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PRIMARY NON-HODGKIN'S LYMPHOMA OF THYROID REPORT OF TWO CASES

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INTRODUCTION

Primary thyroid lymphoma (PTL) is a rare entity comprising 1-5% of thyroid malignancies and 1-2% of extra nodal lymphomas.[1] Its annual incidence account for about 2 cases per million per year.[2]

It has a female preponderance in the 5th-8th decade of life.[3] Normal thyroid gland does not have native lymphoid tissue and PTL usually arises from a background of chronic lymphocytic thyroiditis.[4,5]

Most of the patients have a pre-existing history of Autoimmune/ Hashimoto's Thyroiditis.[1] Most common type of lymphoma occurring as PTL in 50-80% of patients is B- Cell Non-Hodgkin's lymphoma, Diffuse Large B-cell Lymphoma being the most common type.[6]

Its diagnosis poses a challenge due to its rarity and non-specific clinical presentation. Therefore FNAC is an important modality as it is relatively inexpensive and a non-invasive procedure that helps in providing an early diagnosis. Further it is confirmed on histopathology along with immunohistochemical analysis. We hereby present two cases of PTL in a 56 year old male and a 76 year old female.

The aim of this report was to emphasize the role of FNAC in the initial diagnosis of PTL.

CASE PRESENTATION

CASE 1

A 76 year old female presented with a midline neck swelling more towards the right side since 6 months. The swelling rapidly increased in size. Patient had ATT 7 years back for Pulmonary Koch's. There was no history of hypothyroidism or hyperthyroidism. No history of dysphagia or hoarseness of voice was noted. Family history was insignificant. General and systemic examinations were within normal limits. No cervical lymphadenopathy was noted. There was no history of radiation exposure. Thyroid function tests were within normal limits. TSH was high (31.18 mu IU/ML).

On ultrasonography, mass occupying the right lobe of the thyroid gland was having heterogeneous echogenicity with hypoechoic nodules and irregular borders. CT neck revealed a grossly enlarged thyroid gland with diffuse heterogeneous attenuation causing tracheal compression, a diagnosis of Multinodular Goitre was given. Anti-thyroglobulin Antibody (Anti Tg) was 338.30 IU/ml and Antithyroid Peroxidase Antibody (Anti TPO) was >1300 U/ml.

First FNAC was done outside, which revealed equivocal cytological features (? population of intermediate sized lymphoid cells). After three months again FNAC was repeated outside and there a diagnosis of Lymphocytic thyroiditis was given. After 1 year FNAC was performed at our lab. FNA smears showed a dispersed population of large cells ? lymphoid with large nuclei, prominent nucleoli and scant cytoplasm. Background showed few small mature lymphocytes, cyst macrophages, occasional binucleate and multinucleate cells were seen. No follicular cells, hurthle cells or amyloid was seen. A possibility of Non- Hodgkin's lymphoma was suggested. Patient was advised thyroid antibody profile and biopsy along with immunohistochemistry. Patient underwent Trucut biopsy. Histopathological examination revealed diffuse population of monotonous cells with high nuclear: cytoplasmic ratio, hyperchromatic nuclei and scant cytoplasm. Possibilities suggested were NHL and High grade Carcinoma. On immunohistochemistry (IHC), CD45, CD20 (Score 4+) was positive. CD3 showed immunoreactivity in few interspersed T cells. CK was negative. A diagnosis of B-cell NHL was given.

CASE 2

Second patient was a 56 year old female who presented with a rapidly enlarging neck mass with complaints of dysphagia since 3 months. There was no history of associated pain, hoarseness of voice or dysphagia. No past history of any thyroid disorder was noted. Family

history was insignificant. General and systemic examinations were normal. No palpable lymph nodes were noted. FNAC was performed from the midline neck mass. Smears showed dispersed population of lymphoid cells, 2-3 times the size of small mature lymphocytes. Cells showed fine clumped chromatin, inconspicuous nucleoli and scant to moderate amount of cytoplasm. Background showed lymphoid cell population, transformed lymphocytes, plasma cells and lymphoglandular bodies. Focal areas showed few clusters of follicular epithelial cells. No nuclear grooves or intracytoplasmic inclusions were identified. No papillae or microfollicular arrangement of cells seen. No epithelioid granulomas identified. A diagnosis Suspicious of Malignancy, Suspicious of Lymphoproliferative disorder, Bethesda category V was rendered. Patient was advised biopsy and IHC.

CASE 1

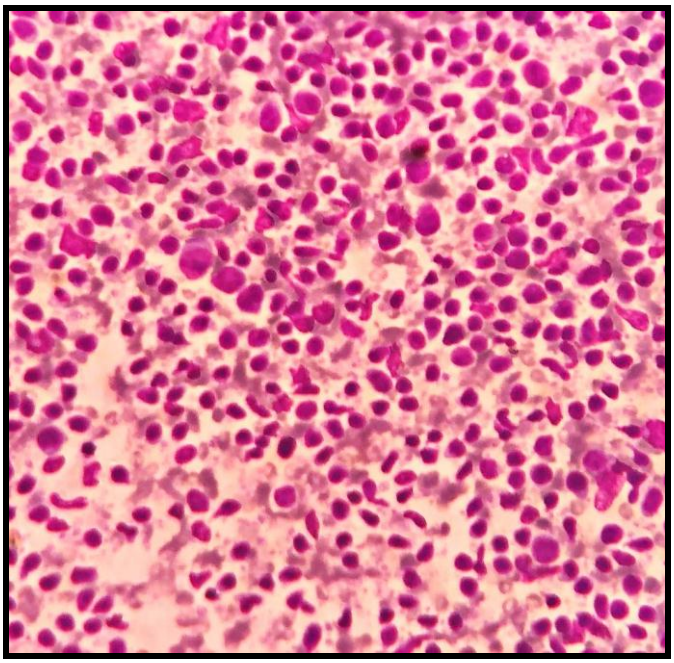

Fig. 1: Microphotograph shows proliferation of atypical lymphoid cells. (Giemsa stain, 10X).

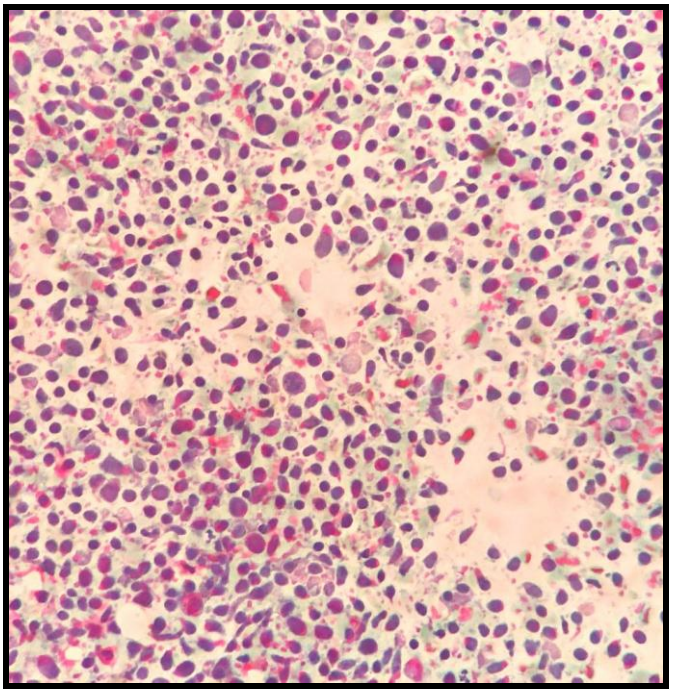

Fig. 2: Pap stain (10X).

CASE 2

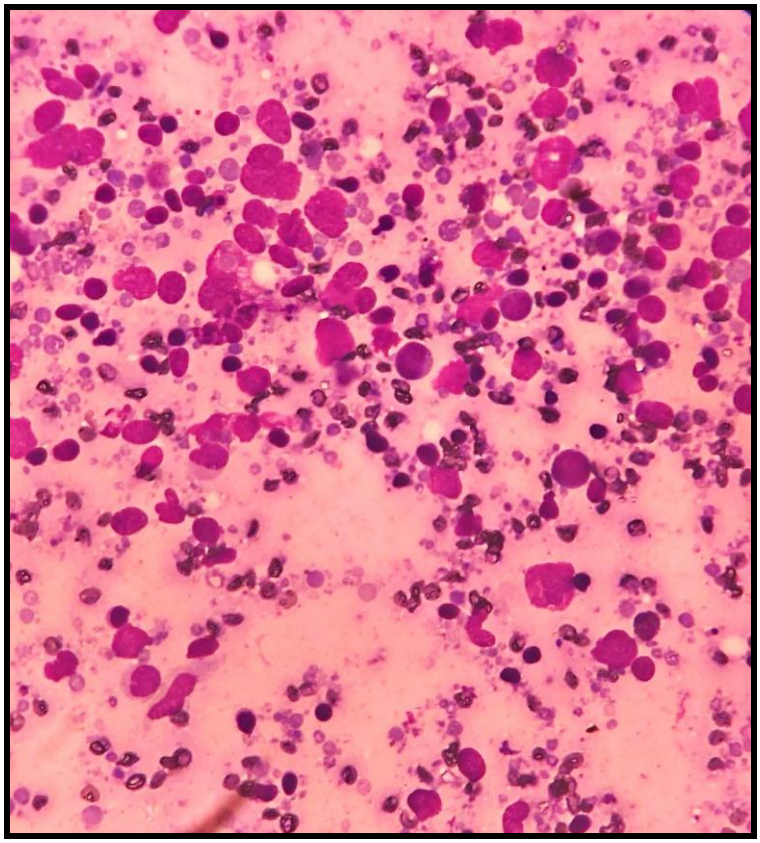

Fig 3: Microphotograph showing population of atypical lymphoid cells, 2-3 times the size of small mature lymphocytes. Cells showed fine clumped chromatin, inconspicuous nucleoli and scant to moderate amount of cytoplasm. (Giemsa stain, 40X).

DISCUSSION

Primary thyroid lymphoma is a disease of rarity. Annual incidence is 2 per million and it constitutes of less than 5 % of all thyroid tumors.[7]

An early diagnosis of PTL remains challenging and should be suspected in patients with a rapidly enlarging neck mass.

PTL has a female preponderance (female: male ratio is 3-4:1) and most commonly occurs in the seventh decade of life. (Mean age is 67 years).[8] One of our cases was a male patient.

Patients most commonly presents with dysphagia, hoarseness and dyspnea. In one of the case, patient presented with dysphagia.

In about 80% of the patients, there is increased TSH levels.[9,10] Approximately 0.6% of all patients with Hashimotos thyroiditis develop thyroid lymphoma. In one of our cases TSH levels were high.

Due to chronic antigenic stimulation, abnormal B- cell clones with genetic abnormalities can thereby replace the normal B-cell population giving rise to lymphoma.[11] However, in autoimmune diseases, impaired immunosurveillance may also contribute to development of lymphomas.[12,13]

Fine needle aspiration cytology is the gold standard in pinpointing to the diagnosis, however in combination with flow cytometric analysis of aspirated material.[14] Confirmatory diagnosis is by biopsy with immunohistochemical analysis. FNAC plays an important role in clinching to the primary diagnosis.[15]

Most common type of thyroid lymphoma is B-cell derived Non-Hodgkin's lymphoma, mainly Diffuse large B cell lymphoma which constitutes for more than 50-70% cases. Mucosa associated lymphoid tissue (MALT) accounts for about 10-15% of all cases.[16]

Treatment of PTL is still controversial. PTL is sensitive to both chemotherapy and radiotherapy and the regimen depends upon the subtype of lymphoma. Because of its aggressive clinical course, a combination of chemotherapy and monoclonal antibodies is preferred.[15]

Prognosis of PTL depends on the age of the patient, subtype of lymphoma as well as on the stage of the disease. DLBCL subtype has a lower survival rate than that of MALT subtype. Five year survival rate for stage I is 86%, 81% for stage II, 64% for stage III/IV.[3]

Treatment depends upon the histological confirmation and staging of the tumor at the time of diagnosis. Primary thyroid lymphomas respond well to chemotherapy and radiotherapy.

According to a study conducted by Mayo clinic,[17] a combination of total thyroidectomy with adjuvant radiotherapy did not demonstrate better survival rate.

With recent advances in immunophenotypic analysis, the accuracy of FNAC in diagnosing PTL is about 80-100%.[18,19,20]

Differential diagnosis of PTL includes Hashimotos thyroiditis and Poorly differentiated Carcinoma, Undifferentiated or Anaplastic thyroid carcinomas.

It is clinically important to distinguish primary and secondary thyroid lymphomas as the treatment and prognosis differ significantly. Secondary lymphoma is a widespread disease with a higher mortality rate.[21]

Five year survival rate is 90%, in patients with primary thyroid lymphoma with intrathyroidal disease and it decreases to 35% in patients with secondary lymphoma.[22]

In both the cases, PTL was diagnosed on FNAC and was then confirmed by trucut biopsy. One of the patients did not survive after two years of chemotherapy. Other patient is currently receiving chemotherapy. Both the patients did not undergo surgery.

This highlights the role of FNAC as an important tool in the early diagnosis followed by trucut biopsy along with immunohistochemistry and typing of lymphoma. This can significantly reduce the surgery associated morbidity.

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