Association between Thyroiditis and Multifocality in Papillary Thyroid Carcinoma

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Abstract

Introduction Hashimoto thyroiditis (HT) shares many characteristics with papillary thyroid carcinoma (PTC), and some studies show that, when associated, PTC is diagnosed mostly with smaller lesions and multifocal pattern.

Objective To evaluate the relationship between HT and PTC.

Methods A retrospective study of 155 patients who underwent total thyroidectomy from 2009 to 2015. Demographical, clinical and ultrasonographical data, as well as anatomopathological findings were evaluated.

Results There were signs of thyroiditis in 35 patients, and 114 patients had a unifocal disease. There was no statistical significance between the variables studied and thyroiditis. However, when compared with the occurrence of unifocal or multifocal lesions, there was statistical significance regarding age (p = 0.038) and mass (p = 0.031). There was no direct relationship between thyroiditis and multifocality (p = 0.325) nor between thyroiditis and cervical extension of the disease (p = 0.300 and p = 0.434).

Conclusion There was no relationship between thyroiditis and multifocality in cases of PTC.

Keywords
► thyroiditis
► papillary thyroid carcinoma
► thyroid cancer

Introduction

Hashimoto thyroiditis (HT) was first described in 1912 by the Japanese surgeon Hakaru Hashimoto, in Berlin, Germany.1 It is the most common disease in the thyroid gland, and it occurs mainly in women.2 It is an inflammatory autoimmune disease with diffuse infiltration of the gland by lymphocytes, leading to fibrosis and atrophy, and is the most common cause of hypothyroidism.3–5 Papillary thyroid carcinoma (PTC) is the most common thyroid cancer, responsible for ~ 70% to 80% of cases of this tumor.

The first causal association between both conditions was proposed in 1955 by Dailey et al.6 However, some
controversy still remains. Some papers suggest a strong relationship between them,²⁻⁹ whereas others do not.¹⁰,¹¹

Hashimoto thyroiditis shares many characteristics with PTC, such as similar morphology, immunohistochemical pattern, and molecular profile, suggesting that it could be a predisposing factor for PTC.¹⁰ Thus, some papers show that, in patients with HT, there is an increase of ~ 30% in cases of PTC. When associated with HT, PTC is diagnosed mostly in young women, with smaller lesions, in an early and multifocal pattern, and with better prognosis.³⁵,⁷,⁸,¹²

The objective of the present study was to evaluate the relationship between these diseases.

Methods

The present study was approved by the Ethics and Research Committee of the institution in which it was performed under number 83977318.4.0000.5509.

It is a retrospective study to evaluate the medical records of patients treated in a tertiary reference facility. In total, 155 patients treated between 2009 and 2015 were evaluated. They underwent total thyroidectomy, with or without neck dissection and radioiodine therapy, according to the protocol of the institution.

Demographical data (gender and age), clinical and ultrasonographic data, as well as anatomo-pathological findings (presence of chronic thyroiditis, size and multicentricity of the lesions and staging of the neck) were evaluated. All histopathological data was reviewed by the same pathologist. Based on the histopathological findings, the possible risk factors for multicentricity, including the presence of chronic thyroiditis, were evaluated.

Frequency distribution was used to describe the categorical variables, (number of cases and percentage) the central measurement tendencies (average and median) and dispersion measurements. The Student t-test was used to check the association between the numerical variables, and the Fisher exact test was employed to compare the categorical variables. A significance level of 5% was used for all statistical tests.

Results

In total, 155 files of patients were evaluated after the anatomo-pathological analysis of the surgical specimens: 120

Table 1 Patient distribution (n = 155)

| Aspect         | With thyroiditis (n = 35) | Without thyroiditis (n = 120) | Total |
|----------------|--------------------------|------------------------------|-------|
| Men            | 6 (17.1%)                 | 13 (10.9%)                   | 19    |
| Women          | 29 (82.9%)                | 107 (89.1%)                  | 136   |
| Unifocal       | 28 (80%)                  | 86 (71.6%)                   | 114   |
| Multifocal     | 7 (20%)                   | 36 (28.4%)                   | 41    |
| N0             | 34 (97.1%)                | 109 (90.8%)                  | 143   |
| N1a            | 1 (2.9%)                  | 8 (6.6%)                     | 9     |
| N1b            | 0                         | 3 (2.6%)                     | 3     |

Table 2 Average characteristics of the patients according to the presence of thyroiditis

|                        | Without thyroiditis | With thyroiditis | p-value |
|------------------------|--------------------|------------------|---------|
| Age (years)            | 50.37              | 52.71            | 0.434   |
| Mass (grams)           | 26.91              | 25.20            | 0.795   |
| Measurement of the higher focus (mm) | 12.77 | 12.26 | 0.737 |

showed no signs of thyroiditis, 114 showed unifocal disease, and 143 didn’t developed regional metastasis (→Table 1).

After the evaluation and comparison of the results, the main variables were age, size of the largest focus and glandular mass. There was no statistical significance when these variables were related to the presence of thyroiditis (→Table 2). However, when compared with the occurrence of unifocal or multifocal lesions, there was statistical significance for age (p = 0.038) and mass (p = 0.031) (→Table 3). Nevertheless, the tests did not show the same results for multifocality and uni/bilaterality (→Tables 4).

There was no direct relationship between thyroiditis and multifocality (p = 0.325) nor between thyroiditis and cervical extension of the disease (p = 0.300 and p = 0.434) (→Table 5).

Discussion

Some controversy in the literature still remains about the relationship between HT and PTC. Some papers³⁻⁵,¹² suggest a strong positive relationship between them, as well as a cause and effect relation in which the inflammatory process

Table 3 Average characteristics of the patients according to multifocality

|                        | Unilateral multifocal lesions | Bilateral lesions | p-value |
|------------------------|-------------------------------|-------------------|---------|
| Age (years)            | 48                            | 46                | 0.707   |
| Mass (grams)           | 28.16                         | 19.37             | 0.53    |
| Measurement of the higher focus (mm) | 15  | 16.48 | 0.99 |

Table 4 Comparison between unifocal and multifocal lesions

|                        | Unifocal lesion | Multifocal lesions | p-value |
|------------------------|-----------------|--------------------|---------|
| Age (years)            | 52.45           | 46.59              | 0.038   |
| Mass (grams)           | 28.17           | 21.95              | 0.031   |
| Measurement of the higher focus (mm) | 11.43 | 16.05 | 0.104 |
The mechanism of such an association is unknown. It is possible that TgAb has a tumorigenic effect or is strongly associated with a specific tumorigenic inflammatory response. Changed processing or mutation in the molecular structure of thyroglobulin can increase its antigenicity. On the other hand, some studies suggest that there is no relation-ship or difference in age and glandular mass with unifocal or multifocal PTC. Thyroiditis was more frequently observed in multifocal PTC than in the unifocal disease; however, a significant statistical heterogeneity was verified in the studies.7

Our study showed positive and statistical significance between multifocality, age and glandular mass. Some articles28–30 in the literature remain controversial on this point. In spite of the fact that the age of the patients is similar in the studies, some28,29 point out that there is no relationship or difference in age and glandular mass with unifocal or multifocal lesions, whereas others30 show a positive relationship between these variables. It is possible that more studies, with a larger number of patients enrolled, would be necessary in order to reach a definitive conclusion.

We did not find statistical significance in the analysis of cervical extension (neck metastasis) when compared with multifocality and thyroiditis when associated, just like many studies.31–33 However, other studies show that multifocality is an independent risk factor for the occurrence of neck metastasis, mainly in the central neck34–43 and regarding young male patients.29

### Conclusion

There was no relationship between thyroiditis and the occurrence of multifocality in cases of PTC. However, we found statistical significance between multifocality, glandular mass and the age of the patients in the study.
Conflict of Interests
The authors have no conflict of interests to declare.

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