets and clusters of rounded cells with enlarged, vesicular nuclei, high nuclear:cytoplasmic ratio, prominent nucleoli, amphophilic cytoplasm and lymphocyte-rich background were among the commonest cytological features noted (4). Other notable features that were reported include the presence of keratinized cells with blunted cell borders, halos within the cytoplasm, inclusions and grooves within the nucleus, clumped chromatin, low mitotic activity, spindle-cell morphology, formation of papillary structures, and rosetting of tumour cells (4).

CASTLE is a solid, well-defined tumour lacking encapsulation. Following fixation, the cut surface appears striking ivory-white (2). Calcifications or cystic changes were not reported (2). According to WHO tumour classification, the histopathological features of CASTLE are indistinguishable from those of mediastinal thymic carcinoma. However, immunohistochemical staining assists in differentiating CASTLE from other malignant thyroid tumours. (2)

Case report

A 46-year-old man presented to the ENT unit with progressive dysphagia, difficulty in breathing and cough for eight months. Clinical examination revealed an enlarged thyroid gland.

The fibreoptic laryngoscopy examination revealed subglottic stenosis. The ultrasound scan revealed a 5 mm-sized nodule of TIRADS IV in the isthmus of the thyroid gland and a large hypoechoic nodule in the right lobe of the thyroid. The contrast-enhanced CT scan of the neck showed an irregular enhancement of the right thyroid lobe with retrosternal extension and level III and level IV left cervical lymphadenopathy. There was no evidence of liver, lung or bone metastases.

Non-US-guided FNAC from the nodule in the right thyroid lobe revealed highly cellular smears with papillary clusters and cells showing nuclear grooves, pseudoinclusions and powdery chromatin, compatible with “Thy5/Bethesda VI, papillary thyroid carcinoma”. The nodule in the isthmus was not palpable for non-guided FNAC.

A total thyroidectomy and an extended tracheostomy were performed as the thyroid gland was adhered to the adjacent structures including the carotid sheath and trachea.

Macroscopy revealed a non-encapsulated solid tumour in the right lobe, with a tan cut surface, measuring 45x40x25 mm. The lesion focally invaded the isthmus. There were no cystic areas or gross evidence of tumour necrosis or calcification. Resection margins were involved macroscopically (Figure 1).

Microscopically, the lesion was composed of solid cell nests containing squamoid cells in a lymphocyte-rich stroma. Frequent mitoses were observed. Keratin pearl formation, sarcomatoid differentiation or follicular/papillary structures were not seen (Figure 2).

There was no lymphovascular or perineural invasion. Margin involvement with extra thyroid extension of the tumour was noted. A separate papillary microcarcinoma was present in the isthmus, 5 mm away from the
main lesion. The background thyroid tissue exhibited evidence of chronic autoimmune thyroiditis. Lymph nodes were not present in the specimen.

The tumour cells were diffusely and strongly positive for CD5, KIT, keratin5/6 and keratin19 (Figure 3). There was a positive focal expression of synaptophysin. TTF1 and calcitonin were negative. The Ki-67 proliferation index was 25%. PAX8 was not available. The immunomorphological features confirmed the diagnosis of CASTLE.

The patient completed a course of radiotherapy, and the post-treatment period was uneventful to date.

Figure 1. Macroscopic appearance of the solid tan tumour in the right lobe of thyroid

Figure 2. Microscopic appearance of the tumour. A. Solid nests of cells (H&E x40)  B. Squamoid cell nests in a lymphoid cell-rich stroma (H&E x200)

Figure 3. Immunohistochemistry. Tumour cells showing strong immunoreactivity for KIT (A) and CD5 (B)
Discussion

CASTLE is believed to arise from ectopic thymic tissue residing in the thyroid gland or branchial pouch remnants. The immunohistochemical findings of the solid nests of branchial pouch remnant and cell nests of CASTLE are strikingly similar, indicating a potential common origin. (5). Molecularly, CASTLE shows chromosomal abnormalities similar to thymomas and thymic carcinomas, such as gain on 1q and losses on 6p, 6q and 16q. The commonest genetic mutation noted in the CASTLE is the TERT mutation (5).

According to the WHO classification of endocrine organ tumours, CASTLE is classified as a separate and unique entity (2). Clinical features of CASTLE can vary and are not specific to the disease (6). Imaging modalities such as ultrasound scans, contrast-enhanced CT scans, and MRI scans may be helpful but are usually nonspecific (7).

FNAC is of limited use for the preoperative diagnosis of CASTLE (8). FNAC findings of CASTLE overlap with those of poorly differentiated thyroid carcinoma, anaplastic thyroid carcinoma and squamous cell carcinoma. The lack of awareness of the presence of cytological features that overlap with papillary thyroid carcinoma may have resulted in classifying CASTLE as papillary thyroid carcinoma in cytopathology.

CASTLE exhibits histopathological characteristics that closely resemble those of mediastinal thymic carcinomas (2). The tumour displays squamous cell carcinoma morphology with an abundant lymphocyte-rich stroma. Notably, there is absence of follicular or papillary structures (2).

The tumour cells display positivity with CD5, P63, KIT, BCL2, P53 and cytokeratins, establishing its connection with the thymic origin. Furthermore, the absence of thyroglobulin, TTF1, calcitonin and LCA in the tumour excludes the possibility of thyroid malignancies and lymphomas (2). The neuroendocrine nature of certain cases was confirmed by synaptophysin and chromogranin A positivity (2). The Ki-67 proliferation index typically ranges between 10% and 30%. KIT, P63 and CD5 are valuable markers for distinguishing CASTLE from other aggressive thyroid malignancies (2,9). CD5 is helpful in differentiating CASTLE from other carcinomas of the region (2,10). P63 shows a strong positive correlation with thymic tumours, while it is negatively associated with both thyroid follicular carcinomas and poorly differentiated carcinomas (9,11).

The intrathyroid thymic carcinoma is known for its aggressive local invasion (2) and is characterized by its favourable prognosis (8). The disease-specific survival rates reported for 5 years, and 10 years are 90% and 82%, respectively (2). One-third of the reported cases showed nodal metastases (9). Invasion into the adjacent soft tissue is about 60% (12). Previous studies have demonstrated that the existence of nodal metastasis and local invasion can serve as indicators of a challenging prognosis (2). It has been shown that postoperative external radiation therapy can offer an effective result (2).

References


