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Primary Thyroid Lymphoma- a Close Association with Hashimotto's Thyroiditis

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Abstract :
PTL or Primary Thyroid Lymphoma is uncommon but potentially life threatening disorder of thyroid gland. The likelihood that a thyroid nodule turns out to be lymphoma is less than 1 in 1000, whereas secondary involvement of thyroid with generalized lymphoma occurs in 10% of patients who die of the disease. Despite the relative rarity, the incidence of PTL is increasing and now it constitutes 5% of all thyroid malignancies.
Here, we report a case of PTL who was being treated for chronic autoimmune lymphocytic thyroiditis with little response. 2 years later, sudden increase in size of the tumour leads her to consult the surgeon to get operated. The growth turned out to be Non Hodgkin's Lymphoma post operatively after histopathological examination and immunohistochemistry.

1. Introduction

Autoimmune Thyroiditis is one of the most common cause of spontaneous Primary Hypothyroidism,in Iodine sufficient patients. Hashimoto thyroiditis is associsted with goitre with lymphocytic infiltration. It is a genetic disorder commonly seen in women of 40-50 years of age. High concentration of Iodine (from amidorone , Iodine contrast material, KI etc.) may inhibit thyroid hormone synthesis and release, in human beings. Lithium also induces Hypothyroidism in underlying autoimmune thyroiditis. PTL is difficult to differentiate from Hashimoto's disease, with latter consisting of well differentiated lymphocytes, plasma cells, macrophages and lymphoid follicles with germinal centres and also scattered Langhans type of giant cells. The reactive lymphoid follicles are largely composed of B lymohocytes that mainly produce polyclonal IgG. The inflammatory cells are associated with damage and stimulation of thyroid follicular cells causing atrophy, metaplasia and hyperplasia leading to loss of thyroid colloid. Inflammatory cells lie in the interstitial tissue between thyroid follicles and are typically confined to thyroid parenchyma with minimal infiltration of the thyroid capsule.

Whereas, in lymphoma, the normal thyroid tissue is extensively infiltrated with abnormal lymphoid cells which often penetrate the thyroid capsule, extending into adjacent soft tissue. The lymphoma is usually composed of small cell, monotonously similar to another, which represents a distinct difference from those seen in Autoimmune thyroiditis. The border between the two, may be sharply defined or there may be a transitional zone in which mixed elements are seen. The lymphoma cells tend to displace, distort and replace the normal thyroid epithelium. Most thyroid follicles are packed and distended with lymphoma cells and loose colloid. Lymphoma cells infiltrate blood vessel wall in atleast one-fourth of the cases. Lymphoma cells may undergo necrosis and Leukocyte Common Antigen can usually be found. Substantial properties of Lymphoma contain both monoclonal heavy chains and light chains immunoglobulin characterstics that allow their differentiation from small cell carcinoma. Also identification of monoclonal light chains allows differentiation of malignant proliferation from a polyclonal benign lymphocytic inflammation. Occasionally monoclonal gammapathy can be seen in Hashimoto's disease.

2. Case Report

A 58 years old female presented with swelling in neck occupying right lobe of thyroid about 7x6 cm, quite firm and multinodular in consistency. There was no dysphagia or dyspnoea or any change in voice. She was investigated for thyroid nodule. Thyroid functions were showing hypothyroidism with TSH-70 and FNAC suggestive of lymphocytic thyroiditis. Colour Doppler USG neck did not show any vascular or soft tissue compression. ANA was borderline with normal ^{131}Iodine uptake. She was known case of Hypertension and lumbar spondylitis. 50mg Thyroxine was started with anti-inflammatory and antibiotic coverage, with initial regression of mass only 25% of the size. Surgery was advised which was refused by the patient. Goitre kept on changing its size,

nodularity. Repeated thyroid functions were showing increased TSH level. The dose of thyroxine was increased by her local physician during 2 years' regular follow up. Consistency also kept on changing from firm to hard.

Patient reported to our hospital after two and a half years, when the size started increasing with nodularity and consistency turning hard with little heaviness of voice. FNAC was lypmphocytic thyroiditis, which was repeated, to confirm the same report. This time there was huge mass which was extending from right lower border of mandible to clavicle and laterally upto posterior border of sternomastoid, crossing midline anteriorly with slight extension towards the retrosternal region and left lobe. There were no symptoms like dysphagia, respiratory obstruction or weight loss.

CT scan was showing extensive mass involving comlplete right lobe, isthumus and left lobe was also enlarged with few lymph nodes. Right lobe was compressing and pushing trachea and larynx to left side, causing compression over oesophagus and extending upto its posterior surface. ANA and ATA was found to be positive. Thyroidectomy was planned.

All other investigations like CBC, ECG, X-Ray chest including Liver functions, Renal functions were normal.

During surgery, the gland was found to be hard and encapsulated with few pretracheal and mid cervical nodes. Total thyroidectomy was done as both lobes were hard and nodular. Frozen section of nodes was reactionary. There was no extracapsular extension, so gland was removed as a single mass. Left parathyroid glands were saved.

Postoperative period was uneventful with little vertigo. Histopathological report was primaryThyroid lymphoma (PTL) and gland was completely replaced by lymphocytes, which were malignant, with no capsular invasion. On Immunohistochemistry, it was B cell Lymphoma.

Postoperative CT scan and ^{131}Iodine uptake was showing no evidence of any residual gland or nodular tissue.

PET scan was advised, which the patient could not get done.

As tumor was huge; early chemotherapy was planned

- R-CHOP was decided to be the best and was started.
- 6 cycles of R-CHOP
  - Ritutsimab
  - Cyclophosphamide
  - Adriamycin
  - Vincristine
  - Prednisolone

Patient got PET scan done after 3 cycles of chemotherapy, which was absolutely normal with no evidence of any hot areas or FDG uptake. Maintenance therapy was given for 1 year (i.e. Ritutsimab 600 mg i.v. infusion) at the interval of 3 months – " 4 cycles ".

3. Discussion

Primary thyroid lymphoma is a rare entity. Its incidence is gradually increasing due to following few reasons observed -

- Cases of PTL were incorrectly diagnosed as anaplastic small cell carcinoma thyroid (ATC).
- Pathologists have become more adapt at differentiating lymphoma from advanced Hashimoto thyroiditis; since PTL typically develops in setting of pre-existing Hashimoto thyroiditis.
- More aggressive diagnostic evaluation of thyroid nodule these days.
- Increasing incidence of Hashimoto thyroiditis.

  Association of Hashimoto thyroiditis and thyroid lymphoma is not very clear; but, its seen that the average interval between diagnosis of chronic thyroiditis and PTL is 9.2 years.

  Virtually all PTL are B cell type which can be identified by monoclonal antibodies. Many extra nodal lymphomas including those in thyroid arise from mucosa associated lymphoid tissue (MALT). They are special group of B cell lymphoma. Most of them are diffuse, with variable cellular features typical of low grade malignancies. Immunoblastic B cell lymphoma are uncommon but are quite aggressive.

3.1. Clinical Features of PTL Are Typical of Malignancies

1. Duration of symptoms, which are quite short. They are rapidly expanding goiters which are invading and compressing the neck structures within 5 months.
2. Compression symptoms are due to tracheal (19%), laryngeal nerve (21%), oesophageal (19%) and muscle (5%) involvement. This gives poor outcome.
3. Rapid enlargement of goitre , may be nodular or discrete with consistency usually firm to hard, non-tender, maybe fixed. Ill defined thyroid border fixity shows extra thyroidal spread and poor prognosis.
4. Lymph node involvement and retrosternal spread also show poor prognosis.

3.2. Important Investigations

- Thyroid function test may be normal or mild hypothyroidism.
- Hyperthyroidism is extremely rare.
- Anti thyroglobulin and antimicrosomal antibodies are found to be increased in 75% cases.

Early diagnosis is important because low grade non hodgkins lymphoma can undergo transformation to high grade tumour, over the time; Incidence of high grade PTL is decreased since people started diagnosing it early.

4. Conclusion

PTL is a rare entity, but the incidence seems to be increasing because of early diagnosis due to suspicion and early decision of doing surgery. As the transformation of low grade lymphoma to high grade is known; and there is a close association of lymphoma with Hashimoto thyroiditis. So it is mandatory to consider PTL in all cases of thyroid swelling with thyroiditis;

Whenever there is-

- Rapid enlargement
- Compression symptoms
- Hypofunctional areas seen in Hashimoto disease during uptake study
- Entire gland or part of thyroid start increasing during hormone therapy in Hashimoto disease
- Cervical node development
- Swelling changing consistency to hard

Early management of PTL with R-CHOP therapy cures most of the cases , if it is intracapsular with no nodal involvement or surrounding tissue infiltration.

- SLIDES:

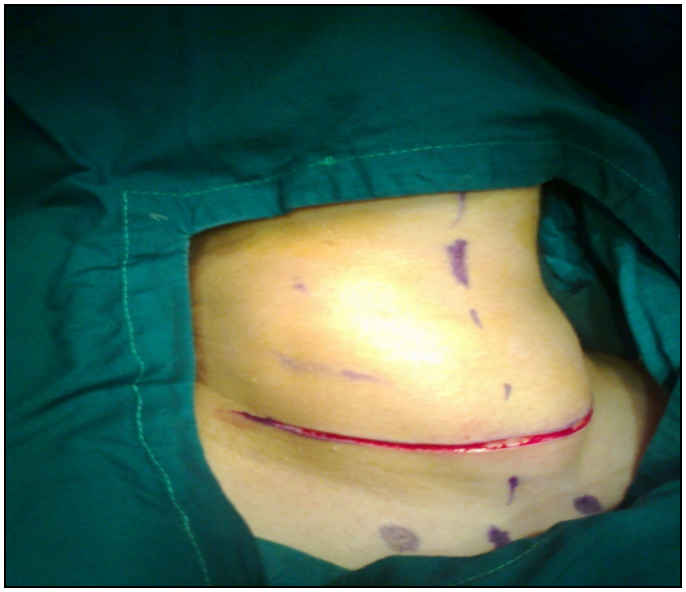

Figure 1: Classical Incision for Thyroidectomy

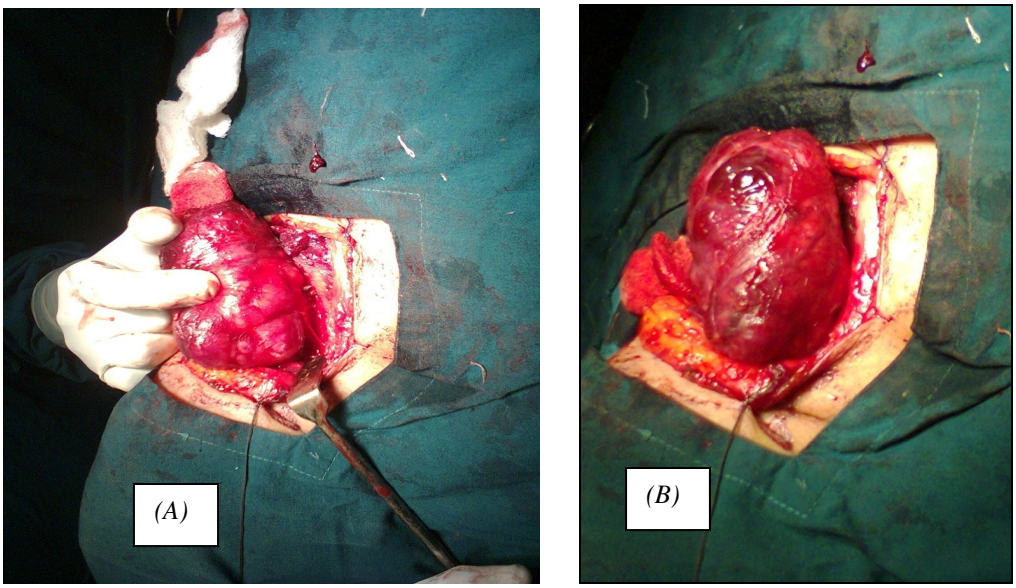

Figure 2: Intraoperative Pictures-

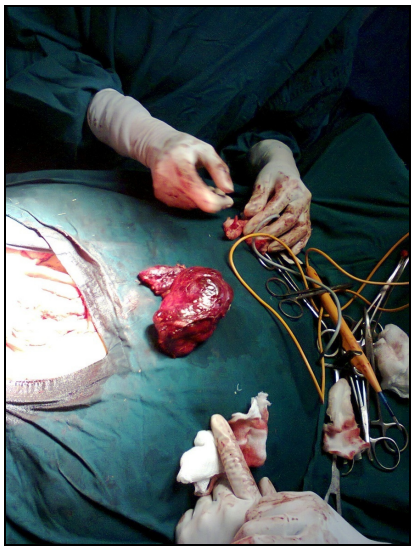

Figure 3: Total Throidectomy Specimen

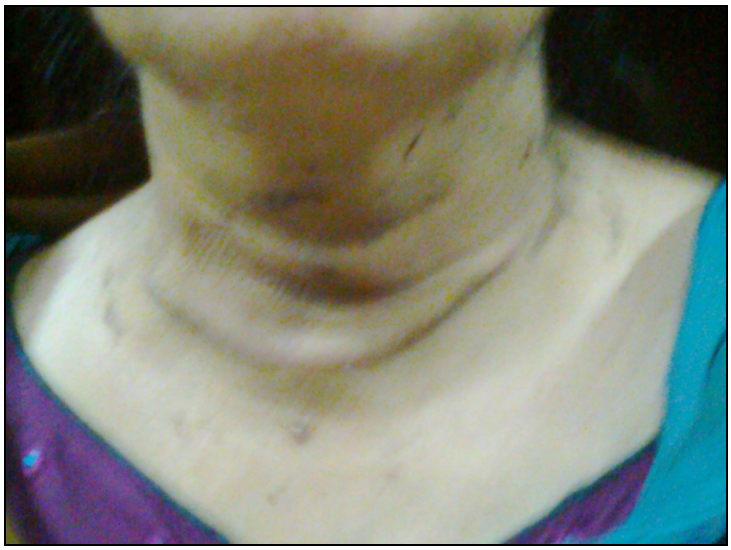

Figure 4: Post-OP Picture after Suture Removal

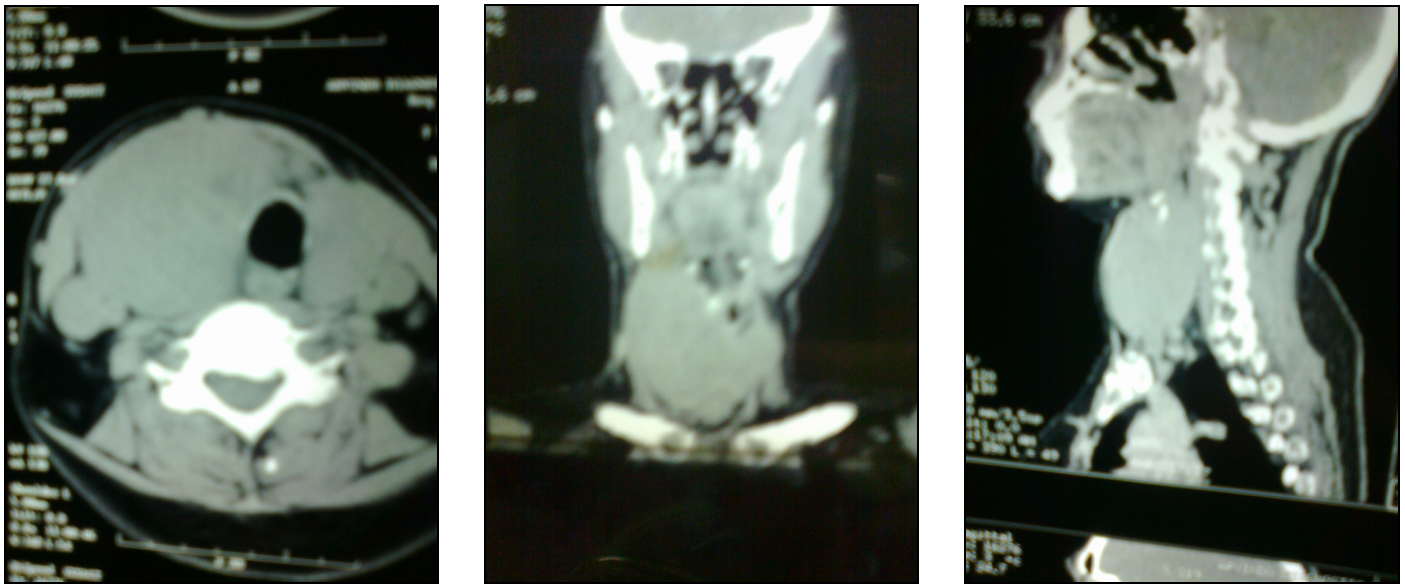

Figure 5: CT SCANS –PRE-OP

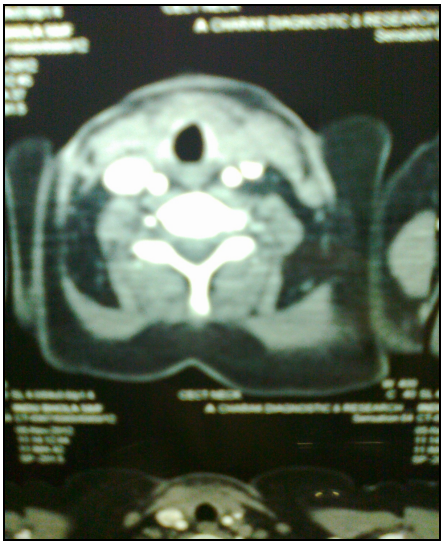

Figure 6: POST OP-CT SCAN

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