Primary Thyroid Lymphoma: Case Series with Review of Literature

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Abstract Primary thyroid lymphoma (PTL) is a rare disorder accounting for about 2 % of all malignant lymphomas. It is an aggressive extranodal non Hodgkin lymphoma mostly of B lineage. We report four cases of PTL and highlight the clinical issues and challenges posed by this rare disease.

Introduction

Primary thyroid lymphoma (PTL) accounts for 1–5 % of thyroid tumors and 1–2.5 % of all lymphomas. The most common clinical presentation of PTL is a rapidly enlarging thyroid mass associated with compressive symptoms like dyspnea, dysphagia and pain in an elderly female [1]. Chronic antigen stimulation is involved in the pathogenesis of non Hodgkin lymphoma (NHL) and virtually all PTL derive from antigen experienced B-cells harbouring immunoglobulin heavy chain variable region genes extensively targeted by the somatic hypermutation process. Up to two-thirds of PTL harbour mutation of genes namely CD95/FAS which are expressed in the germinal centre [2].

Association of chronic lymphocytic thyroiditis (CLT) with PTL has been found to be between 25 and 75 % [3]. However not all patients of CLT develop lymphoma of the thyroid gland (TG). Pathologically two-thirds of PTL are represented by diffuse large B cell lymphoma (DLBCL) arising either de novo or in the context of a concomitant indolent NHL of the mucosa associated lymphatic tissue (MALT) [2]. The optimal management for a PTL be it chemotherapy, radiation therapy or monoclonal antibodies is still debatable. The role for surgery has its utmost importance in emergency situations to relieve compression and for diagnostic purposes.

Case Reports

Case 1

A 56 year old woman having psychiatric illness presented with rapidly progressing neck swelling, dyspnea, dysphagia and hoarseness of voice of 3 weeks duration. Ultrasonography (USG) neck revealed enlarged thyroid lobes having heterogenous parenchyma. Computerized tomographic (CT) scan revealed well defined thyroid masses 100 × 55 mm (right side) and 75 × 22 mm (left side) with multiple bilateral small cervical lymph nodes. She was euthyroid and underwent total thyroidectomy. Histopathology (HPE) revealed replacement of the whole gland by atypical cells with immunohistochemistry (IHC)-CD45+, CD20+, CD3–, CD5–, CD10–, BCL6+, BCL2– and was diagnosed as mixed diffuse and marginal zone lymphoma. She received combination chemotherapy R-CHOP protocol (rituximab-cyclophosphamide, doxorubicin, oncovin, prednisolone) 6 cycles and currently is under follow up for the last 16 months.

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Case 2

A 57 year old male presented with progressively increasing tender neck swelling of 2 months duration. USG neck revealed enlarged left thyroid lobe and isthmus with heterogeneous parenchyma. CT scan findings were thyroid mass extending down to retrosternum with absence of lymphadenopathy. Patient was euthyroid and subjected to left thyroid lobectomy. HPE revealed DLBCL with perivascular, perineural, skeletal and adipose tissue extension. IHC-CD45+, CD20+, CD3–, CD5–, M1B1+ (70 % cells). He was treated with R-CHOP protocol (6 cycles) and is currently under follow up for the last 45 months.

Case 3

A 54 year old female initially presented about 5 years ago with neck swelling of 6 months duration. She was diagnosed as hypothyroid and was started on thyroxine 100 mcg/day. Two years later she started complaining of malaise, night sweats and weight loss. USG neck revealed two large right sided nodules with bilateral cervical lymphadenopathy. She underwent right hemithyroidectomy and HPE revealed diffuse replacement of thyroid parenchyma by heavy lymphoid infiltrate with large follicular structures containing centrocytes, centroblasts and follicular dendritic cells. Small amount of residual thyroid tissue revealed oncocyctic change. IHC-follicles were CD45+, CD20+, CD10+, BCL2+, CD3–, CD5– within a meshwork of CD21+ and CD23+ follicular dendritic cells. She was diagnosed as follicular lymphoma (FL) CD20+ and she is under follow up since last 24 months.

Case 4

A 57 year old female who was known to have Hashimoto's thyroiditis with hypothyroidism for last 5 years presented with neck swelling of 2 months duration. USG and CT scan showed diffusely enlarged TG with mediastinal lymphadenopathy. Incisional biopsy revealed DLBCL with IHC-CD45+, CD20+, CD3–, CD5–. She received R-CHOP protocol (6 cycles) and achieved clinical and radiological remission but 6 months later she developed central nervous system lesions and died.

Discussion

PTL are uncommon tumours with peak incidence in the fifth to seventh decade and the male–female ratio being 1:3 [4]. The classical presentation of PTL occurs in women in the sixth decade with a history of CLT and rapidly growing firm diffuse thyroid mass. Approximately 50–80 % of PTL are of

B-cell origin most commonly DLBCL with MALT lymphomas accounting for 6–27 % of all cases [5]. All our patients had B cell lymphoma and fell in the same age group. Present studies recommend USG of the TG and needle biopsy as initial diagnostic procedures whenever PTL is suspected [6]. Importance of histological type is controversial with some authors stating that nodular lymphomas have a better prognosis than diffuse tumours. All our cases demonstrated diffuse pattern. Extension of tumor outside the gland, bulky tumours and lymph node metastases decrease the survival. Reported 5 year survival rates for PTL range from 40 to 60 percent (70–80 % for stage I disease and 30–40 % for stage III and IV disease [7]. One patient had retrosternal extension of thyroid mass and three had lymph node involvement. Three patients were in stage II and one was in stage III. Surgery played a major role in the diagnosis and treatment of PTL in the past [3]. Recently surgical management has been limited to cases of localized MALT lymphoma where response rate of more than 90 % has been seen [8]. Surgery also plays an important role in the early control of symptoms especially in patients with severe airway obstruction or those with severe pain [1]. DLBCL which constitutes majority of PTL cases are aggressive tumors. They have been shown to be both chemosensitive and radiosensitive. The risks of aggressive thyroid surgery include damage to the recurrent laryngeal nerves, trachea, esophagus, large vessels and parathyroid glands [9]. Surgery followed by local radiation therapy is indicated only if the malignancy is completely intrathyroidal [10]. Local irradiation alone can lead to systemic relapse in about one-third of the patients so use of combination chemotherapy is preferred which should constitute an anthracycline based regimen and consists of three to six cycles of CHOP regimen [11]. A study revealed that the long term survival rate after treatment with combined chemotherapy and radiation therapy was nearly 100 % [12]. All our patients underwent surgery for diagnosis and as treatment for FL but patients with DLBCL were treated with chemotherapy.

In conclusion PTL should also be considered in the differential diagnosis of a thyroid mass especially when there is a rapid increase in size of mass, obstructive symptoms, history of CLT or hypothyroidism. USG and biopsy should be the preferred diagnostic tools. The best modality of treatment was found to be combination of chemotherapy with radiation therapy.

References

1. Sipple RS, Gauger PG, Angelos P, Thompson NW, Mack E, Chen H (2002) Palliative thyroidectomy for malignant lymphoma of the thyroid. *Ann Surg Oncol* 9:907–911
2. Rossi D (2009) Thyroid lymphoma: beyond antigen stimulation. *Leuk Res* 33:607–609

3. Abdel A, Ayman A, Alaa K, Gamal EH, Yasser K, Nasser AR, Gamal G, Dahish A, Alan A, Henrik S, Adnan E (2001) Primary thyroid lymphoma. A retrospective analysis of prognostic factors and treatment outcome for localized intermediate and high grade lymphoma. *Am J Clin Oncol* 24:299–305
4. Schlumberger M, Caillon B (1996) Miscellaneous tumours of the thyroid. In: Braverman LE, Utiger RD (eds) *the thyroid*. Lippincott Raven, Philadelphia, pp 961–965
5. Moshynska OV, Saxena A (2008) Clonal relationship between Hashimoto thyroiditis and thyroid lymphoma. *J Clin Pathol* 61:438–444
6. Aozasa K (1986) Malignant lymphoma of the thyroid. *Cancer* 58:100–104
7. Singer John A (1988) Primary lymphoma of the thyroid. *Am JSurg* 64:334–338
8. Widder S, Pasieka JL (2004) Primary thyroid lymphomas. *Curr Treat Options Oncol* 5:307–313
9. Pyke CM, Grant CS, Haberman TM (1992) Non-Hodgkin's lymphoma of the thyroid: is more than biopsy necessary. *World J Surg* 16:604–609
10. Pasieka JL (2000) Hashimoto's disease and thyroid lymphoma: role of the surgery. *World J Surg* 24:366–370
11. Doria R, Zckel Z, Cooper D (1994) Thyroid lymphoma: the care for combined modality therapy. *Cancer* 73:200–206
12. Mat S, Zuka F, Miyauchi A, Katayama S (1993) Clinical aspects of primary thyroid lymphoma: diagnosis and treatment based on our experience of 119 cases. *Thyroid* 3:93