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Case Report

A Rare Case of Thyroid Carcinoma Showing Thymus-Like Differentiation in a Young Adult

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Keyterms
CASTLE · Thyroid cancer · Thymus-like differentiation

Abstract
Thyroid carcinoma showing thymus-like differentiation (CASTLE) is thought to originate from ectopic thymic tissue or remnants of the developing thymus within or adjacent to the thyroid. This case report describes a mass located on the left thyroid of a 28-year-old man. Fine-needle aspiration cytology revealed a number of lymphoid cells without atypia that were similar to those seen in a malignant lymphoma of the thyroid, and surgery was performed. Based on additional histopathological findings, the tumor was finally diagnosed as a CASTLE. It is difficult to diagnose this neoplasm using fine-needle aspiration cytology. However, it is possible to differentially diagnose CASTLE based on its histological features. CD5 is useful for diagnosing CASTLE with immunohistochemical staining.

Introduction

Carcinoma showing thymus-like differentiation (CASTLE), also known as intrathyroid thymic carcinoma, is the malignant counterpart of ectopic thymoma of the thyroid gland [1, 2]. It is currently designated as an independent clinicopathological entity from thyroid neoplasms according to the 2004 World Health Organization classification of endocrine tumors [3]. CASTLE is a very rare thyroid cancer, with an estimated incidence of 0.083% (8

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Table 1. Blood test results

WBC/μL	5,650	CRP, mg/dL	<0.02
Hb, g/dL	14.1	Na, mEq/L	141
PLT × 10^4/μL	20.8	K, mEq/L	4.5
Total protein, g/dL	7.2	Cl, mEq/L	104
Albumin, g/dL	4.7	TSH, μIU/mL	1.993
AST (GOT), IU/L	17	FT4, ng/dL	1.15
ALT (GPT), IU/L	18	FT3, ng/dL	2.96
LD, IU/L	142	Tg, ng/mL	50.3
Creatinine, mg/dL	0.94	Tg-Ab, IU/mL	<10.0
Glucose, mg/dL	97	TPO-Ab, IU/mL	<100

AST, aspartate aminotransferase; ALT, alanine aminotransferase; WBC, white blood cells; Hb, hemoglobin; PLT, platelets; GOT, glutamic oxaloacetic transaminase; GPT, glutamic pyruvic transaminase; LD, lactate dehydrogenase.

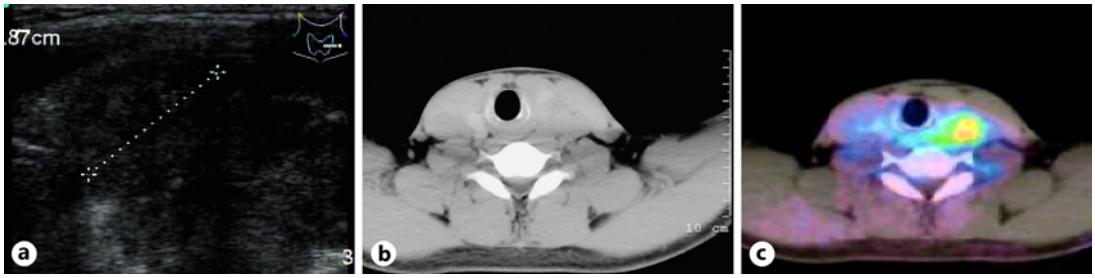

Fig. 1. Preoperative imaging. **a** Cervical ultrasonography shows a low echoic and unclear solid mass in the lower pole of the left thyroid lobe. **b** CT image reveals a low-density mass in the left thyroid lobe. **c** Positron-emission tomography shows ^{18}F-FDG accumulation in the left thyroid tumor (standardized uptake value of 5.29).

out of 9,582 cases) of primary thyroid malignancy in Japanese patients and 0.15% (3 out of 2,033 cases) in Chinese patients [4, 5]. Herein, we report a rare malignant neoplasm of the thyroid gland in a young adult patient.

Case

The patient, a 28-year-old man with a 3-month-old mass in the neck was referred to our department. The mass, located on the left thyroid lobe, was elastic, hard, showed limited mobility, and measured approximately 30 × 20 mm. There was no remarkable tenderness over the mass.

Blood examination results were normal, including levels of thyroid-stimulating hormone, free thyroid hormone, and thyroglobulin (Table 1). Ultrasonography revealed a hypoechoic solid mass in the lower pole of the left thyroid lobe with a poorly marginated heterogeneous pattern (Fig. 1a). Computed tomography revealed a heterogenic tumor in the left thyroid lobe (Fig. 1b). ^{18}F-fluorodeoxyglucose (^{18}F-FDG) accumulated in the thyroid tumor on positron-emission tomography. The standardized uptake value of ^{18}F-FDG was 5.29 (Fig. 1c). Fine-needle aspiration cytology (FNAC) showed a number of lymphoid cells without atypia that were similar to those seen in malignant lymphoma of the thyroid (Fig. 2).

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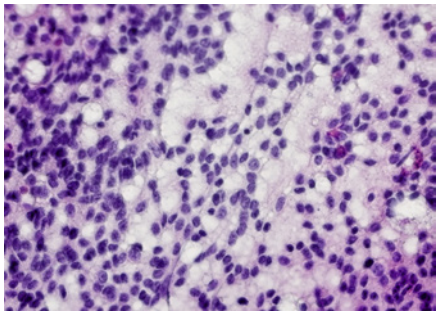

Fig. 2. FNAC shows numerous lymphoid cells without atypia.

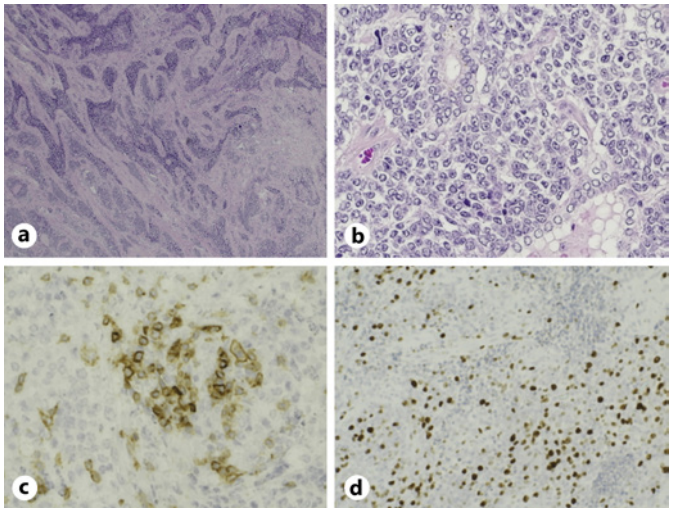

Fig. 3. Histological findings. **a** Thick fibrous septa intersecting the tumor cells into lobules. Hematoxylin-eosin stain, ×40. **b** Tumor cells have a round nucleus with remarkable nucleolus. Hematoxylin-eosin stain, ×400. Immunohistochemical studies showed the tumor was CD5 partially positive (**c**) and Ki-67 positive (**d**).

As we diagnosed a highly malignant thyroid cancer (cT2N0M0), we performed a left hemithyroidectomy with central neck dissection (ND). Histopathological findings showed that the tumor was composed of irregular insular nests of neoplastic cells and had an expansive growth pattern in the thyroid (Fig. 3a). The carcinoma cells had round nuclei or polymorphonuclei with well-defined nucleoli and ill-defined cell borders (Fig. 3b). Immunohistochemical studies showed that the tumor was partially positive for CD5, positive for Ki-67 (approx. 30%), and negative for CD20, calcitonin, and thyroglobulin (Fig. 3c, d). Based on these histopathological findings, the tumor was finally diagnosed as CASTLE. There were no signs of recurrence without additional treatment after 10 years of follow-up.

Discussion

CASTLE is a rare malignant neoplasm that was originally described by Miyauchi et al. [1] in 1985. Their group reported 25 patients with CASTLE, including 11 men and 14 women [6]. The patients' mean ages were 52.4 years (SD ±18.6). Chan et al. [7] reviewed 26 patients with an age range of 25–71 years; this showed that middle-aged individuals are susceptible to CASTLE [8]. Moreover, there were no distinguishing characteristics, even with FNAC. Preoperative examinations are usually unable to provide a conclusive diagnosis for CASTLE [8]. Therefore, it is very difficult to diagnose CASTLE in young adults before surgery.

Histologically, CASTLE shares typical morphological characteristics with thymic carcinoma, such as pleomorphic or spindle-shaped cells, with oval or vesicular nuclei having

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prominent nucleoli, fibrous septa dividing the tumor nests, peritumoral and intratumoral infiltration of lymphocytes and plasma cells, infrequent mitoses, and mild nuclear atypia [1, 3, 8, 9]. These features were also seen in our case.

CD5 is a transmembrane protein associated with the T cell receptor that is expressed by all mature T cells and some leukemic B cells. It negatively modulates T cell activation and differentiation, and is also expressed in thymic carcinoma [10]. Therefore, CD5 is used as a marker of thymic origin. Ito et al. [6] reported a sensitivity and specificity of 82 and 100%, respectively, for CD5-based diagnoses of CASTLE. Although its negative expression does not completely rule out CASTLE, CD5 can sufficiently help us diagnose CASTLE.

Surgical resection of the tumor is the gold standard for CASTLE treatment [8]. When it was performed, CASTLE had a favorable prognosis; the 5- and 10-year cause-specific survival rates were 90 and 82%, respectively [6]. However, it is said that about one-third to half of the patients have lymph node metastases [6, 11, 12]. Previous reports suggested thyroidectomy with ND to achieve more favorable outcomes. In particular, CASTLE with extrathyroidal extension might be more susceptible to lymph node metastasis. Therefore, thyroidectomy with central ND should always be performed, including prophylactic ND in all CASTLE patients with tumors of clinical stage N0 in the neck [6, 8, 11, 12]. Furthermore, Dong et al. [12] suggested that therapeutic ipsilateral or bilateral ND should be performed for patients with suspected or biopsy-proven lateral cervical lymph node metastasis.

There is still a controversy over whether postoperative radiotherapy and chemotherapy should be performed. Dong et al. [12] reported 6 patients with CASTLE who had extrathyroidal extensions, including 2 with lymph node metastases who underwent radical surgery without postoperative radiotherapy or chemotherapy. Only 1 patient developed lateral cervical lymph node metastasis 26 months after initial treatment. The authors concluded that radical surgery can yield favorable outcomes for CASTLE patients [12]. Reports of postoperative radiation to prevent locoregional recurrence have been gaining traction in the literature. However, there are also reports of patients who received radiotherapy for distant recurrence after surgery. Gao et al. [8] reported that lymph node metastasis and tumor invasion into adjacent tissue had a negative effect on survival, while radiotherapy significantly improved survival. Currently, postoperative radiation seems promising, but further examination of its long-term efficacy is needed. The efficacy of chemotherapy is unknown because there are insufficient data substantiating this treatment. In our case, the patient refused postoperative radiotherapy and was disease-free for 10 years.

Conclusion

Here, we report a rare case of CASTLE. Although it is difficult to diagnose using FNAC, CASTLE may be suspected by its histological features. CD5 is useful for diagnosing CASTLE in immunohistochemical staining. Curative surgery is effective in managing thyroid CASTLE tumors.

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Statement of Ethics

This study was approved by the Ethics Committee of the institutional review board of Wakayama Medical University (No. 2964), and informed consent was obtained in the form of an opt-out on the Japanese website due to loss of contact.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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Author Contributions

Eri Kimura and Keisuke Enomoto drafted the manuscript; Saori Takeda and Naoko Kumashiro provided the clinical information; Shun Hirayama and Takahito Kimura made the imaging diagnosis; Shunji Tamagawa, Masamitsu Kono, and Muneki Hotomi participated in manuscript revision.

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