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Primary Thyroid Lymphoma Arising in a Background of Hashimoto Thyroiditis, A Rare Case of Marginal Zone B Cell Lymphoma

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Abstract: ***Primary thyroid lymphoma (PTL) is very rare and as per definition it is a lymphoma involving the thyroid gland alone or non-contiguous lesions involving thyroid gland and lymph nodes. (1) Localized thyroid lymphomas have a good outcome. The outcome depends also on the type of the lymphoproliferative disorder. We present a case of an 83-year-old lady who presented with diffuse neck swelling for 2 years with a recent increase in size over the past 3 months. Total thyroidectomy was done and the histopathology revealed Hashimoto thyroiditis with lymphoproliferative disorder. IHC was done and a diagnosis of Marginal zone B cell lymphoma was made.***

Keywords: Primary Thyroid lymphoma, Hashimoto thyroiditis, Marginal Zone B cell lymphoma, Lymphoproliferative disorder

1.Introduction

Lymphoma involving either the thyroid gland alone or thyroid gland along with regional lymph nodes without any contiguous extension or metastasis to any other sites can be considered as Primary Thyroid Lymphoma. It constitutes 0.5-5% of all the malignancies involving thyroid gland and approximately 2% of extranodal lymphomas. The incidence is two per million persons (2). It affects women more often than men with a women to men ratio of 2-8:1. Common presentation is with a rapidly growing mass in the thyroid gland in the sixth-seventh decades of life. Thyroid lymphoma is often associated with Hashimoto thyroiditis. The risk of lymphoma is higher in patients with Hashimoto Thyroiditis. (3) Most Lymphomas are B-cell derived non-Hodgkin lymphoma. Distinguishing between primary and secondary lymphoma is significant as there is a major difference in treatment and outcome. (4) The Primary thyroid lymphomas can be further subtyped into Diffuse large B-cell lymphoma, MALT lymphoma and Follicular lymphoma. On microscopy, DLBCL is composed of large atypical lymphoid cells with amphophilic cytoplasm, vesicular nuclei and prominent nucleoli infiltrating and destroying thyroid follicles. A typical microscopic finding seen in MALT lymphoma is presence of lymphoepithelial lesions (lymphocytes within glandular lumen) in a background of lymphocytic thyroiditis. Follicular lymphoma shows follicles of similar sizes, with interfollicular neoplastic infiltrate.

Histopathological examination along with IHC is the gold standard for the diagnosis of Primary lymphomas involving Thyroid gland. Combined chemoradiotherapy is regarded as the best treatment modality, irrespective of the subtype of lymphoma. Ki 67 and MUM1 IHCs are helpful in diagnosing DLBCL, especially in small biopsies. The literature on Primary Lymphoma involving thyroid is limited from India to date. (5)

2.Case Presentation

An 83-year lady presented with a diffuse neck swelling which was noticed 2 years prior to presentation. There was a history of recent increase in size over the past 3 months. She also gave a history of difficulty in swallowing and hoarseness of voice. She had a history of hypothyroidism of 20 years duration and was on treatment with Levothyroxine Sodium 50mcg OD (Thyronorm). Physical examination showed a swelling of size 12x8 cm in front of neck which moved on deglutition. Blood investigations included Thyroid function test, Renal function test and serum electrolytes and all the parameters were within normal limits.

Ultrasound examination of the neck showed diffuse enlargement of thyroid gland with compression of trachea. The Fine Needle aspiration cytology was done from the left lobe and it showed monolayered sheets and singly scattered thyroid follicular cells. A few clusters showed lymphocytic impingement and hurthle cell change. A few other clusters showed nuclear enlargement. Background showed sheets of lymphocytes. A cytological diagnosis of Atypia of undetermined significance, TBSRTC category 3 was made. Later the patient underwent Total thyroidectomy with lymph node dissection and the specimen was sent for histopathological examination. Intraoperatively, both lobes of thyroid gland were enlarged and multiple central and lateral level cervical lymph nodes were identified. There was dense adhesion to strap muscles on the right side. Post operative period was uneventful.

Grossly, right lobe measured 10.5x7.5x4.5 cms, isthmus 1.5x1x1cm and the left lobe 8.5x6.5x6 cm. Serial sectioning of both lobes and isthmus showed pale white lobulated and fleshy areas (Figure A). Identified 23 lymph nodes. Microscopic examination of the thyroid showed marked infiltration by small lymphocytes with lymphoid follicle formation. Marginal zones showed prominent expansion by small lymphocytes with attenuated mantle zone. (Figure B, C) Marked atrophy of

thyroid follicles noted. Preserved thyroid follicles showed Hurthle cell change and lymphoepithelial lesion (Figure D). There was no evidence of necrosis in the sections studied. 13 of the 23 lymph nodes identified showed the same morphology as in the thyroid tissue. IHC was done. CD 20 was immunoreactive, in the atypical lymphoid cells in the expanded marginal zone. BCL2 was immunoreactive in the lymphoid cells in expanded marginal zone and in the small lymphoid cells infiltrating the follicles. CD3 was immunoreactive in the scattered small T lymphocytes in the paracortical area and in the follicular T cells. Cyclin D1 was non immunoreactive (Figure E). In view of the presence of lymphoepithelial lesions and IHC profile, a diagnosis of marginal zone B cell lymphoma was made and further cytogenetic/molecular studies were advised for confirmation. Following surgery, the patient had no fresh complaints. CT thorax and abdomen showed no lymphadenopathy and was advised PET CT to rule out any metastasis. Patient wished to continue the treatment at Regional Cancer Centre, Thiruvananthapuram due to financial constraints and therefore was referred.

3.Discussion

Primary thyroid lymphoma is thyroid malignancy which is very rare and contribute less than 2% of thyroid malignancies. (6) Average age of presentation is 65 years. Patients present with a rapidly growing neck mass with or without cervical lymph node enlargement. (7) The typical B-symptoms of lymphoma like fever, sweating and weight loss are seen in not more than 20% of patients. The only risk factor identified is Hashimoto thyroiditis. It is important to distinguish between Hashimoto thyroiditis with lymphoid hyperplasia from a lymphoma composed of small lymphocytes which is sometimes difficult. (4) The risk of primary thyroid lymphoma in patients with autoimmune thyroiditis is 40 times greater compared to that of the general population. The duration from the onset of lymphocytic thyroiditis and development of primary thyroid lymphoma is about 20-30 years. (7) Correctly diagnosing lymphoma is important because the treatment of lymphoma is different from that of other thyroid malignancies. (6) The secondary thyroid lymphoma originates from a widespread non-thyroidal lymphoma that metastasizes to the thyroid gland. It is clinically important to differentiate primary from secondary lymphoma of the thyroid as the therapy and outcome is significantly different. The secondary lymphoma of the thyroid is a widespread disease and the rate of mortality is higher when compared to early stages of primary thyroid lymphoma. (8) We therefore present a case of primary thyroid lymphoma that developed in a background of Hashimoto thyroiditis which was a diagnostic challenge.

Most primary thyroid lymphomas are of B-cell origin. The most common subtype of primary thyroid lymphoma is DLBCL and almost 70% of primary thyroid lymphoma cases are DLBCL. The most aggressive clinical course is seen in DLBCL and almost 60% of these tumors are diagnosed with disseminated disease. The next subtype is mucosa-associated lymphoid tissue (MALT) lymphomas which contribute of 6-27% of all primary thyroid lymphomas. These have comparatively an indolent course. Diffuse large B-cell lymphomas are characteristically positive for CD20. 75% of the cases are BCL6 positive and almost 50% are BCL2 positive. Diffuse large B-cell lymphoma is further subclassified now into a germinal center B-cell-like lymphoma with a favourable prognosis and activated B-cell-like subgroup with a more aggressive clinical course. Activated B-cell type are positive for the markers like MUM1 and FOXP1. (9) Mucosa-associated lymphoid tissue lymphoma of the thyroid follows a comparatively benign clinical course and they often present at an earlier stage and is found to have a better response to treatment. (10) The treatment includes Radiation and Chemotherapy. (6) Surgical intervention may be needed in cases of critical airway obstruction. Intervention in such situations carries high morbidity and should be done with extreme care. (11) Surgery alone has been considered to be sufficient for the treatment of localized intrathyroidal lymphoma. Chemotherapy can control distant spread of the disease and radiotherapy can control local spread of the lymphoma. (12) The overall prognosis of thyroid lymphoma as per the British Thyroid Association guidelines is excellent but the prognosis is dependent on the subtype and 5-year survival rates can be as low at 45%. (11)

4.Conclusion

Therefore, our case report highlights the need for a multidisciplinary approach for the early diagnosis of primary thyroid lymphoma and thereby prevent delay in treatment and unnecessary surgeries. It is definitely a diagnostic challenge. A strong clinical and radiological suspicion and correlation with histopathological and immunohistochemical findings is needed to arrive at a definitive diagnosis.

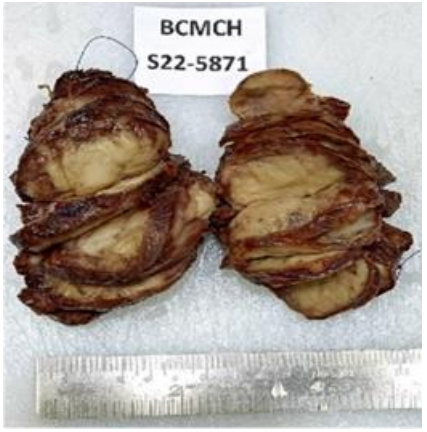

Figure A: Gross image showing the pale white lobulated homogenous appearance

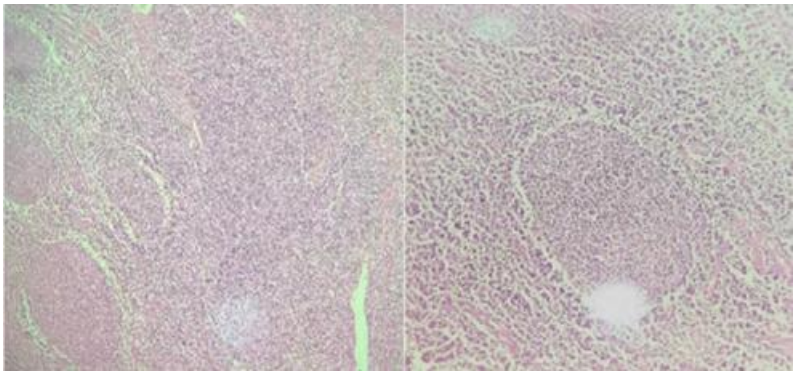

Figure B, C: H&E, 4X and 10X showing marginal zone expansion and attenuation of mantle zone.

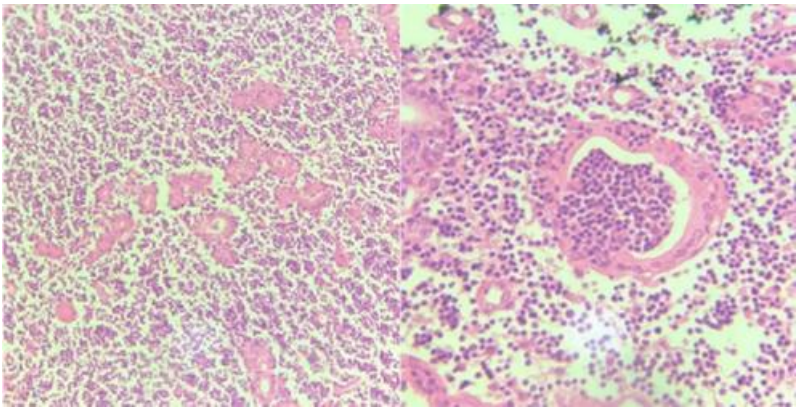

Figure D: H&E, 10X and 40X showing preserved thyroid follicle with hurthle cell change and lymphoepithelial lesion

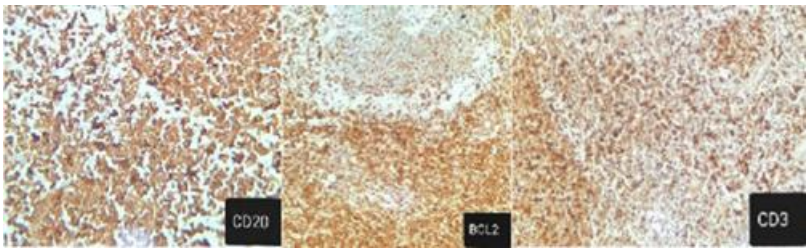

Figure E: IHC-CD20, BCL2 showing positivity in the atypical lymphoid cells in the expanded marginal zone and CD3 positivity in small T cells in the intervening areas.

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