

Original research article

The association of chronic lymphocytic thyroiditis and papillary carcinoma and its clinicopathological effects

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Abstract

Objective: To compare clinicopathological characteristics of patients with papillary thyroid carcinoma in association with the presence or absence of chronic lymphocytic thyroiditis in tertiary care hospital who underwent thyroidectomy.

Material and Method: This was a cross sectional retrospective study carried out by the Department of pathology, NAMO Medical Institute of Medical Science, Silvassa. In the present study, histopathological record of patients who underwent for total thyroidectomy were reviewed NAMO Medical Institute of Medical Science, Shree Vinoba Bhav Hospital, Silvassa, during the period of December 2019-December 2022. Total 20 cases of thyroidectomy specimen with papillary carcinoma were included in the present study. Following variables were taken in the present study: Age and gender of patient, presence of chronic lymphocytic thyroiditis, type of thyroid malignancy, tumor size and lymph node metastasis. The cancer other than papillary carcinoma and benign thyroid lesion were not included in the present study.

Result: Total 200 Thyroidectomy were done within December 2019-december 2022 (3 years period), from which 170 (85%) cases were benign thyroid lesion which were excluded from the study. Only 30 (15%) cases were malignant thyroid lesion from which 20 (66.67%) cases were of papillary carcinoma of thyroid, 6 (20%) cases were of follicular carcinoma, 1 (3.33%) case was of medullar carcinoma, and 3 (10%) cases were others like lymphoma and poorly differentiated malignancy. Among the 20 patients, there were 16 (80%) men and 4 (20%) women. Mean age was 48.23 ± 12.54 years. The mean tumor size was 2.5 ± 0.97 cm. Based on univariate analysis, the mean age of patients with and without CLT was 40.45 ± 10.64 and 46.6 ± 11.18 years, respectively (P-value=0.143). Predominance of female gender was observed in patients without CLT compared to patients with CLT. The mean tumor size was smaller in patients with CLT than patients without CLT (1.7 ± 0.88 cm vs 2.2 ± 0.92 cm, respectively; P=0.033).

Conclusion: The chronic lymphocytic Thyroiditis is positively associated with papillary carcinoma of Thyroiditis. The influence of Thyroiditis on prognosis of well differentiated thyroid epithelial malignancy needs to be evaluated on the larger sample size.

Keywords: Papillary, thyroid cancer, lymphocytic thyroiditis

Introduction

Chronic lymphocytic thyroiditis (CLT) is an autoimmune disease characterized by widespread lymphocytic infiltration, fibrosis, and late-stage parenchymal atrophy of thyroid tissue. It is the most common inflammatory disorder of the thyroid gland [1]. Papillary thyroid cancer (PTC) is the most common form of thyroid cancer, comprising approximately 80% of all thyroid cancers [2, 3]. Well-differentiated thyroid carcinoma and chronic lymphocytic thyroiditis are commonly encountered conditions in clinical practice [4-5]. Although the frequency of CLT varies widely from 0.5%-38%, the coexistence of CLT and PTC has been reported in several studies since first reported in 1955 [6, 7].

Chronic inflammation has been well established as a risk factor for the development of certain malignant tumors. Lymphocytic infiltration is frequently observed in differentiated thyroid carcinoma, suggesting immunological factors might be involved in tumor progression [8, 9]. The prevalence of CLT in patients with PTC has been reported to be significantly higher than with benign thyroid tumors [10]. Patients with CLT are believed to be at higher risk for PTC compared with patients without CLT [11].

The pathogenic mechanism explaining why PTC and CLT develop concurrently remains controversial,

although a number of theories have been suggested. One suggestion is that CLT may represent the host's immune response to preexisting PTC. Conversely, PTC may be induced or triggered by preexisting CLT. Alternatively, both diseases may result from an imbalance between apoptotic and anti-apoptotic pathways^[12]. Several previous reports have shown that the coexistence of CLT with PTC is associated with a better prognosis, a lower recurrence rate, and a less aggressive clinical presentation^[13-15]. However, other investigators have reported that the coexistence of CLT has no protective effect on patient outcome^[16, 17].

The results of most of the studies do not lead to definitive conclusions. Some evidence suggests that nonspecific focal or multifocal lymphocytic infiltrates may occur more frequently in cases of papillary thyroid carcinoma, possibly indicating that the tumor can exert some degree of influence on the rest of the gland. Some authors have reported that the presence of chronic lymphocytic thyroiditis, especially Hashimoto's thyroiditis in patients with papillary thyroid carcinoma, is associated with a less aggressive clinical presentation and course^[18, 19], while other studies have not found a similar effect^[20, 21]. The objective of this study was to evaluate the prevalence of an association between chronic lymphocytic thyroiditis and papillary thyroid carcinoma, and to compare clinicopathological characteristics of patients with papillary thyroid carcinoma in association with the presence or absence of chronic lymphocytic thyroiditis in tertiary care hospital who underwent thyroidectomy.

Material and Methodology

This was a cross sectional retrospective study carried out by the department of pathology, NAMO Medical Institute of Medical Science, Silvassa. In the present study, histopathological record of patients who underwent for total thyroidectomy were reviewed NAMO Medical Institute of Medical Science, Shree Vinoba Bhav Hospital, Silvassa, during the period of December 2019- December 2022. Total 20 cases of thyroidectomy specimen with papillary carcinoma were included in the present study.

Following variables were taken in the present study: Age and gender of patient, presence of chronic lymphocytic thyroiditis, type of thyroid malignancy, tumor size and lymph node metastasis. The cancer other than papillary carcinoma and benign thyroid lesion were not included in the present study.

In this study, tumors were considered multifocal when two or more malignant foci were found in the same gland. Capsular invasion was determined based on evidence of tumor infiltration beyond the capsule of the thyroid gland on microscopic examination. All data were collected by the same researcher and all pathologic reviews were performed by the same consultant pathologist.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics included computation of percentages, means and standard deviations were calculated. Statistical test applied for the analysis was student t-test. The level of confidence interval and p-value were set at 95% and 5%.

Result

Total 200 Thyroidectomy were done within December 2019-December 2022 (3 years period), from which 170 (85%) cases were benign thyroid lesion which were excluded from the study. Only 30 (15%) cases were malignant thyroid lesion from which 20(66.67%) cases were of papillary carcinoma of thyroid, 6(20%) cases were of follicular carcinoma, 1(3.33%) case was of medullary carcinoma, and 3(10%) cases were others like lymphoma and poorly differentiated malignancy. The malignancy other than papillary carcinoma were not included in the study. Females (53.33%) were more likely to have papillary carcinoma in our population compared with males. In our study patient with chronic lymphocytic Thyroiditis were more likely to have papillary carcinoma than those without Thyroiditis. Mean tumor size was smaller in patients with thyroiditis than those without Thyroiditis. Lymph node metastasis was common in patient without Thyroiditis than those with Thyroiditis (3 vs 1).

Table 1: Total no of thyroid malignancy with frequency of different type of thyroid malignancy in histopathological reports

| Variables | No. (%) |
|---|-------------|
| Total cases of thyroidectomy | 200 |
| Total cases of thyroid malignancy | 30 (100%) |
| Papillary carcinoma of thyroid | 20 (66.67%) |
| Follicular carcinoma of thyroid | 6 (20%) |
| Medullary carcinoma of thyroid | 1 (3.33%) |
| Others like lymphoma and poorly differentiated malignancy | 3 (10%) |

Table 2: Correlation of PTC without CLT and PTC with CLT in association with age, gender, maximum tumor size, Lymph node metastasis

| Parameters | All patients (100%) | Papillary carcinoma of thyroid with chronic lymphocytic thyroiditis (50%) | Papillary carcinoma of thyroid without chronic lymphocytic thyroiditis (50%) | P-value |
|--|---------------------|---|--|--------------|
| Age at the time of operation (mean age in years) | 48.23±12.54 | 40.45±10.64 | 46.6±11.18 | 0.143 |
| Gender | | | | |
| Female | 16 (80%) | 07 (70%) | 09 (90%) | 0.001 (Sig.) |
| Male | 04 (20%) | 03 (30%) | 01 (10%) | |
| Maximum tumor size in cm (mean size) | 2.5±0.97 | 1.7±0.88 | 2.2±0.92 | 0.033 (Sig.) |
| Lymph node metastasis | 3 (15%) | 2 (20%) | 1 (10%) | 0.642 (NS) |

Among the 20 patients, there were 16 (80%) men and 4 (20%) women. Mean age was 48.23±12.54 years. The mean tumor size was 2.5±0.97 cm. Based on univariate analysis, the mean age of patients with and without CLT was 40.45±10.64 and 46.6±11.18 years, respectively (P-value=0.143). Predominance of female gender was observed in patients without CLT compared to patients with CLT. The mean tumor size was smaller in patients with CLT than patients without CLT (1.7±0.88 cm vs 2.2±0.92 cm, respectively; P=0.033).

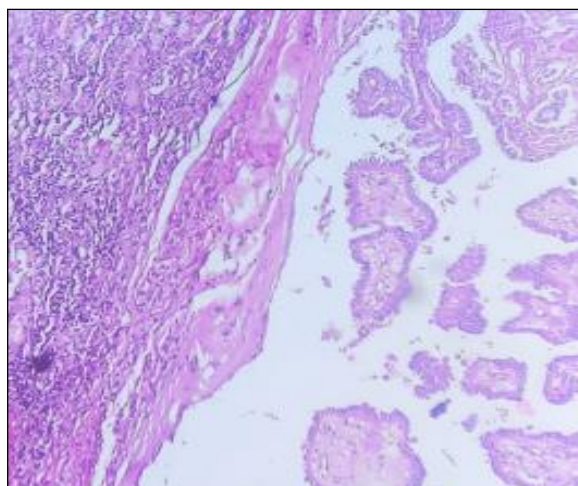


Fig 1: Papillary carcinoma with chronic lymphocytic Thyroiditis (x40)

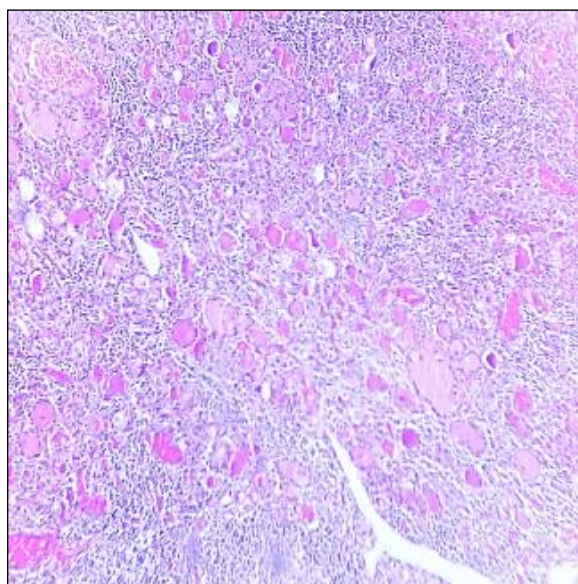


Fig 2: Chronic lymphocytic Thyroiditis (x40)

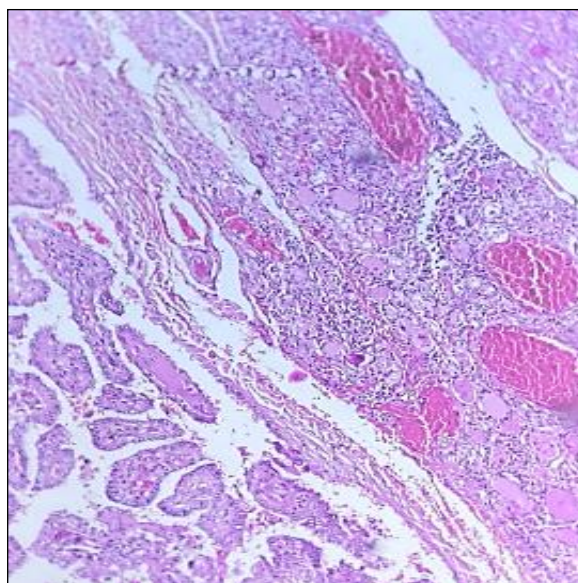


Fig 3: Papillary carcinoma with chronic lymphocytic Thyroiditis (40 x)

Discussion

In the present study presence of chronic lymphocytic Thyroiditis, age and gender were studied in papillary carcinoma and were significant predictor of presence/absence of thyroid carcinoma. Association between chronic lymphocytic Thyroiditis and papillary carcinoma is well established in many parts of world but in our country, it needed to be studied. In the present study chronic lymphocytic Thyroiditis was defined as presence of lymphoid follicles with germinal centers, presence or absence of hurthle cell changes and atrophic changes in the area of normal thyroid parenchyma and excluded the only lymphoid cell infiltration around the tumor cells.

In our study 50% of papillary carcinoma patient had chronic lymphocytic Thyroiditis is similar to other reports in thyroidectomy patients [7, 22]. In the different studies, the incidence of thyroid cancer developing against the background of chronic lymphocytic Thyroiditis has been reported to be between 0.5-23% [23, 24]. Singh *et al.* [25] and Replinger *et al.* [26] reported that the prevalence of thyroid cancer was significantly higher in patient with Thyroiditis compared with those without Thyroiditis.

In our study, females (53.33%) were more likely to have papillary carcinoma in our population compared with males which is similar to Nadeesha J nawaratha *et al.* study [27]. In our study, patient with chronic lymphocytic Thyroiditis were more likely to have papillary carcinoma than those without Thyroiditis which is compared to Nadeesha *et al.* study [27] and Jun Soojeong *et al.* study [28]. In our study, mean tumor size was smaller in patients with thyroiditis than those without Thyroiditis compared to Jun soo jeong *et al.* study [28]. Lymph node metastasis was common in patient without Thyroiditis than those with Thyroiditis which is also comparable to Jun soo jeong *et al.* study [28].

Bagnasco *et al.* [29] reported a higher proportion of cytotoxic T cells with natural killer (NK)-like or lymphokine-activated killer activity in PTC infiltrating T cells compared to those occurring in autoimmune thyroid disorders (Hashimoto's thyroiditis and Graves' disease). In addition to the primarily cell-mediated inflammatory reaction observed in PTC. Lucas *et al.* [30] demonstrated that more humoral-mediated immune reactions occur with PTC (80% of PTC cases) than with other thyroid neoplasms or autoimmune thyroid disorders. This study suggests that a humoral-specific tumor immune response consisting of an immunoglobulin/complement-mediated reaction may also occur with PTC.

In a retrospective study conducted by Kim *et al.*, [31], the presence of CLT in patients with PTC was associated with a smaller tumor size, younger age, and female predominant. The Fas-mediated apoptotic pathway activated by Fas and Fas ligand is expressed in follicular cells in patients with CLT and involved in the destruction of tumor cells in patients with Hashimoto's thyroiditis, which is quite similar to CLT histopathologically [32]. Kimura *et al.* [33] reported that interleukin-1 inhibits human thyroid carcinoma cell growth. So, the destruction of tumor cells via humoral and cytotoxic T cell-mediated immune mechanisms might be related to the favorable effect of CLT on PTC.

Prognosis of thyroid cancers is affected by multiple clinicopathological factors, such as gender, age, tumor size, multifocality, capsular invasion, lymphovascular invasion, lymph node metastasis, and distant metastasis [34]. However, the influence of coexisting nonspecific chronic lymphocytic thyroiditis on the behavior of thyroid carcinoma is still debatable. Although majority of studies showed a protective effect of associated chronic lymphocytic thyroiditis, some studies reported a worse prognosis, while others pointed that it does not affect its prognosis [35].

Conclusion

In conclusion, in our study, we found a significant correlation between chronic lymphocytic thyroiditis and papillary carcinoma of thyroid. In our study, patients with Thyroiditis were of younger age ground and had small tumor size and lower rate of lymph node metastasis. The influence of Thyroiditis on prognosis of well differentiated thyroid epithelial malignancy needs to be evaluated on the larger sample size.

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