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Hyperthyroidism in Patients with Chronic Lymphocytic Leukemia

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Abstract

Background Chronic lymphocytic leukemia (CLL) is a hematological malignancy characterized by the accumulation of immunologically mature cluster of differentiation (CD) 5+ B-lymphocytes in the blood, bone marrow and lymphatic tissues. Hyperthyroidism can occasionally be caused by non-thyroid cancers infiltrating the thyroid and cause hyperthyroidism.

Objective To assess the thyroid function of patients with CLL.

Methods Patients and participant controls are subjected to prevalence tests of thyroid function as thyroid stimulating hormone (TSH), thyroxine (T4) and triiodothyronine (T3). Serum samples were analyzed by specialized kits of immunodiagnostic mini VIDAS Industry system (BioMérieux, France).

Results Out of 37 males and 17 females CLL patients and 60 volunteer controls (36 males and 24 females), only two male patients at their sixth decade were diagnosed with hyperthyroidism, these patients were classified as Stage (A) to the Binet staging system. The test results were showed as follow: TSH; <0.05 miu/ml (Normal range 0.25-5.0 miu/ml); T4; 172.11, 182.34 nmol/l (Normal range 60-120 nmol/) and T3 3.4, 3.6 nmol/l (Normal range 0.9-2.3 nmol/l) for both patients respectively. All controls subject's thyroid function test results were normal.

Conclusion Accurate assessment of thyroid function and determination the origin of hyperthyroidism to identify any thyroid gland infiltration by chronic lymphocytic malignant cells in CLL patients using medical advanced diagnostic techniques can help treating hyperthyroidism.

Keywords Chronic lymphocytic leukemia (CLL), hyperthyroidism, malignancy, metastasis, infiltration, thyroid gland

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List of abbreviations: CD markers = Cluster of differentiation markers, CLL = Chronic lymphocytic leukemia, SLL = Small lymphocytic lymphoma, T3 = Triiodothyronine, T4 = Thyroxine, TSH = Thyroid stimulating hormone

Introduction

Chronic lymphocytic leukemia (CLL) is a clonal disorder characterized by the accumulation of morphologically mature cluster of differentiation (CD) 5+ B-lymphocytes in the peripheral blood, bone marrow and lymphatic tissues [(1)]. In patients with CLL as a result of defective apoptosis, B lymphoid cells build up and invade the spleen, lymph nodes, bone marrow, and, in extremely rare circumstances, other organs [(2)].

A heterogeneous category of malignant lymphocyte neoplasms known as lymphoma diseases accounts for about 2% of all thyroid gland malignancies [(3)]. The thyroid gland infiltration in patients with CLL is a part of systemic disease involvement [(4)].

Rare cases of CLL/SLL (chronic lymphocytic leukemia/small lymphocytic lymphoma) manifesting as thyroid abnormalities have been documented [(5)]. Instances of CLL affecting the thyroid have been reported to be extremely

rare, accounting for only 3-4% of all thyroid lymphoproliferative neoplasms [6].

Clinical diagnosis of thyroid cancer with metastatic illness is uncommon. But there have been a rising number of clinical cases with metastases to the thyroid gland, as a result of the development of new diagnostic methods [7].

Hyperthyroidism can occasionally be caused by non-thyroid cancers infiltrating the thyroid gland. It is possible for hematological cancers to invade the thyroid gland and this process may be combined with euthyroidism, hypothyroidism, or hyperthyroidism [8].

The aim of the study is the assessment of thyroid gland function in patients with CLL.

Methods

At the Hematology Clinics at the Nanakali and Azadi Hospitals in the cities of Erbil and Duhok in Iraqi Kurdistan region, a total of 54 patients with CLL were enrolled and 60 normal individuals with no history of hematologic malignancies were included as controls. The World Health Organization (WHO) diagnostic criteria were used to diagnose these patients. Absolute lymphocytosis, characteristic morphology, and immunophenotyping by immunohistochemistry and flow cytometry are some of these criteria [9]. Equal to or more than 5×10^9/l small monoclonal cells in peripheral blood are needed for diagnosis of CLL. These patients were identified as having CLL according to the WHO criteria, and flow cytometry showed clonality as indicated by kappa or lambda light chain restriction. CLL cells are frequently positive for CD5, CD23, CD19, and CD20 [9].

All patients were divided into staging categories (stage A, B, and C) in accordance with the International Working Party categorization created by Binet and his colleagues [10].

All patients were initially informed about the study and written consent was obtained. Three milliliters of peripheral venous blood were drawn from patients and control subjects clot activator gel tubes, and a centrifugation technique was utilized to obtain clear serum.

Thyroid function tests were performed using mini VIDAS system (BioMérieux, France).

For statistical analysis, the obtained data were analyzed using (statistical package for social sciences (SPSS) 24 program system. Frequency and its percentage value were used for description of the data.

Results

As shown in table (1), out of the 54 CLL patients and 60 healthy individuals with no history of malignancy (including CLL disease) were subjected to thyroid function tests during this study. The age of hospitalized CLL patients as revealed in table (2) were ranged from 44 to 82 years old (mean 61.31), of which 37 patients (68.5%) were males and the remaining 17 patients (31.5%) were females, with a male to female ratio (M:F) 2.18:1. For control participants, their ages ranged from 40 to 90 years (mean 57.53) with 36 (60%) males and 24 (40%) females. CLL cases were seen most frequently in males and according to decades of age among (61-70) year old patients with coincidence of hyperthyroidism disorder within same age's decade.

The Binet staging system was used to categorize CLL cases [10]. Stage A was more common than the other stages, as illustrated in table (3). Stage A was represented by 29 (53.7%) patients of the cases, Stage B by 15 (27.8%) patients, and Stage C, which was the least prevalent, by 10 (18.5%) patients.

Thyroid stimulating hormone (TSH), thyroxine (T4), and triiodothyronine (T3) tests were performed on all patients to evaluate the thyroid gland function, 2 patients age 63 and 67 years old men revealed thyroid dysfunction as hyperthyroidism and represented 3.7% of patients with CLL with TSH, <0.05 miu/ml (Normal range 0.25-5.0 miu/ml); T4, 172.11, 182.34 nmol/l (Normal range 60-120 nmol/l) and T3, 3.4, and 3.6 nmol/l (Normal range 0.9-2.3 nmol/l) respectively as illustrated in table (4). Noteworthy, both patients were within Stage (A) of CLL disease.

Table 1. Thyroid function Status of CLL patients according to gender

Patient gender	Thyroid function Status		Total	
	Euthyroidism	Hyperthyroidism	No.	%
Male	35	2	37	68.5
Female	17	0	17	31.5
Total	52	2	54	100
Controls gender				
Male	36	0	36	60
Female	24	0	24	40
Total	60	0	60	100

Table 2. Thyroid function Status of CLL patients according to age group

Age group (yr)	Thyroid function Status		Total	
	Euthyroidism	Hyperthyroidism	No.	%
40-50	6	0	6	11.11
51-60	16	0	16	29.63
61-70	21	2	23	42.60
71-80	8	0	8	14.81
81-90	1	0	1	1.85
Total	52	2	54	100

Table 3. Thyroid function Status of CLL patients according to disease stage

Age group (yr)	Thyroid function Status		Total	
	Euthyroidism	Hyperthyroidism	No.	%
A	27	2	29	53.7
B	15	0	15	27.8
C	10	0	10	18.5
Total	52	2	54	100

Table 4. Frequency and percentage of CLL patients related to thyroid function

Thyroid function	N	%
Euthyroidism	52	96.3
Hyperthyroidism	2	3.7
Total	54	100

Discussion

Previous researches have shown that leukemia and lymphoma, particularly CLL malignant cells infiltrate the thyroid gland [8]. The thyroid disorders can be developed by metastatic disease in the sixth or seventh decades of life in older people [11,12]. Due to their plentiful blood supply, endocrine glands generally can serve as targets for metastases from a variety of non-endocrine tumors [13]. The majority of individuals with metastases to the thyroid gland are euthyroid, although some patients may also have hypothyroidism or hyperthyroidism [8].

In the current study, thyroid gland function tests were performed on all CLL patients to investigate any abnormalities of its function, such as hypothyroidism or hyperthyroidism. Only two patients were 63- and 67-years old men revealed thyroid dysfunction as hyperthyroidism identified throughout this study, making up just 3.7% of all patients, while the participant volunteers control revealed non-hyperthyroidism status (euthyroidism). However, according to another study, the prevalence of CLL affecting the thyroid is remarkably low, accounting for only 3-4% of all thyroid lymphoproliferative neoplasms [6]. Obviously, these patients were located within CLL disease stage (A) according to Binet staging system and was reported by another study as having the same staging by Andrysiak-Mamos and his colleagues [14].

In conclusion, infiltration of malignant cells like CLL cells into the thyroid gland may induce tissue damage and hyperthyroidism. Therefore, a pathologist's correct determination of the origin of hyperthyroidism utilizing a variety of diagnostic procedures (for instance, cytological evaluation by fine needle aspiration biopsy) may allow a therapist to make the best decision for managing hyperthyroidism.

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Conflict of interest

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References

1. Gaidano G, Foà R, Dalla-Favera R. Molecular pathogenesis of chronic lymphocytic leukemia. J Clin Invest. 2012; 122(10): 3432-8. https://doi.org/10.1172/JCI64101
2. Derringer GA, Thompson LD, Frommelt RA, et al. Malignant lymphoma of the thyroid gland: a clinicopathologic study of 108 cases. Am J Surg Pathol. 2000; 24(5): 623-39. doi: 10.1097/00000478-200005000-00001.
3. Thieblemont C, Mayer A, Dumontet C, et al. Primary thyroid lymphoma is a heterogeneous disease. J Clin Endocrinol Metab. 2002; 87(1): 105-11. doi: 10.1210/jcem.87.1.8156.
4. Reid-Nicholson M, Moreira A, Ramalingam P. Cytologic features of mixed papillary carcinoma and chronic lymphocytic leukemia/small lymphocytic lymphoma of the thyroid gland. Diagn Cytopathol. 2008; 36(11): 813-7. doi: 10.1002/dc.20894.
5. Shin J, Chute D, Milas M, et al. A rare case of chronic lymphocytic leukemia/small lymphocytic lymphoma presenting in the thyroid gland. Thyroid. 2010; 20(9): 1019-23. doi: 10.1089/thy.2010.0089.
6. Gonçalves A, Vale S, Nobre E, et al. Thyroid nodule: first manifestation of chronic lymphocytic leukaemia. Arch Endocrinol Metab. 2015; 59(2): 190-4. doi: 10.1590/2359-3997000000034.
7. Nixon IJ, Coca-Pelaz A, Kaleva AI, et al. Metastasis to the thyroid gland: A critical review. Ann Surg Oncol. 2017; 24(6): 1533-9. doi: 10.1245/s10434-016-5683-4.
8. Jonklaas J. Infiltration of the thyroid gland by non-thyroid malignancy: A literature review reveals this to be an unusual cause of hyperthyroidism. J Clin Transl Endocrinol. 2020; 20: 100221. doi: 10.1016/j.jcte.2020.100221.
9. Rawstron AC, Kreuzer KA, Soosapilla A, et al. Reproducible diagnosis of chronic lymphocytic leukemia by flow cytometry: An European Research Initiative on CLL (ERIC) & European Society for Clinical Cell Analysis (ESCCA) Harmonisation project. Cytometry B Clin Cytom. 2018; 94(1): 121-8. doi: 10.1002/cyto.b.21595.
10. Binet JL, Auquier A, Dighiero G, et al. A new prognostic classification of chronic lymphocytic leukemia derived from a multivariate survival analysis. Cancer. 1981; 48(1): 198-206. doi:

10.1002/1097-0142(19810701)48:1<198::aid-cncr2820480131>3.0.co;2-v.

11. Autelitano F, Santeusanio G, Mauriello A, et al. Patologia latente della tiroide: studio epidemiologico e statistico di tiroidi prelevate in corso di 507 autopsie consecutive [Latent pathology of the thyroid: an epidemiological and statistical study of thyroids sampled during 507 consecutive autopsies]. Ann Ital Chir. 1992; 63(6): 761-81.
12. Mistelou A, Papadatos SS, Kousi C, et al. Thyroid gland as a target of secondary malignancies - an autopsy study and review data. Folia Med (Plovdiv). 2019; 61(2): 277-88. doi: 10.2478/folmed-2018-0077.
13. Angelousi A, Alexandraki KI, Kyriakopoulos G, et al. Neoplastic metastases to the endocrine glands. Endocr Relat Cancer. 2020; 27(1): R1-R20. doi: 10.1530/ERC-19-0263.
14. Andrysiak-Mamos E, Becht R, Sowińska-Przepiera E, et al. Case report: rare case of infiltration of small lymphocytic B-cell lymphoma in the thyroid gland of female patient with B-cell chronic lymphocytic leukemia (CLL-B/SLL-B). Thyroid Res. 2013; 6(1): 1. doi: 10.1186/1756-6614-6-1.

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