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Diffuse Large B-Cell Lymphoma of Thyroid

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Abstract

Primary thyroid lymphoma (PTL) is a rare malignancy and represents <5% of all thyroid malignancies, <3% of extranodal lymphomas and 1–3% of all malignant lymphomas [1,2]. This rare disease usually affects middle to older aged individuals with a female predilection, and presents with a rapidly enlarging anterior neck mass with or without cervical lymphadenopathy, often leading to compressive symptoms [2]. To diagnose it accurately and to differentiate it from other thyroid malignancies, along with Fine needle aspiration cytology(FNAC), True cut needle biopsy and immunohistochemistry studies are very important, as primary thyroid lymphoma is highly curable with combination chemotherapy and radiotherapy, without thyroidectomy. We report a case of a 55years old female who presented with a thyroid swelling and was diagnosed with Primary Thyroid Lymphoma- Diffuse Large B-cell Lymphoma of Thyroid (DLBCL), after cytology and histopathology.

Keywords: Primary Lymphoma, DLBCL, Thyroid

Introduction

The global burden of Non-Hodgkin's lymphoma (NHL) has been steadily increasing, with NHL causing significant morbidity and mortality.[3] Around 25% of NHL arise in tissues other than the lymph node, spleen, Waldeyer's ring and thymus, and are referred to as primary extra nodal NHL (EN-NHL). It has been observed that the incidence of EN-NHL has increased more rapidly than the nodal type. [3] Primary thyroid lymphoma (PTL) is a rare malignancy. It represents <5% of all thyroid malignancies and 1–3% of all malignant lymphomas [1,2]. This rare disease usually affects middle to older aged individuals, with a female predilection and presents with a rapidly enlarging anterior neck mass with or without cervical lymphadenopathy, often leading to compressive symptoms [2,3]. Diagnosing it accurately and to differentiate it from other thyroid malignancies is very important, as primary thyroid lymphoma is highly curable without thyroidectomy. Most primary thyroid lymphomas are B cell Non-Hodgkin's lymphoma and are usually treated by a combination of chemotherapy and radiotherapy.[4] Ultrasonography (USG) guided fine-needle aspiration cytology (FNAC) of the thyroid lesion is a simple, cost effective, accurate and rapid to perform investigation for thyroid lesions. Fine needle aspiration cytology added with flow cytometry and immunohistochemical studies may be more sensitive and specific.

Case Report

A 55years old female came with complaints of pain and swelling in the anterior aspect of neck, increasing

progressively in size for four months. She had difficulty in swallowing since five days. No significant past history. On examination: Thyroid swelling of size 5×4 cm, oval, firm to hard in consistency, was present. Overlying skin was normal. Swelling moved with deglutition. Bilateral supraclavicular lymph nodes were palpable, firm to hard in consistency. On the right side, it was 3×2cm and on the left side, it was 1.5×1cm[Figure 1]. Laryngoscopy was normal.

USG Thyroid showed Left lobe msg. 5.9×1.9×1.7cm, with evidence of few anechoic cystic areas with increased vascularity. Right lobe showed hypoechoic lesion of size 3.2×2.7×2.6cm, with increased vascularity.

Investigation- CBC: Hb: 9.1gm% TLC: 4,200/mm^3,

DLC: P64, L31, M1, E4; Platelet:1,01,000/mm^3.

Peripheral Smear- Normal. Urea: 18.4 mg/dL. Creatinine: 0.2mg/dL, HIV/HBsAg: Negative. Thyroid profile: Normal.

FNAC smears from right lobe of thyroid and right supraclavicular lymph node revealed similar morphology. They were cellular and showed mainly dispersed as well as few groups of cells with scanty cytoplasm. The cells were large with large nuclei showing pleomorphism, with prominent nucleoli. Few nuclei appeared lobulated. Lymphocytes were also seen. [Figure 2] The cytological features were suggestive of Poorly differentiated malignancy, Thyroid and right supraclavicular lymph node.

Differential diagnosis: 1) Anaplastic large cell lymphoma.

2) Anaplastic carcinoma of thyroid

The right cervical lymph node was biopsied and sent for histopathology. Histopathological examination of cervical lymph node revealed many large tumour cells arranged in diffuse pattern, with large vesicular nuclei with prominent nucleoli and moderate amount of cytoplasm. Few nuclei showed multilobation. There was moderate pleomorphism. Lymphocytes were also seen. [Figure 3]

Histopathological features were suggestive of Non Hodgkin's Lymphoma-Diffuse Large B-cell type.

Immunohistochemistry study revealed Tumour cells positive for CD20 and negative for Bcl2 and CD10.

Final diagnosis-Diffuse Large B-cell lymphoma, thyroid & cervical lymph node.

Our patient was referred to the oncologist for further treatment.

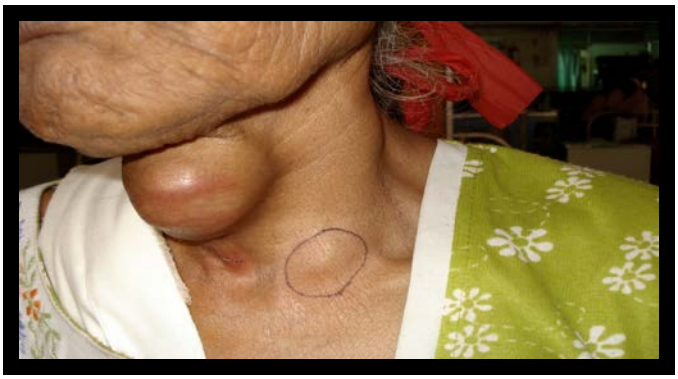

Figure 1: Thyroid swelling of size 5×4 cm, oval, firm to hard in consistency, was present. Overlying skin was normal. Bilateral Supraclavicular lymph nodes were palpable, firm to hard in consistency.

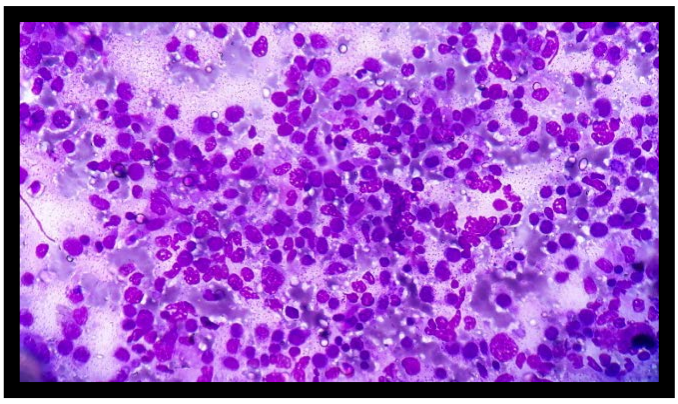

Figure-2: FNAC aspirate from lobe of thyroid showed cellular smears showing dispersed as well as few groups of large cells with large pleomorphic nuclei with prominent nucleoli and scanty cytoplasm intermixed with few lymphocytes.

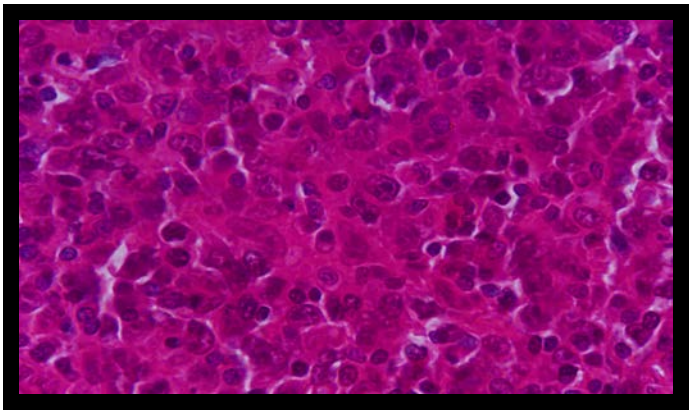

Figure 3: Right cervical lymph node histopathology showed lymphoid tissue with diffuse large sized atypical cells showing large pleomorphic nuclei with prominent nucleoli and scanty cytoplasm (Haematoxylin and Eosin stain, 40x).

Discussion

Primary thyroid lymphoma is an unusual entity, comprising of around 5% of all thyroid malignancies, 1–2.5% of malignant lymphomas and ,<3% of Extra Nodal lymphomas.[1] Dawson et al. defined primary EN-NHL as those lymphomas that present at non nodal sites with the main manifestation of their disease, with or without regional lymph node involvement.[5] PTL usually affects middle aged and elderly women with a peak incidence in sixth to seventh decade of life.[6] Three fourths of thyroid lymphomas are B-cell NHL. Hodgkin's and T-cell lymphomas are unusual. [3,7] PTLs are classified based on pathological subtypes, with each carrying a different prognosis. The two most common subtypes are diffuse large B-cell lymphoma (DLBCL) and MALT lymphoma. DLBCL accounts for more than three fourths of the cases, others being MALT and follicular lymphoma. [8] Differential diagnosis of primary thyroid lymphoma includes Hashimoto's thyroiditis (HT), secondary thyroid lymphoma and anaplastic thyroid carcinoma. Hashimoto's thyroiditis (autoimmune chronic lymphocytic thyroiditis) is the most prevalent autoimmune thyroid disorder [9]. Hashimoto's thyroiditis is associated with MALT lymphoma type of the primary thyroid lymphomas and due to this close association, often both can be misdiagnosed for one another on FNAC. [1]

DLBCLs are typically positive for CD20, with 75% also positive for the Bcl-6 oncogene and up to 50% positive for the Bcl-2 oncogene [4]. Historically, it is the most aggressive subtype, with 60% of patients exhibiting metastatic disease at first presentation and hence classically associated with poor prognosis. DLBCL itself has now been divided into two major cell of origin phenotypes with differing prognosis: a favourable germinal centre B-cell-like lymphoma and a more aggressive activated B-cell like subgroup with overexpression of the activated B-cell immunophenotype markers MUM1 and FOXP1 [4]. 40-70% patients with primary thyroid DLBCL treated with combined chemotherapy, radiotherapy and surgery showed complete remission, compared with MALT lymphomas, showing significantly higher complete response. [6] MALT lymphomas account for majority of the remaining 30% of PTLs. MALT lymphomas are characterized by the presence of lymphoepithelial lesions, (lymphocytes "stuffing" glandular lumina), representing colonization of the thyroid follicles by the lymphoma cells [4]. MALT is identified by the presence of immunoglobulin light chains, pan-B-cell antigens, and Bcl-2 and the absence of CD5, CD10, and CD23[4]. MALT lymphoma of the thyroid follows a relatively benign indolent clinical course and thus demonstrate a better response to treatment. [9]

Advanced and disseminated lymphoma can involve the thyroid as secondary thyroid lymphoma. As with widespread disease burden, secondary lymphoma of the thyroid has poor treatment outcome compared to primary thyroid lymphoma [9]. The presence of non-cohesive atypical large cells, irregular nuclear membrane, vesicular

nuclei with prominent nucleoli and presence of lymphoglandular bodies in the background as cytology features, supported by CK and EMA negativity in IHC goes against the diagnosis of anaplastic carcinoma thyroid [10].

Conclusion

DLBCL type of Primary thyroid lymphoma (PTL), is a rare and unique disease, more commonly seen in females of 60 to 70 years age group. They present with rapidly growing masses in the thyroid gland region with or without cervical lymphadenopathy. Ultrasonography guided fine-needle aspiration cytology and histopathology with immunohistochemistry helps to make the final diagnosis. Primary thyroid lymphomas have excellent response to chemotherapy and radiotherapy.

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