

Primary Thyroid Lymphoma: A Rare Thyroid Malignancy

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ABSTRACT

Incidence of thyroidal masses is very high with predominance in females. Most of these masses are benign. Malignancy can be of thyroid or non-thyroid origin. Surgery is treatment of choice in the former but not in latter. Primary thyroid lymphoma (PTL) is a rare cause of thyroid malignancy of non-thyroid origin which is highly treatable without surgery but early diagnosis is important requisite to have better outcome. Fine needle aspiration cytology (FNAC) is an important tool in early diagnosis of PTL, which enables doctors to treat patient better without major surgery and its morbidity. Two cases of primary thyroid lymphoma are hereby presented. The patient diagnosed on FNAC had better outcome than the one who had major surgery.

Key words: *Thyroid mass. Non-Hodgkin's lymphoma (NHL). Fine needle aspiration cytology (FNAC). Primary thyroid lymphoma. Chemotherapy.*

INTRODUCTION

Thyroid mass is a common problem more in females than males and elders than younger. Most of these are benign but can be malignant. Few malignancies have better treatment results without surgery. Non-Hodgkin Lymphoma (NHL) is one of them which are rare,^{1,2} and highly curable if diagnosed and managed correctly. It usually presents with rapidly enlarging thyroid mass.³ So early diagnosis with tissue cytology is important for better treatment in time with good prognosis and without major surgical trauma.

CASE REPORT

CASE 1: A 63 years old female patient presented with history of rapid increase in size of mass in front of neck that was present for the last 10 years, causing pressure symptoms of dysphagia and shortness of breath. She was operated in emergency of surgical department for subtotal thyroidectomy and tracheostomy to relieve pressure symptoms. Histopathology of the surgical specimen revealed it to be diffuse large B cell lymphoma; on immunohistochemistry CD 20 was positive. There was no history of B symptoms (fever, weight loss, increased sweating).

On clinical examination, neither the lymph node nor the abdominal viscera were palpable. All routine investigations including complete blood counts (CBC), routine urine examination (RUE), renal parameters (RPMs), liver function tests (LFTs) and fasting blood sugar (FBS) were within normal limits. She was euthyroid as thyroid

function tests (TFTs) were normal while thyroid scan revealed multinodular goiter (MNG, Figure 1). X-ray chest and abdominal ultrasonography was normal. Lactate dehydrogenase (LDH) was raised (877 U/dl; normal value < 450 U/dl). Bone marrow biopsy (BMB) was negative for lymphomatous infiltration (Table I). So patient was staged as IE according to Anarbour classification. She was planned for six cycles of multidrug regime chemotherapy including Cyclophosphamide, Doxorubicin, Vincristine and Prednisolone (CHOP). Doses were calculated according to body surface area and chemotherapy cycles were repeated

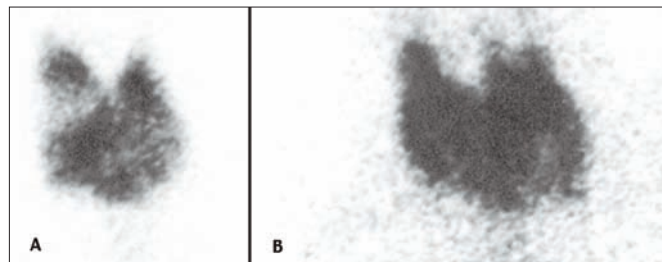


Figure 1: Thyroid scan A (case 1); B (case 2).

Table I: Comparison of the staging work-up of the two cases.

Investigations	Results	
	Case 1	Case 2
Routine investigations i.e. CBC, RPMs, LFTs, FBS, RUE	WNLs	WNLs
Clinical examination	No lymph node palpable	No lymph node palpable
CXR	No mediastinal widening	No mediastinal widening
USG Abdomen	No visceromegaly or lymphadenopathy	No visceromegaly or lymphadenopathy
Serum LDH (U/dl)	877	977
Bone marrow biopsy	No lymphomatous infiltration	No lymphomatous infiltration
TFTs	WNL	WNL

WNL = Within normal limits; CBC = Complete blood counts; RPMs = Renal parameters; LFTs = Liver function tests; FBS = Fasting blood sugar; RUE = Routine urine examination.

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after every 3 weeks. She failed to continue chemotherapy after two cycles because she developed septicemia and tracheo-esophageal fistula (TEF). Absence of neutropenia on blood count excluded chemotherapy-related septicemia. Ultimately the patient died.

CASE 2: A 55 years old female patient presented with gradually progressive swelling in front of neck for the last 2 months. Thyroid scan revealed MNG. The patient was euthyroid as TFTs were normal. Routine investigations including CBC, RUE, FBS, RPMs, and LFTs were within normal limits. FNAC revealed diffuse large B cell NHL. Serum LDH level was two times the normal limits i.e. 977 U/dl. Staging work-up including clinical examination, X-ray chest, USG abdomen and BMB was done showing no positive findings.

Thus, patient was staged as IE according to Anarbour classification. Six cycles of chemotherapy with CHOP were planned. Doses were calculated according to body surface area. This patient successfully completed chemotherapy with good compliance and had follow-up for one year. Clinical examination, LDH levels, X-ray chest and USG abdomen were done on each follow-up that was at 4-6 months. She remained disease-free during her entire follow-up of one year.

DISCUSSION

Thyroid mass is a common clinical presentation. Incidence increases with increasing age and has high predominance in females. Most of these (95%) are benign with only 5% being malignant.⁴ Malignant mass can be primary or metastatic in origin. Primary thyroid malignancy can be of thyroid or non-thyroid origin. Surgery has an important role in the former but not in the latter. Factors suggesting a malignant diagnosis include male gender, age younger than 20 years or older than 70 years, associated symptoms of dysphagia or dysphonia, history of neck irradiation, prior history of thyroid carcinoma, firm, hard, or immobile nodule and presence of cervical lymphadenopathy. Of importance, the factors mentioned above are only guidelines to assist in decision-making and do not provide absolute diagnostic information.

Primary thyroid lymphoma (PTL) is a rare cause of thyroid malignancy which is defined as lymphoma that arises from the thyroid gland. This definition excludes lymphomas that invade the thyroid gland because of either metastasis or direct extension from an adjacent lymph node.³ The thyroid gland contains no native lymphoid tissue. Intrathyroid lymphoid tissue is accrued in various pathological conditions, but more evidently in the course of autoimmune thyroid disease, notably autoimmune thyroiditis (Hashimoto's thyroiditis).⁵

Lymphoma is monoclonal malignant proliferation of lymphoreticular cells and is of two histological types, Hodgkin's lymphoma (HD) and non-Hodgkin's lymphoma

(NHL). Approximately one-third lymphoma occur in extra nodal sites other than lymph nodes, spleen, bone marrow and even in sites which normally contain no native lymphoid tissue.³

Incidence ranges from 0.6 to 5% of all thyroid malignancies in most series and occurs in less than 1% of all non-Hodgkin's lymphomas.² Most PTL are non-Hodgkin's B cell lymphomas (small/large cells) also called high grade lymphoma because of its aggressive clinical course or mucosa associated lymphoid tumour (MALT) called low grade lymphoma which has indolent clinical course.⁶ T-cell lymphomas are exceedingly rare. The median age of presentation is over 60 years old, and women are affected more commonly than men. The most common clinical presentation is that of a rapidly enlarging thyroid mass, frequently in association with neck adenopathy or pressure symptoms like dysphagia and shortness of breath.⁶ With the exception of anaplastic thyroid carcinoma, thyroid NHL usually grows faster than any other thyroid neoplasm.³

Of interest, these disorders are frequently associated with Hashimoto thyroiditis, and the incidence of primary thyroid lymphomas in patients with Hashimoto thyroiditis is markedly increased.⁷ Some believe that a pathogenetic link exists between this autoimmune disorder and thyroid NHL.

PTL continues to produce diagnostic and therapeutic dilemmas.² FNAC has become the procedure of choice for the initial pathological diagnosis of thyroid nodule.² FNAC is a useful tool in the diagnosis of PTL. The two most important critical diagnoses in FNAC of thyroid are lymphoma and anaplastic carcinoma. Proper evaluation of aspirates in these cases can avoid unnecessary surgical trauma.⁵ High grade lymphomas can be diagnosed easily but the diagnosis of low grade lymphomas may be difficult.² This method of clinical investigation is now practiced worldwide and has become the cornerstone in the management of all types of thyroid nodules.⁸

Surgery is an invasive procedure and, therefore, thyroidectomy is not indicated for clinically evident lymphoma diagnosed by fine needle or core biopsy. Surgical debulking is done if the mass is very large and is causing mechanical discomfort. Chemotherapy is the mainstay of treatment in B cell NHL.⁵ Radiotherapy (RT) may be required in cases of recurrences and local spread. Some authors recommend that the combination of chemotherapy and radiotherapy is the standard treatment of localized aggressive lymphoma, but in some patients, under 60 years and without any adverse prognostic factors, chemotherapy alone may be proposed.⁴ With chemotherapy (Anthracycline-containing regimen with Rituximab, full 6 cycles) and loco regional RT (35-40 Gy), local control is achieved in the majority of patients, and survival and relapse free survival should exceed 75%.⁹

Out of the total 5530 cancer patients registered at our institute over last 8 years, incidence of NHL was 3.7% (204 patients) and only 2 of these 204 patients were diagnosed as PTL. Good survival was achieved in one patient diagnosed on FNAC treated with chemotherapy alone without any surgical intervention or radiotherapy, while the other patient had major surgery (thyroidectomy and tracheostomy). She developed postsurgical tracheo-esophageal fistula and septicemia which are recognized complications of tracheostomy and thyroidectomy.¹⁰ She failed to complete chemotherapy and died because of these complications.

It is imperative to use FNAC as a diagnostic aid in cases with rapidly enlarging thyroid mass. It plays an important role in the diagnosis of rare causes of thyroid mass like thyroid lymphoma, which once diagnosed on FNAC, can be treated successfully with chemotherapy alone preventing surgical morbidity and mortality as was in one of our cases.

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