Case Report

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Follicular dendritic cell sarcoma presenting as a thyroid mass: an unusual case report and literature review

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Abstract

Thyroid follicular dendritic cell sarcoma (FDCS) is an extremely rare malignancy that originates from follicular dendritic cells of the germinal centers and is characterized by the neoplastic proliferation of spindled to ovoid cells. As there have been only five cases reported in the literature until now, the diagnostic and therapeutic information available to clinicians regarding thyroid FDCS is fairly limited. To our knowledge, this is the first case report of thyroid FDCS without a history of Hashimoto's thyroiditis. A 48-year-old woman was found to have a slow-growing mass in the left thyroid. After total thyroidectomy and left modified radical neck dissection, the specimen demonstrated morphologic and immunohistochemical features of FDCS. The patient had a favorable prognosis with no evidence of disease 11 months after tumor excision.

Keywords

Follicular dendritic cell sarcoma, thyroid, diagnosis, treatment, thyroidectomy, Hashimoto's thyroiditis

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Introduction

Follicular dendritic cell sarcoma (FDCS) was first described by Monda et al.[1] based on four cases of unilateral cervical adenopathy in 1986 and is an uncommon lymph node malignancy of antigen-presenting

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cells of the B-cell follicles. FDCS acts as an essential element of the germinal centers of B-cell follicles, and thus is commonly present not only in nodal but also extranodal lymphoid follicles.[2] Most FDCS described in the literature have occurred in the lymph nodes, while approximately 30% of the reported cases were located in extranodal sites throughout the body, including the pharynx, tonsil, pancreas, peritoneum, spleen, stomach, liver, and lung.[3–10] FDCS involving the thyroid is extremely rare, and until now, only five cases had been reported in the English and Chinese literature.[11–14] Therefore, it remains challenging for clinicians to make a rapid diagnosis of thyroid FDCS, which is easily confused with poorly differentiated and undifferentiated carcinomas, spindle epithelial tumor with thymus-like differentiation (SETTLE), and spindle cell carcinoma. To our knowledge, the previous five thyroid FDCS cases were accompanied by a history of Hashimoto's thyroiditis. Here, we report the first case of thyroid FDCS without a history of Hashimoto's thyroiditis, summarized the related clinical symptoms and pathological changes, thereby broadening the ability to recognize this neoplasm.

Case presentation

Clinical findings

A 48-year-old female farmer in northeast China sought clinical attention owing to the swollen feeling of a cervical mass for 1 month. She had no family history and had not received any treatment or medication. The patient denied cervical pain, dysphagia, hoarseness, and other past medical conditions. On the local examination, a 5-cm painless movable nodule could be touched in region III of the left neck. Ultrasonography demonstrated that a hypoechoic nodule (size: 57.4×42.4 mm) was located in the left lobe of the thyroid, accompanied by regional lymph node enlargement in ipsilateral region IV. Doppler scan showed augmented internal blood flow in the mass. Subsequent computed tomography (CT) of the thyroid found a heterogeneous enlargement at the left lobe of the thyroid, a metastatic lesion in left cervical lymph node, and slight airway constriction (right shift of the trachea, Figure 1a and 1b). Endocrinological tests showed that thyroxine and thyroid autoantibody levels were within the normal range (Table 1), indicating that the thyroid function of the patient was normal. The patient underwent left thyroidectomy and lymph node biopsy, and the initial diagnosis was SETTLE or FDCS. Subsequently, the patient was sent back to the operating theater for a total thyroidectomy and left modified radical neck dissection. Based on the histologic morphology and the immunohistochemical features of the resected cervical lesions, a pathological diagnosis of thyroid FDCS was ultimately made. Only one metastatic lymph node was distinguished in the left cervical dissection sections. After L-thyroxine replacement therapy, the patient became euthyroid with no evidence of disease 11 months after treatment.

Histopathological findings

Grossly, the left lobe of the thyroid was almost completely affected by the tumor (measured size: $6.0 \times 4.0 \times 4.0$ cm), and the right lobe showed a diffuse goiter. The encapsulated tumor was solid, grayish yellow, tough, and did not show obvious necrosis or hemorrhage (Figure 1c and 1d). Microscopically, the tumor comprised oval to spindle cells with various architectural patterns including storiform, fascicle, and concentric whorl patterns (Figure 2a and 2b). Scattered multinucleated giant cells that were similar to Warthin–Finkeldey giant cells were occasionally seen in the tumor.

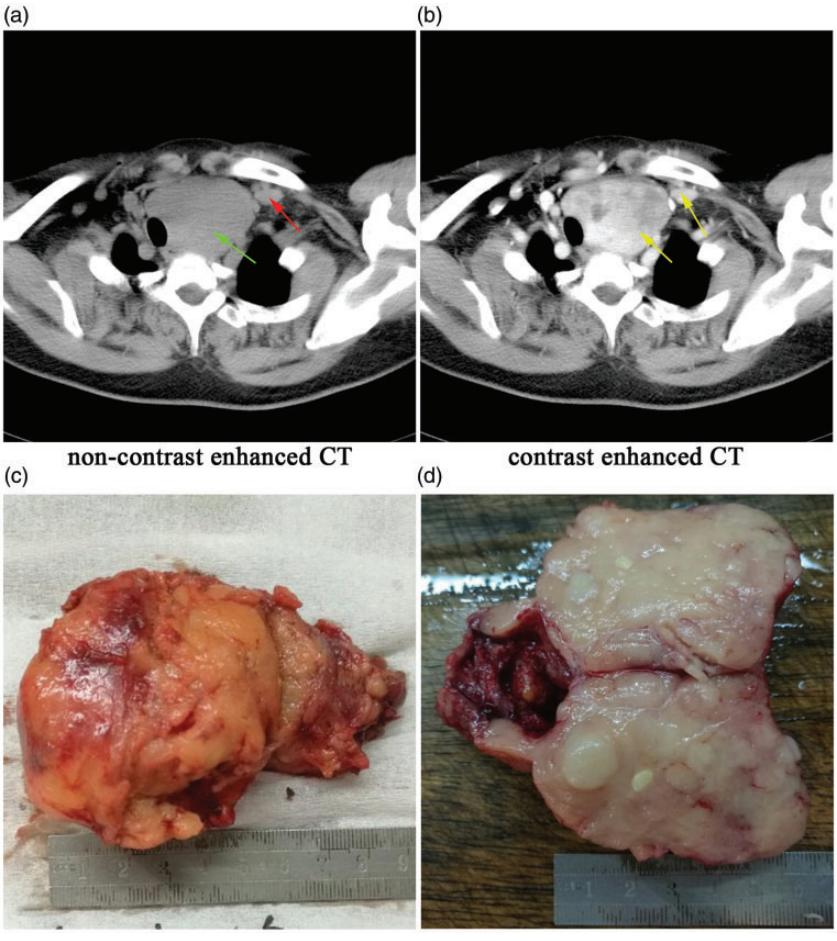

Figure 1. Thyroid follicular dendritic cell sarcoma (FDCS). (a) The left thyroid lobe (green arrow) and cervical lymph node (red arrow) were heterogeneously enlarged. (b) The lesions were significantly enhanced (yellow arrows). (c) Panoramic view of the thyroid FDCS that was located in the left lobe. (d) The cut surface of the thyroid FDCS without obvious necrosis or hemorrhage.

Table 1. Endocrinological tests for thyroxine and thyroid autoantibodies before surgery.

	Reference range	Test value
Thyrotropin	0.35–4.94 mIU/L	75.42
Free triiodothyronine	2.63–5.7 pmol/L	7.73
Free thyroxine	9.01–19.05 pmol/L	3.34
Anti-thyroglobulin antibody	0.00–4.11 IU/mL	1.66
Anti-thyroid microantibody	0.00–5.61 IU/mL	0.33

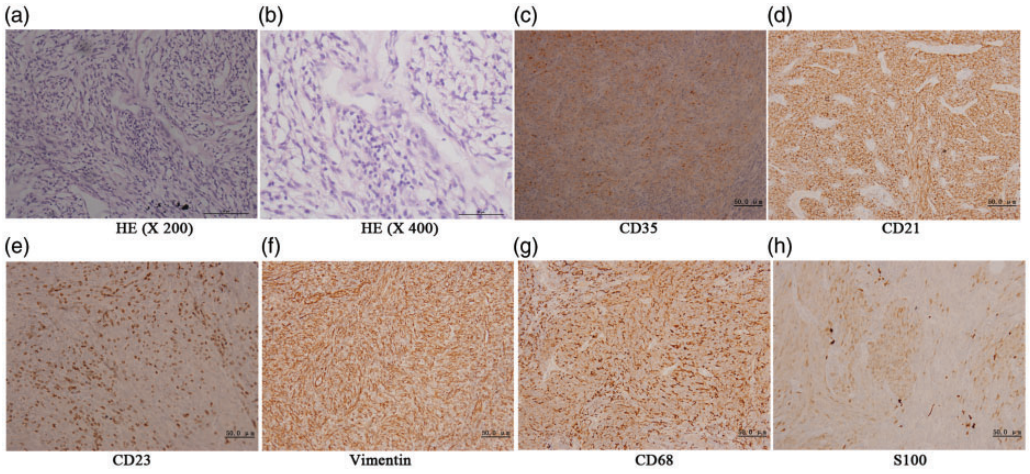

Figure 2. Cytomorphology and immunohistochemistry of the follicular dendritic cell sarcoma (FDCS) located in the left thyroid lobe. The thyroid FDCS was primarily composed of oval to spindle cells with eosinophilic cytoplasm, prominent nuclei and dispersed chromatin. Images of hematoxylin and eosin stained tissues at 200× (a) and 400× (b) magnification. The thyroid FDCS was positive for CD35 (c), CD21 (d), CD23 (e), vimentin (f), CD68 (g), and S100 (h) (magnification: 200×).

The tumor cells possessed indistinct borders, moderately abundant cytoplasm, and a syncytial appearance, which were consistent with the typical characteristics of FDCS. Their nuclei, round to elongated with a thin nuclear membrane, were vesicular and hyperchromatic. Immunohistochemically, tumor sections were positive for CD21, CD35, CD23, vimentin, CD68, S100 (partial) (Figure 2c–2h), CD5, and terminal deoxynucleotidyl transferase (TdT, sporadic) (Figure 3a–3d). Staining for Lysozyme, thyroglobulin (TG), and transcription termination factor-1 (TTF-1) were all negative (Figure 4). These immunohistochemistry results confirmed the diagnosis of thyroid FDCS.

Ethics

The study was approved by the ethics committee of The First Hospital of China Medical University. Written informed consent from the patient was obtained before presentation of the study.

Discussion

FDCS is an uncommon neoplasm that originates from the follicular dendritic cells of the germinal centers, which are primarily located in lymph nodes. Therefore, the thyroid gland is an extremely rare location to find a FDCS. To date, only five previous cases of thyroid FDCS have been reported in the literature (Table 2).[11–14] Thyroid FDCS cases primarily involve middle-aged patients (average age: 50.2-years-old). Thyroid FDCS is more likely to occur in women based on four (80%) of the reported cases having involved female patients. Thyroid FDCS patients have clinically presented with a single, slow growing, well-circumscribed mass in the neck, without a history of pain, dysphagia, hoarseness, or loss of weight and appetite. The majority of thyroid FDCS patients were euthyroid. Positivity for Epstein–Barr virus (EBV) *in situ* hybridization and Castleman's disease, which are FDCS-related risk factors, were not found in three of the previously reported thyroid FDCS cases.[15,16]

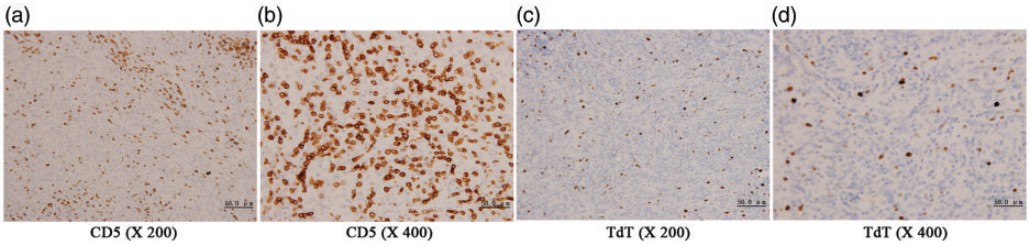

Figure 3. Immunohistochemistry for T lymphocytes. Immunohistochemical staining for CD5 and TdT in the thyroid follicular dendritic cell sarcoma (magnification: 200× and 400×).

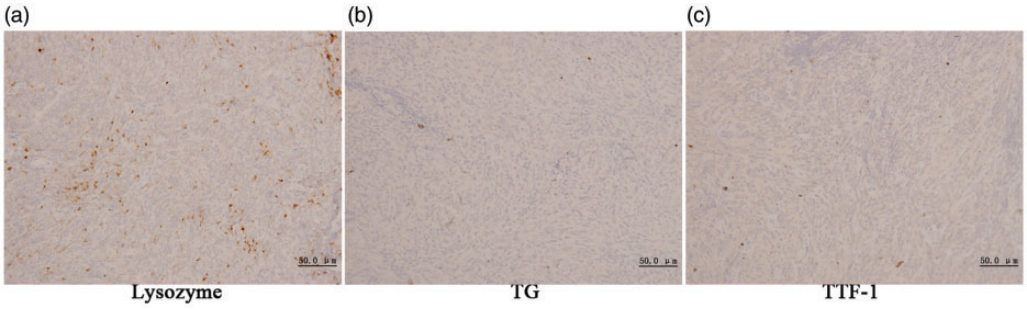

Figure 4. Representative immunohistochemical staining images of the thyroid follicular dendritic cell sarcoma tissue. The thyroid follicular dendritic cell sarcoma tissue was weakly positive for Lysozyme (a) and negative for TG (b) and TTF-1 (c) (magnification: 200×).

Interestingly, all previously reported thyroid FDCS cases have had a history of Hashimoto's thyroiditis and lymphatic infiltration in the tumor and adjacent thyroid tissues.[11–14] Except for Hashimoto's thyroiditis history, the clinical manifestations of our case were consistent with those of previous cases. Hence, we preliminarily inferred that Hashimoto's thyroiditis was not an essential cause of FDCS.

Thyroid ultrasonography is the preferred method for imaging thyroid nodules and helps clinicians identify the indolent and aggressive types. However, thyroid FDCS usually presents as hypoechoic or isoechoic nodules without typical imaging features.[13] CT scan is the secondary imaging procedure for FDCS, and allows confirmation of the presence of a thyroid mass, determining tumor extension, and ensuring the status of local lymph nodes. Ultrasonography-guided fine needle aspiration cytology (FNAC) can be a valuable tool for diagnosing thyroid FDCS. However, considering the accuracy of FNAC and the infrequency of thyroid FDCS, it continues to be difficult to get a firm diagnosis from an expert cytologist. As described in the previous case studies, FNAC results of thyroid FDCS might be confused with poorly differentiated and undifferentiated carcinoma of the thyroid.[13] Although clinicians cannot directly obtain a final diagnosis from routine imaging and cytology tests, such as ultrasound examination, CT scan, and FNAC, these examinations remain indispensable.

On gross examination, thyroid FDCS is usually described as a single, well circumscribed, resilient tumor, occasionally with

Table 2. Summary of previous thyroid follicular dendritic cell sarcoma cases in the literature.

No.	Sex/Age (years)	Primary diagnosis	Treatment	Tumor size (cm)	IHC positivity	Adjuvant therapy	Follow-up	Reference
1	Female/65	Poorly differentiated non-small cell carcinoma	Total thyroidectomy, right modified radical neck dissection	4	CD 21, vimentin	Radiotherapy	36 months, NED	11
2	Female/58	NA	Subtotal thyroidectomy	2	CD35, vimentin, CD68, lysozymes, S100, Fascin, CD45, CD45RO, HLA-DP, DQ, HLA-DR	NA	NA, NA	12
3	Female/44	Anaplastic thyroid carcinoma	Total thyroidectomy, central compartment dissection, parathyroid reimplantation	2.5	CD21, CD23, vimentin, clusterin, Fascin, podoplanin, CXCL13	Radiotherapy	NA, NA	13
4	Female/48	Thyroid spindle cell tumor	Thyroidectomy	5	CD21, CD23, CD35, vimentin, CD68 (weak)	Chemotherapy, radiotherapy	6 months, NED	14
5	Male/36	Spindle cell tumor	NA	2.6	CD21, CD23, CD35, vimentin, CD68 (weak)	None	14 months, NED	14

Notes: IHC, immunohistochemistry; NA, not available; NED, no evidence of disease.

necrotic and hemorrhagic areas. In this case, the cut surfaces of the tumor showed a rather homogeneous gray tissue. It has been reported that the diameter of thyroid FDCS ranges from 2 to 4 cm, with an average of approximately 3.22 cm. Histopathologically, thyroid FDCS is typically composed of oval to spindle cells with eosinophilic cytoplasm, prominent nuclei, and dispersed chromatin. Additionally, the characteristic growth patterns include concentric whorls, fascicles, and focal storiform, accompanied by scattered multinucleated tumor cells. All of these typical morphologic features must be simultaneously considered in the differential diagnosis of thyroid FDCS. While the differential diagnoses could cover malignant lymphoma, undifferentiated carcinoma, and SETTLE, thyroid FDCS can be differentiated from these by immunohistochemical staining. Thyroid FDCS cells are typically positive for CD21, CD23, CD35, and vimentin, show variable positivity for CD68, CD45, S100, and epithelial membrane antigen (EMA), and are negative for cytokeratin, smooth muscle actin (SMA), CD34, and CD3. Unlike thyroid FDCS, positive CD3 expression is observed in malignant lymphoma.[17,18] The tumor cells of thyroid undifferentiated carcinoma are generally positive for cytokeratin and EMA.[19] SETTLE is a rare slow-growing tumor commonly composed of epithelioid and spindle cells, but is easily distinguished from thyroid FDCS by positive staining for cytokeratin.[20,21] Recently, it was demonstrated that podoplanin (D2-40) is a mucin-type transmembrane glycoprotein that shows strong expression in FDCS but is not expressed in normal or neoplastic lymphoid cells.[22–24] Positive diffuse podoplanin staining may be a sensitive and specific marker for thyroid FDCS. Additionally, Clusterin is another apoptosis-related glycoprotein that is highly expressed in FDCS and could be used to distinguish FDCS.[25] Thus, thyroid FDCS possesses a distinctive immunophenotype, namely, expressing dendritic cell markers and absence of cytokeratin expression. In this case, immunohistochemical staining for CD5 was positive, which might be due to the presence of intratumoral T lymphocytes. Additionally, TdT-positive T lymphocytes were only present in the bone marrow and thymus during physiologic motion.[26] Our thyroid FDCS section was sporadically positive for TdT, which might be related to paraneoplastic pemphigus; however, the recruitment mechanisms of TdT-positive immature T lymphocyte remain unknown. As a defined diagnostic criteria for thyroid FDCS has not yet been established, these histopathological and immunohistochemical analyses should be implemented simultaneously to avoid misdiagnoses.

While FDCS is a low-grade malignancy, the literature indicates that the rates of local recurrence and distant metastasis are approximately 40% to 50% and that the mortality rate is approximately 20%, which suggests that FDCS is a higher grade lesion.[27–29] Tumor location and size, mitotic count, and significant cellular atypia are important prognostic factors for FDCS. Combining the recommend treatment from the World Health Organization Classification of Tumors of Hematopoietic and Lymphoid Tissues (Revised 4th Edition) and the five previous cases studies of thyroid FDCS, complete surgical excision with or without adjuvant radiotherapy or chemotherapy appears to be the uniform therapeutic modality. However, owing to the lack of a uniform indication for use, the value of chemotherapy and radiotherapy and the best therapeutic regimen remains to be explored.

In this study, we report the first case of thyroid FDCS without a history of Hashimoto's thyroiditis in a 48-year-old woman and review the related literature.

Our experience highlights the need to obtain clinical imaging to ascertain tumor location and lymph node status. Histopathology and immunohistochemistry are essential indicators to identify thyroid FDCS from related malignancies. Thyroid FDCS is relatively indolent and has preferable clinical outcomes. Complete surgical resection is the best treatment for thyroid FDCS, but the effects of adjuvant chemotherapy and radiotherapy remain to be rigorously tested.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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