Primary Thyroid Lymphoma: A Series of Two Cases and Review of Literature

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Abstract

Primary Thyroid Lymphoma (PTL) is lymphomatous process involving the thyroid gland without contiguous spread or distant metastases from other areas of involvement at diagnosis. It is a rare tumor usually presenting in 60s with rapidly enlarging thyroid mass. Proper evaluation of FNAC specimens is essential in diagnosis as they may be confused with Hashimoto’s Thyroiditis or Anaplastic Carcinomas. With the advent of rituximab (monoclonal antibodies binding B-lymphocytes), chemotherapy is the mainstay therapy – CHOP + rituximab. However, there may still be some role of local therapies. We present here two cases which had presented at our OPD in last year. Both our patients had presented with rapidly enlarging neck masses with compressive features. Both were reported as Hashimoto’s Thyroiditis on initial FNAC. We present here two cases which had presented at our OPD in last year. Both our patients had presented with rapidly enlarging neck masses with compressive features. Both were reported as Hashimoto’s Thyroiditis on initial FNAC. Both underwent thyroidectomy followed by chemotherapy with CHOP + rituximab and are now doing well with no recurrence till date.

Case 1

Mrs. LM, 44yr female presented with swelling right side of neck which had appeared exactly 3 wks back and had rapidly increased in size. No history of associated pain, dysphagia or hoarseness of voice. History of feeling suffocated sometimes and difficulty in breathing esp. on lying down was present. No history suggestive of hypo- or hyper thyroidism. She was eumenorrhic. There was no history of similar illness or previous thyroid disorder and family history was not significant. The general physical and systemic examinations were normal. She had Goiter grade 2 with a discrete firm, nontender nodule at the right upper pole. There was no retrosternal extension and no palpable Lymph Nodes. Not adherent to skin or surrounding structures and there was no bruit. Bilateral carotids were palpable.

Possibilities we considered on the basis of history were differential diagnosis of painless rapidly enlarging goiter and included Colloid cyst, Anaplastic carcinoma, Lymphoma of thyroid, Medullary thyroid carcinoma and Papillary carcinoma.

Investigations that she was carrying with her (from another center) revealed subclinical hypothyroidism (T3 1.32 ng/dl, T4 7.00 µg/dl and TSH 9.26 µIu/ml). She was ANA positive and Anti TPO was 3740 Iu/ml. The uSG showed that both lobes of the thyroid were bulky with nodule 2.9 x 2.3 cm at superior pole of right lobe with irregular margins without any calcification. An FNAC done previously was suggestive of Hashimoto’s thyroiditis. We ordered a repeat FNAC under uSG guidance which revealed sheets of lymphocytic cells with almost absent Thyroid follicular cells and colloid. Histiocytes were frequently present (Figure 1a).

Near total thyroidectomy was done as compressive features were present. Final histopathological diagnosis was Non-Hodgkin’s lymphoma of diffuse large B cell phenotype arising in a background of Hashimoto’s thyroiditis. The tumor cells express CD 20 and are immunonegative for CD 3. The Mib-1 labeling index was more than 90%.

The patient underwent post operative chemotherapy with CHOP + rituximab.

Case 2

Mr. BLB, 58 yr male with diabetes mellitus for 3 years well controlled on oral hypoglycemic agents, presented with progressively enlarging neck swelling for past 1 month. No history of pain, dysphagia or hoarseness. Patient had some breathing difficulty especially on lying down. On examination patient was clinically euthyroid. Thyroid was enlarged (grade 2), nontender, no definite nodule or cystic area was palpable. Investigations revealed Subclinical hypothyroidism (TSH was 8.30). USG evaluation revealed enlarged thyroid with few small areas of calcification. Note was made of few small lymph nodes

Fig. 1: Microscopic pictures of the FNAC specimen. (A) Light microscopic picture showing sheets of lymphocytic cells with frequent histiocytes. Sparse follicular cells with minimal colloid. (B) High power view showing large atypical lymphoid cells with occasional areas of necrosis.
in the anterior neck. FNAC done was suggestive of autoimmune thyroiditis. CT scan showed enlarged thyroid gland with encasement of right jugular vein. A repeat FNAC was reported as being suggestive of Non Hodgkin’s Lymphoma (Figure 1b). In view of compressive symptoms and possibility of malignancy the patient underwent total thyroidectomy. Interoperatively the right lobe of the gland was fixed to the surrounding structures with extensive extrathyroidal disease. Left lobe of the thyroid was also enlarged. Few matted lymph nodes were seen. Final diagnosis was Non-Hodgkin’s lymphoma of diffuse large B cell type (Figure 1b). Patient received follow up chemotherapy with CHOP + rituximab.

In both our cases the patients presented with rapidly enlarging thyroid masses with some compressive features. Both our patients were reported as having Hashimotos thyroiditis on initial FNAC. It was only on high clinical suspicion that a correct preoperative diagnosis was made. Both our patients underwent thyroidectomy with follow up chemotherapy with CHOP and rituximab.

**Discussion**

Primary Thyroid Lymphoma (PTL) is lymphomatous process involving the thyroid gland without contiguous spread or distant metastases from other areas of involvement at diagnosis. It is a rare tumor. It constitutes about 1–5% of all thyroid malignancies and 1–2% of all extranodal lymphomas, with an annual incidence of two per million.1,3 PTL is more common in women (3:1 predominance) between the age of 50 and 80 years, with a peak incidence in the 60s. 3,8

The patients usually present with a rapidly growing thyroid mass.3,5,8,10 They may experience hoarseness, stridor, or dysphagia. B symptoms, such as fever, night sweats, weight loss, pruritus, or all may be present. They are usually euthyroid but there may be associated thyroid dysfunction. Circulating antibodies to thyroid peroxidase are positive in 60–80% of patients suggesting underlying lymphocytic thyroiditis as a predisposing factor.10

Major histological types include Diffuse Large B-Cell Lymphoma (DLBCL), Marginal Zone B-Cell Lymphoma of the Malt and Thyroid follicular lymphomas of which DLBCL is the most common. It may arise from preexisting MALT lymphoma. It is the most aggressive and carries worst prognosis with a 5-year disease-specific survival of 75%. Marginal Zone B-Cell Lymphoma of the MALT is the second most common type and comprises approximately 6% to 27% of thyroid lymphomas. It has relatively, indolent course. The majority have Hashimoto’s thyroiditis, which increases the risk by 50 times. Thyroid follicular lymphomas have a prognosis between MALT and DLBCL and have a 5-year disease-specific survival of 87%.1

Fine Needle Aspiration cytology (FNA) plays an important role in the diagnosis of thyroid lymphoma and it is imperative to use it as a diagnostic aid. Low grade lymphomas can be mistaken for chronic thyroiditis. In thyroiditis, a polymorphic mixed population of mature and transformed lymphocytes is seen. The presence of monotonous population of large atypical lymphocytes or rarely small cells is seen in lymphoma. The distinguishing features may be the abundance of lymphoid tissue and a high proportion of intermediate centrocyte-like cells in low-grade NHL as compared to Hashimoto’s thyroiditis. False negative results may be due to sampling error also as low-grade B- cell MALT lymphoma originates from HT and the two usually coexist. PTL is usually of large cell type and a diagnosis of large cell lymphoma is easy on FNA and features like lack of cellular cohesion and presence of lymphoglandular bodies in the background are features strongly against a diagnosis of anaplastic carcinoma. Immunocytochemistry confirms the lymphoid origin of the cells and their B or T-lineage. By contrast, cytological diagnosis of MALT- lymphomas is difficult, because of heterogeneous appearance of the neoplastic infiltrate.11

Proper evaluation of aspirates can avoid unnecessary surgery.11,12 In one recent series, FNA accurately diagnosed PTL in only 60% of patients who were later proven to have the malignancy. In a case series from India of 10 cases13, nine out of ten cases (90%) of the cases of PTL were correctly diagnosed by FNA. There continues to be a role for surgical biopsy to ensure that aggressive histologies are not missed.

Cervical ultrasound is the standard initial imaging study in case of thyroid mass. PTL may present as a pseudocystic, hypoechoic region that can be mistaken for a benign cyst on sonography. It is particularly valuable in guiding appropriate FNA or core needle biopsies. Once the diagnosis of PTL has been established, imaging of the entire body is necessary in order to stage the patient accurately.

To date, no randomized, controlled trials evaluating the efficacy of chemotherapy in PTL exist. Use of chemotherapy, most commonly CHOP (cyclophosphamide, doxorubicin, vincristine, prednisolone), in patients with extranodal lymphomas is both well tolerated and efficacious. Most PTL patients who present with recurrent disease relapse at a distant site, further supporting the case for systemic treatment. Approved in 2006 for first-line treatment, rituximab is a monoclonal B-cell antibody that selectively binds to the CD20 antigen found on pre-B and mature B lymphocytes. In DLBCL, rituximab approved for use with CHOP or other anthracycline-based chemotherapy regimens. In Follicular lymphoma, rituximab improves outcomes when used in conjunction with CHOP or CVP (cyclophosphamide, vincristine, and prednisone).1

Surgery / Radiotherapy is useful for Stage I or II (regardless of histology) in DLBCL, MALT and follicular lymphomas and Bulky tumors with airway obstruction. Thyroid resections can be difficult due to inflammatory nature of thyroiditis and possible extrathyroidal extension. Stages IE and IIE thyroid NHL have been traditionally treated by surgical resection; however, modern treatment consists of chemotherapy and local radiotherapy, and surgery is often reserved for tissue diagnosis and relief of airway compression.13 In patients with solitary thyroid nodule and diagnosed as PTL after surgical resection, radiation therapy can be curative.

The more indolent, MALT lymphomas when localized to the thyroid (stage IE), responds well to total thyroidectomy or with a complete response rate of more than 90%, leading some authors to recommend surgery as primary therapy. Therefore, surgery as a primary treatment for thyroid lymphomas would only be recommended under ideal conditions, such as MALT subtype stage IE only, and completely resectable with minimal morbidity.14

Primary thyroid gland lymphomas have a favorable outcome with appropriate therapy, but prognosis depends on both clinical stage and age at presentation. Because of the risk of both local-regional and distant failure, combined modality approaches that use chemotherapy with radiotherapy are warranted for intermediate- and high grade thyroid lymphoma.9,15
References


