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Original Article

A Clinical Study on Primary Lymphoma of the Thyroid in a Tertiary Hospital

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Abstract

Background: The incidence of primary thyroid lymphoma is uncommon and accounts for <5% of all thyroid malignancies. Diagnosis by fine needle aspiration cytology (FNAC) is difficult due to its rarity, and therefore patients may undergo thyroidectomy unnecessarily.

Aim of the Study: The aim of the study was to study the review the incidence of primary thyroid malignancies in a tertiary hospital and study the diagnostic as well therapeutic methods available.

Materials and Methods: A total of 37 patients with primary lymphoma of thyroid over a period of 13 years managed were reviewed retrospectively for their clinical presentation, FNAC reports and modes of management.

Observations and Results: Among 37 patients 26 (70.27%) were women and 11 (29.72%) were male patients. The previous history of thyroid disease was seen in 13 (35.13%) patients. The most common clinical presentation was mass in the neck in 31 (83.78%), dysphagia in 21 (56.75%), dyspnea in 18 (48.64%), and hoarseness of voice in 14 (37.83%). All the patients underwent FNAC. Primary diagnosis of primary thyroid lymphoma was made by FNAC in 12 (32.43%) of the 37 patients. Primary thyroiditis was reported in 4 (10.81%), follicular thyroid carcinoma in 7 (18.91%). In 14 patients (37.83%) FNAC was inconclusive and required hardcore biopsy in 6 (16.215), and 8 (21.62%) required incisional biopsy. Two patients required emergency debulking for airway obstruction. Overall among the 37 patients B-cell Non-Hodgkin's Lymphoma (NHL) was observed in 31 (83.78%) and T-cell NHL in 6 (16.21%) patients.

Conclusions: In rapidly growing thyroid goiters the diagnosis of primary thyroid lymphoma should be considered. FNAC is limited in diagnosing thyroid lymphoma but useful in the initial workup of thyroid goiters. However, surgical intervention to take biopsy is required to establish the diagnosis and relieve critical airway compression. A combination of chemotherapy and irradiation is the mainstay of management.

Key words: Anaplastic, Chemotherapy, Follicular, Lymphoma, Thyroid, Tumors

INTRODUCTION

Primary lymphoma of the thyroid gland is a rare entity of malignant tumors of the thyroid gland accounting for only 5% of thyroid malignancies and 2% of extranodal lymphomas.[1] Hodgkin's lymphoma rarely involves the thyroid gland. The diagnosis is usually histological as there are no specific clinical symptoms or signs related to primary lymphoma of the thyroid. The management includes chemotherapy, monoclonal antibody, and radiotherapy. Surgery must be avoided when the diagnosis can be obtained before or intraoperatively. However, thyroidectomy must be done, and it is the main way to get healing in association with chemotherapy with or without radiotherapy. Only rare cases of Hodgkin's lymphoma presenting in the thyroid have been reported in the literature.[2] The diagnosis is made usually after thyroid surgery for suspected carcinoma of thyroid.[3] The increased use of immuno-cyto-chemical lymphoid markers has improved the diagnosis and categorization of thyroid lymphoma.[4] In recent times it is believed that patients previously diagnosed as anaplastic carcinoma could be suffering from primary thyroid lymphoma. Onset of new symptoms and sudden increase in the size of the pre-existing thyroid swelling are the hallmarks of both thyroid lymphoma and anaplastic

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carcinoma.[5,6] As the anaplastic carcinoma has poor prognosis, it is important to differentiate it from primary thyroid lymphoma with only surviving beyond 2 years. Whereas primary thyroid lymphoma has a favorable outcome with cyclophosphamide-based multimodality chemotherapy in combination with radiotherapy.[7-9] In the present retrospective study, 37 patients with lymphoma of thyroid were reviewed for their fine needle aspiration cytology (FNAC) reports final histopathological diagnosis and diagnostic as well therapeutic methods used.

Period of Study

This study period was from February 2004 to December 2016 (13 years).

Institute of Study

Department of Surgery, General Hospital Attached to Kannur Medical College, Anjarakandy, Kannur, Kerala.

MATERIALS AND METHODS

A total of 37 patients diagnosed with primary thyroid lymphoma in the Department of Surgery between February 2004 and December 2016 were included in this retrospective study. Institutional Ethical Clearance was obtained before commencement of the study.

Inclusion Criteria

1. Patients aged above 36 years and below 60 years were included.
2. Patients with thyroid goiters with rapidly increasing size were included.
3. Patients with dysphagia were included.
4. Patients with dyspnea were included.
5. Patients with hoarseness of voice were included.

Exclusion Criteria

1. Patients below the age of 35 and above the age of 60 years were excluded.
2. Patients with FNAC reports of inflammatory diseases of the thyroid were excluded.
3. Patients with thyrotoxicosis were excluded.

The demographic data and clinical course of the condition were elicited and recorded. FNAC reports (37) were analyzed from the case sheets. Hardcore biopsy and incisional biopsy were done where FNAC was inconclusive. The final diagnosis in all the patients was analyzed. The treatment adopted in each case was studied, and the data were tabulated. The 5 years survival rate was calculated. All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

Among 37, 26 (70.27%) were women and 11 (29.72%) were male patients. The male to female ratio was 1:2.36. The age group of the patients in the study was 36–59 years with a mean age of 49.25 ± 3.50. In 19/37 patients the tumor was observed in the age group of 51–60 years (51.35%), [Table 1].

The previous history of thyroid disease was seen in 13 (35.13%) patients. The most common clinical presentation was mass in the neck in 37 (100%), dysphagia in 21 (56.75%), dyspnea in 18 (48.64%), and hoarseness of voice in 14 (37.83%) [Table 2]. Other signs and lab investigations are also shown in Table 2.

All the patients underwent FNAC. Primary diagnosis was made by FNAC in 12 (32.43%) of the 37 patients. Primary thyroiditis was reported initially in 4 (10.81%), follicular thyroid carcinoma in 7 (18.91%). In 14 patients (37.83%) FNAC was inconclusive and required hardcore biopsy in 6 (16.21%), and 8 (21.62%) required incisional biopsy. Two patients required emergency debulking for airway obstruction. Overall, among the 37 patients B-cell Non-Hodgkin's Lymphoma (NHL) were observed in 35 (83.78%) and T-cell NHL in 1 (02.70%) patients [Table 3].

All the 37 patients were managed with chemotherapy (CHOP regimen: Cyclophosphamide, doxorubicin, vincristine, and prednisolone). Radiotherapy was given in

Table 1: The age and gender incidence in the study group (*n*=37)

Age groups	Male - 11	Female - 26	Percentage
36–40-04	02	02	10.81
41–45-06	02	04	16.21
46–50-08	03	05	21.62
51–55-10	02	08	27.02
56– 60-09	02	07	24.32

Table 2: The symptoms and signs in the study group (*n*=37)

Symptoms/signs	*n* (%)
Previous history of thyroid disease	13 (35.13)
Thyroid swelling	37 (100)
Dysphagia	21 (56.75)
Dyspnea	18 (48.64)
Hoarseness of voice	14 (37.83)
Palpable lymph nodes	15 (40.54)
Imaging showing nodes	11 (35.15)
Euthyroid	25 (67.56)
Hypothyroid	09 (24.32)
Hyperthyroid	03 (08.10)
Antimicrosomal and antithyroglobulin antibodies	10 (27.02)

Table 3: The nature of primary lymphoma in the study (*n*=37)

Final diagnosis	*n* (%)
Non-Hodgkin's Lymphoma	35 (94.59)
Hodgkin's Lymphoma	01 (2.70)

9 patients (24.32%) after completion of chemotherapy. There was a decrease in tumor size in all patients after initial treatment. All the patients except three (34/37) are still alive without any relapse. Our overall survival was 91.89%, with a mean follow-up of 36 months (range: 6–42 months). Two patients who underwent emergency tumor debulking for acute respiratory distress lost for chemotherapy after two cycles. The tumor recurred, and he succumbed 6 months after surgery in spite of restarting chemotherapy.

DISCUSSION

Primary lymphoma of the thyroid is a rare entity reported by many authors in the literature. NHL of the thyroid is reported commonly in females. In this study, the male to female ratio was 1:2.36. In certain clinical reports, the ratio was as high as 1:4.[10] Clinical picture similar to primary lymphoma of the thyroid is also observed in anaplastic carcinoma of the thyroid; rapid growth, which might be associated with dyspnea, dysphagia, pain, and hoarseness of voice. Rh primary lymphoma of the thyroid occurs commonly ion the age groups of the 5th to 7th decades. Among this majority of the patients have a history of Hashimoto's thyroiditis (range: 40–80%) [2,11] Holm *et al.* were of the opinion that patients with Hashimoto's thyroiditis have a greater risk of subsequently developing thyroid lymphoma, with an overall 60–80-fold higher risk than in the general population.[12] In this study, the previous history of Hashimoto's Thyroiditis was found in 04/37 patients. It is estimated that 1 in 200 cases of Hashimoto's disease goes on to develop primary thyroid lymphoma. There is also evidence that large cell lymphoma probably evolves from persistent low-grade mucosa-associated lymphoid tissue (MALT) malignant lymphoma, suggesting a morphological progression from chronic lymphocytic thyroiditis to low-grade MALT lymphoma, and subsequently, to high-grade large-cell lymphoma.[1,13] According to Ben Ezra *et al.*, the time lapse between occurrence of Hashimoto's and malignant transformation is 9–10 years.[14] As the value of FNAC in the diagnosis of NHL true core biopsy or incisional biopsy is often required for confirmation; occasionally even thyroidectomy is required.[15]

Scholefield *et al.*[16] are of the opinion that serial autoantibody assays in patients with Hashimoto's thyroiditis may help predicting the onset of lymphomatous change in this condition. To differentiate between high-grade lymphoma and anaplastic carcinoma by immuno-histochemical grounds using antibodies to cytokeratins and leukocyte common antigens. The essential difference between a reactive and a neoplastic lymphoid infiltrate is the presence of light chain restriction in the latter.[17] Lymphoma tumors usually have a diffuse growth pattern; residual follicles are often seen within the tumor at the border.[13] Similar to the findings of the present study, most thyroid lymphomas are of B-cell origin and predominantly of diffuse large-cell type.[1,2,11,18] The second most common histological type is MALT lymphoma.[18] Other less frequently encountered types include Hodgkin's disease, Burkitt's lymphoma, and Plasmacytoma. T-cell lymphoma is extremely rare, with only a few cases reported in the literature. Most of the T-cell lymphomas reported from Asia; they are associated with a worse prognosis than is B-cell lymphoma.[19] Management is based on its histological subtype, its stage, bulk of the tumor as well as the other associated comorbid factors.[20,21] In this study, majority of patients presented with Stage I and II disease (about 80%). The overall survival ranges from 35% to 79%.[11] The 5-year survival for each stage is 80% for Stage IE, 50% Stage for IIE, and < 36% for Stage IIIE and IVE.[22]

A similar observation was made by DiBiase *et al.* with a relapse rate of 30%.[23] Many centers use the CHOP chemotherapy regimen. Pedersen and Pedersen are of the opinion that histological grading is not a statistically significant factor in survival; however, it is significant in Stage IIIE and IVE disease.[24] In this study overall survival was 91.89%, with a mean follow-up of 36 months (range: 6–42 months). Two patients who underwent emergency tumor debulking for acute respiratory distress lost for chemotherapy after two cycles. The tumor recurred, and he succumbed 6 months after surgery in spite of restarting chemotherapy.

CONCLUSIONS

In rapidly growing thyroid goiters the diagnosis of primary thyroid lymphoma should be considered. FNAC is limited in diagnosing thyroid lymphoma but useful in the initial workup of thyroid goiters. However, surgical intervention to take biopsy is required to establish the diagnosis and relieve critical airway compression. A combination of chemotherapy and irradiation is the mainstay of management.

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