Journal of
Babol University of Medical Sciences
JBUMS
e-ISSN: 2251-7170 p-ISSN: 1561-4107

Correlation between Papillary Carcinoma and Hashimoto's Thyroiditis

L. A. Arkawazi (MD)[*1], K. A. Mahmood (MD)[2], M. A. Salih (MD)[2]

1.Department of Pathology, College of Medicine, University of Sulaimani, Kurdistan Region, Iraq.
2.Department of Surgery, College of Medicine, University of Sulaimani, Kurdistan Region, Iraq.

Article Type

Research Paper

Received:
Feb 28th 2023
Revised:
Apr 15th 2023
Accepted:
May 7th 2023

ABSTRACT

Background and Objective: Papillary thyroid carcinoma (PTC) can be affected by underlying diseases. There is controversy about whether PTC and Hashimoto's thyroiditis are connected. The present study was conducted to evaluate the effect of Hashimoto's thyroiditis on papillary thyroid carcinoma.

Methods: This retrospective study was conducted on 100 cases of total thyroidectomy (TT) referred to pathology centers of public and private hospitals of Kurdistan Region, Iraq, from 2019 to 2021. Data about histopathological findings such as pathology diagnosis, Hashimoto's thyroiditis (HT), toxic goiter, multinodular goiter (MNG), diagnosis based on the physician's report and FNAC (fine needle aspiration cytology) results were collected and compared.

Findings: Out of 100 TT cases examined, 41 cases were diagnosed as HT, 22 cases of PTC were identified, 11 of which were associated with HT background. Out of 100 TT, non-toxic goiter was found in 54 cases and toxic goiter in 5 cases. The most common indication for TT was multinodular goiter, which was found among 10 cases of PTC. There was a significant association between HT and PTC (p=0.036) with Odds ratio of 1.87 (95% CI: 1.19-2.82). FNAC was malignant or suspicious for PTC in 7 cases and histological diagnosis was malignant in 5 cases. Fourteen surgeries were performed depending on the radiological findings of suspicious nodules with the diagnosis of thyroid cancer in 6 cases.

Conclusion: The results of the study showed a potential relationship between Hashimoto's thyroiditis and papillary thyroid carcinoma.

Keywords: *Thyroid Neoplasms, Multinodular Goiter, Papillary Thyroid Carcinoma*.

Cite this article: Arkawazi LA, Mahmood KA, Salih MA. Correlation between Papillary Carcinoma and Hashimoto's Thyroiditis. *Journal of Babol University of Medical Sciences*. 2023; 25(1): 379-85.

[DOI: 10.22088/jbums.25.1.379]

[*]Corresponding Author: L. A. Arkawazi (MD)
Address: Department of Pathology, College of Medicine, University of Sulaimani, Kurdistan Region, Iraq.
Tel: +964 (770) 1520190. **E-mail:** dr.lusan.arkawazi@gmail.com

Introduction

The most prevalent autoimmune thyroid condition, known as Hashimoto's thyroiditis (HT), causes the immune system to target and ultimately destroy the thyroid gland (1). Hakaru Hashimoto initially identified Hashimoto's thyroiditis in 1912, which results in goiter and elevated levels of antithyroid peroxidase and antithyroglobulin antibody in the blood (2). 90-95% of those with HT are female, and the average age range is 45-65. It tends to cluster in families. Blacks and Japanese are less affected than Whites (3). Its presentation is painless along with gradual thyroid tissue destruction, which in early stage may show transient hyperthyroidism (4).

An evaluation of Anti TSH (unique to Hashimoto's and Grave's illness) is part of the laboratory investigation. Antithyroglobulin is comparable in specificity to antithyroid peroxidase but less sensitive (5). Large lymphocytic infiltrations with germinal center development are the histological descriptions of HT. Atrophic follicles with an abundance of Hürthle cells but no reduced colloid. Though visible, fibrosis does not extend past the capsule. Huge cells could be discovered. It is possible to identify epithelial alterations such as larger or overlapping nuclei with incomplete nuclear clearance (6).

The most common kind of thyroid cancer, known as Papillary thyroid carcinoma (PTC), accounts for 80-90% of all thyroid malignancies. In 1955, Dailey et al., became the first to relate neoplastic alterations to chronic inflammation and proposed a relationship between HT and PTC (7). According to 2017 WHO classification, there are 15 different types of papillary thyroid cancer, including prototypical conventional/classic papillary thyroid carcinoma. An increase in papillary thyroid cancer cases has been seen over the past 15 to 20 years, and this association is related to early thyroid nodule detection on imaging (ultrasound and CT) (8).

Female gender was predominant with an F:M ratio of ~3:1 (9). Although the exact etiology of PTC is unknown, exposure to radiation before 20 years of age for conditions like acne, tonsillitis, tinea capitis, and enlargement of the thymus is linked to its occurrence (10). Some articles suggest a possible correlation between HT and PTC which is the subject of the current study and discussion. Papillary thyroid carcinoma may vary in appearance and can be located anywhere in the gland. The typical size of papillary carcinomas is between 2 and 3 cm, however, they can also be as little as a few millimeters in diameter. PTC lesions typically have a hard tone, white, and intrusive appearance. Calcification occurs often. Cyst alteration might be seen (11, 12). Nuclear features are among the histological characteristics of PTC: Nuclear enlargement, elongation, and overlapping, as well as chromatin cleaning and margination (glassy/ground glass nuclei and Orphan Annie nuclei), are examples of changes in nuclear size and form. The abnormality of the nuclear membrane revealed irregular nuclear contours, nuclear grooves, and nuclear pseudoinclusions (cytoplasmic invaginations) (13). The rationale for conducting this study is to explore the potential connection between papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis, which is an autoimmune disorder that can affect the thyroid gland. While there is some evidence to suggest a correlation between these two conditions, the exact nature of the relationship remains unclear and is the subject of ongoing debate in the medical community. Understanding the potential impact of Hashimoto's thyroiditis on the development and progression of PTC is important for several reasons. First, if there is a significant correlation between these two conditions, it could have important implications for how PTC is diagnosed and treated, particularly in patients with a history of thyroid disease. Additionally, identifying risk factors for PTC can help healthcare providers develop more targeted screening and prevention strategies to reduce the incidence and impact of this disease.

[DOI: 10.22088/jbums.25.1.379]

Methods

This was a retrospective study performed on 100 cases of total thyroidectomy (TT) surgeries performed at public and private hospitals in Sulaimani governorate. The ethics in research committee of University of Sulaimani, Kurdistan Region approved the study protocol with meeting NO.22 & issue number 87. Preoperative radiological evaluation and laboratory investigations were taken in consideration. Sampling method was census sampling. All individuals who underwent complete thyroidectomy between 2019 and 2021 comprise the criteria for inclusion. Exclusion criteria: patients leaving outside the 2019-2021 period, and residence of the patient in a province other than Suleimani.

By referring to the pathology centers of public and private hospitals between the years 2019-2021, all cases of total thyroidectomy with PTC diagnosis were extracted. The pathology report of these patients was reviewed. The instrument for gathering data was a two-part checklist. Age and gender were among the demographic details in the first section, the second section includes information related to histopathological and clinical findings such as: Hashimoto's thyroiditis (HT), toxic goiter, multi nodular goiter (MNG) and FNAC (fine needle aspiration cytology) results. Indication of TT was determined based on these reports. Pathological diagnosis and reports were dictated by expert pathologists with the use of Paraffin blocks and hematoxylin and eosin stains for histological evaluation.

The 8th edition of the AJCC (American Joint of Cancer) guideline for the analysis of data from patients who had thyroid gland carcinomas was utilized for PTC staging.

Data were expressed as number and percentages, calculated in SPSS, version 21. Fisher exact test was used to calculate differences in the incidence of diseases between groups, considering 95% confidence interval for the calculation of odds ratio with p value of under 0.05 as significant.

Results

Age-wise, 12 men and 58 women made up the 70 patients who were under 45 years of age. Thirty patients, including 13 men and 17 women, were above the age of 45. Forty-one cases were diagnosed as HT in the examined 100 cases of TT. Twenty-two (22%) cases of PTC were detected, 11 of them were associated with a background of HT. Out of the 100 TT, non-toxic goiter was found in 54 cases and 5 cases of toxic goiter. Only 8 cases of PCT were noted with a background of non-toxic goiter. Three cases of PTC were not associated with any additional pathological findings (Table 1). Based on the Fisher exact test, the test results showed a significant association between HT and PTC (p=0.036). Out of 41 cases with HT, 11 had PTC, while out of 59 cases without HT, 11 had PTC. The odds ratio for the association between HT and PTC was 1.87 (95% CI: 1.19-2.82). We can conclude that there is a significant association between the presence of PTC and the presence of Hashimoto's thyroiditis.

Table 1. Relation between PTC and additional pathological findings

Types of additional pathological findings	Cases Number(%)	Cases with PTC Number(%)	p-value*
HT	41(41)	11(26.82)	0.036
Non-Toxic goiter	54(54)	11(20.37)	0.178
Toxic goiter	5(5)	0(0)	0.999
Total number	100	22(22)	-

*Fisher exact test

[DOI: 10.22088/jbums.25.1.379]

Most common indication for TT was multinodular goiter, by a rate of 61%, with a finding of 10 cases of PTC between them.

The second most common indication was FNAC (Fine needle aspiration cytology) result, which included malignancy or suspicious for PTC by a rate of 7 cases, with histological diagnosis of malignancy in 5 cases (Table 2). 14 surgeries were performed depending on radiological finding of suspicious nodule, with diagnosis of thyroid cancer in 6 cases (PTC and follicular carcinoma). Only 1 case of thyroid adenoma was diagnosed in the total 100 TT in which the surgery was inducted on the bases of MNG (Table 2).

Other indications for surgery included failure of antithyroid drugs, among which one case of PTC was diagnosed (Table 3).

Table 2. Indication of TT

Indication of TT	Number(%)
MNG	61(61)
FNA	7(7)
Radiological suspicious nodule	14(14)
Others	18(18)
Total	100

Table 3. PTC in relation to indication of TT

Indication of TT	Number of cases	Malignancy/suspicious for malignancy	Adenoma
MNG	61	10	0
FNA	7	5	0
Radiological suspicious nodule	14	6	0
Others	18	1	0

Discussion

Our study examined 100 cases of thyroidectomy and found that 41 cases had Hashimoto's thyroiditis (HT) and 22 cases had papillary thyroid carcinoma (PTC), 11 of which were associated with HT. There was a significant association between HT and PTC with an odds ratio of 1.87 (95% CI: 1.19-2.82), indicating a positive association between the two conditions. The correlation between PTC and HT is complicated and not clear till now (14). Although there is an ongoing discussion, several studies have indicated that people with HT had a greater risk of PTC (15-18). The meta-analysis by Lai et al. revealed that HT-predisposed individuals showed a higher risk of developing PTC (19), however others denied any connection between these two lesions (20, 21). Lee et al. published a meta-analysis and found that PTC is significantly associated with pathologically confirmed HT (22). Lee et al. suggested that PTC is a cause of HT, then it would be contradictory to the findings of the current study which suggests that HT may be a risk factor for the development of PTC. However, it's important to note that our study is observational in nature and it may be difficult to establish causality from observational data alone. Further research is needed to better understand the relationship between HT and PTC, including the potential for bidirectional causality. According to

[DOI: 10.22088/jbums.25.1.379]

Tamimi, PTC patients had a higher rate of lymphocytic infiltration, and the associated inflammatory response seen in HT may be a factor in the development of malignant transformation (23).

Through reactive oxygen species, the inflammation can cause DNA damage and mutations that may contribute to PTC carcinogenesis (24). Different retrospective and prospective studies suggested that the link between HT and PTC is antibody mediated reaction (25). Despite our confirmation for the exitance of a relation between HT and PTC, but we cannot agree on blaming the inflammatory response and lymphocytic infiltration in the pathogenesis of PTC, and it's important to keep in mind that some malignancies, like breast cancer, have favorable prognoses when they are accompanied by high rates of inflammatory cell reactions (26).

In fact, the lymphocyte infiltration of HT may represent a positive immune response with a cancer-suppressing impact, which may significantly contribute to the favorable prognosis of PTC (27, 28). It is recommended that subsequent studies be conducted on the relation between HT and PTC on radiological and laboratory aspects.

In conclusion, our study found a significant association between Hashimoto's thyroiditis (HT) and papillary thyroid carcinoma (PTC), indicating a potential link between these two conditions. Although the exact pathophysiology of HT in PTC remains unclear, our findings provide support for further research to investigate this relationship. These results highlight the importance of considering HT as a potential risk factor for the development of PTC in patients undergoing thyroidectomy, and may have implications for screening and management strategies in this population. To improve the results, it is recommended to include more samples in future studies.

Conflicts of Interest: There were no conflicts of interest among the writers in this investigation.

Acknowledgment

We would like to thank the participating patients who helped us in this study.

[DOI: 10.22088/jbums.25.1.379]

References

1.Dayan CM, Daniels GH. Chronic autoimmune thyroiditis. N Engl J Med. 1996;335:99-107.

2.Takami HE, Miyabe R, Kameyama K. Hashimoto's Thyroiditis. World J Surg. 2008;32(5):688-92.

3.Okayasu I, Hara Y, Nakamura K, Rose NR. Racial and Age-related Differences in Incidence and Severity of Focal Autoimmune Thyroiditis. Am J Clin Pathol. 1994; 101(6), 698-702.

4.Demirbilek H, Kandemir N, Gonc EN, Ozon A, Alikasifoglu A. Assessment of thyroid function during the long course of Hashimoto's thyroiditis in children and adolescents. Clin Endocrinol (Oxf). 2009;71(3):451-4.

5.Tozzoli R, Villalta D, Kodermaz G, Bagnasco M, Tonutti E, Bizzaro N. Autoantibody profiling of patients with autoimmune thyroid disease using a new multiplexed immunoassay method. Clin Chem Lab Med. 2006;44(7):837-42.

6.Caillou B. Ductal metaplasia in chronic lymphocytic thyroiditis as a manifestation of phylogenic regression to an exocrine structure. Am J Surg Pathol. 2006;30(6):774-81.

7.Dailey Me, Lindsay S, Skahen R. Relation of thyroid neoplasms to Hashimoto disease of the thyroid gland. AMA Arch Surg. 1955;70(2):291-7.

8.Ahn HS, Welch HG. South Korea's Thyroid-Cancer "Epidemic"--Turning the Tide. N Engl J Med. 2015;373(24):2389-90.

9.Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7-30.

10.De Jong SA, Demeter JG, Jarosz H, Lawrence AM, Paloyan E. Thyroid carcinoma and hyperparathyroidism after radiation therapy for adolescent acne vulgaris. Surgery. 1991;110(4):691-5.

11.Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics, 2009. CA Cancer J Clin. 2009;59(4):225-49.

12.Baloch ZW, LiVolsi VA. Pathology of the thyroid gland. In: LiVolsi VA, Asa SL, editors. Endocrine Pathology, 1st ed. Philadelphia, PA: Churchill Livingstone; 2002. p. 61-88.

13.Vickery AL Jr. Thyroid papillary carcinoma. Pathological and philosophical controversies. Am J Surg Pathol. 1983;7(8):797-807.

14.Guarino V, Castellone MD, Avilla E, Melillo RM. Thyroid cancer and inflammation. Mol Cell Endocrinol. 2010;321(1):94-102.

15.Zhang Y, Dai J, Wu T, Yang N, Yin Z. The study of the coexistence of Hashimoto's thyroiditis with papillary thyroid carcinoma. J Cancer Res Clin Oncol. 2014;140(6):1021-6.

16.Ahn D, Heo SJ, Park JH, Kim JH, Sohn JH, Park JY, Park SK, Park J. Clinical relationship between Hashimoto's thyroiditis and papillary thyroid cancer. Acta Oncol. 2011;50(8):1228-34.

17.Azizi G, Keller JM, Lewis M, Piper K, Puett D, Rivenbark KM, Malchoff CD. Association of Hashimoto's thyroiditis with thyroid cancer. Endocr Relat Cancer. 2014;21(6):845-52.

18.Bradly DP, Reddy V, Prinz RA, Gattuso P. Incidental papillary carcinoma in patients treated surgically for benign thyroid diseases. Surgery. 2009;146(6):1099-104.

19.Lai X, Xia Y, Zhang B, Li J, Jiang Y. A meta-analysis of Hashimoto's thyroiditis and papillary thyroid carcinoma risk. Oncotarget. 2017;8(37):62414-24.

20.Anil C, Goksel S, Gursoy A. Hashimoto's thyroiditis is not associated with increased risk of thyroid cancer in patients with thyroid nodules: a single-center prospective study. Thyroid. 2010;20(6),601-6.

21.Matesa-Anić D, Matesa N, Dabelić N, Kusić Z. Coexistence of papillary carcinoma and Hashimoto's thyroiditis. Acta Clin Croat. 2009;48(1):9-12.

22.Lee JH, Kim Y, Choi JW, Kim YS. The association between papillary thyroid carcinoma and histologically proven Hashimoto's thyroiditis: a meta-analysis. Eur J Endocrinol. 2013;168(3):343-9.

[DOI: 10.22088/jbums.25.1.379]

23.Tamimi DM. The association between chronic lymphocytic thyroiditis and thyroid tumors. Int J Surg Pathol. 2002;10(2):141-6.

24.Jankovic B, Le KT, Hershman JM. Clinical Review: Hashimoto's thyroiditis and papillary thyroid carcinoma: is there a correlation?. J Clin Endocrinol Metab. 2013;98(2):474-82.

25.Azizi G, Malchoff CD. Autoimmune thyroid disease: a risk factor for thyroid cancer. Endocr Pract. 2011;17(2):201-9.

26.Rakha EA, Aleskandarany M, El-Sayed ME, Blamey RW, Elston CW, Ellis IO, et al. The prognostic significance of inflammation and medullary histological type in invasive carcinoma of the breast. Eur J Cancer. 2009;45(10):1780-7.

27.Matsubayashi S, Kawai K, Matsumoto Y, Mukuta T, Morita T, Hirai K, et al. The correlation between papillary thyroid carcinoma and lymphocytic infiltration in the thyroid gland. J Clin Endocrinol Metab. 1995;80(12):3421-4.

28.Gholami A, Mousavie Anijdan SH. The high ratio of thyroiditis as a main cause of thyrotoxicosis in patients referred to the nuclear medicine department of Babol Shahid Beheshti Hospital. J Babol Univ Med Sci. 2018;20(12):33-8. [In Persian]

[DOI: 10.22088/jbums.25.1.379]