

COEXISTENCE OF PAPILLARY CARCINOMA AND HASHIMOTO'S THYROIDITIS

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SUMMARY – The aim of the study was to determine the incidence of coexistence of papillary carcinoma and Hashimoto's thyroiditis in cytologic material. Cytologic findings were collected from 10508 patients that underwent ultrasound-guided fine needle aspiration cytology (FNAC) of the thyroid. Hashimoto's thyroiditis was found in 2156 (20.5%) and papillary carcinoma in 269 (2.6%) of 10508 patients with FNAC, whereas both Hashimoto's thyroiditis and papillary carcinoma were present in 42 (0.4%) patients. Among patients with FNAC diagnosis of Hashimoto's thyroiditis, the prevalence of papillary carcinoma was 1.9%. Among patients with FNAC diagnosis of papillary carcinoma, the prevalence of Hashimoto's thyroiditis was 15.6%. There was no statistically significant association between the presence of papillary carcinoma and Hashimoto's thyroiditis in patients undergoing FNAC ($p=0.0522$). In conclusion, in a large series of patients, the incidence of Hashimoto's thyroiditis and papillary carcinoma coexistence in cytologic material was 0.4%. There was no statistically significant relationship between Hashimoto's thyroiditis and papillary carcinoma in cytologic material.

Key words: *Thyroid neoplasms – cytology; Thyroid neoplasms – surgery; Carcinoma, papillary – cytology; Thyroiditis, autoimmune – pathology; Thyroidectomy*

Introduction

The association between Hashimoto's thyroiditis (HT) and papillary carcinoma (PC) of the thyroid remains controversial. Since the first report by Dailey *et al.* in 1955¹, the relation between HT and PC has been frequently discussed and suggested mostly on the basis of retrospective analyses of surgical series²⁻¹³. A higher rate of PC in patients with HT, and a higher rate of HT in patients with PC was recorded in several studies, indicating the possible correlation between these two diseases^{5,10,13,15-18,20,21}. The main limitation of these studies was that they were carried out in patients that had undergone thyroidectomy and were therefore subject to potential selection bias. In contrast to surgical and pathologic series, large population-based clinical stud-

ies^{6,7,14,19} failed to show any significant increase in the incidence of thyroid cancer in cohorts of patients with HT.

The aim of our study was to determine the incidence of PC and HT coexistence in cytologic material of a large series of patients. We also analyzed the potential association between HT and PC in a retrospective search of cytologic diagnoses.

Patients and Methods

In a retrospective study, we analyzed data on 10508 patients that underwent ultrasound-guided fine needle aspiration cytology (FNAC) of the thyroid during a 12-year period (1995-2006). It was an unselected group of consecutive patients referred to our outpatient service. There were 979 (9.3%) male and 9529 (90.7%) female patients, mean age 52 (age range 2-88) years. Thyroid autoantibodies were determined in 345 patients with cytologic diagnosis of HT and were positive in 309 (89.6%) patients. Aspirates were smeared for conven-

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tional cytology (MGG staining). One to three punctures *per* nodule were performed depending on the nodule size. Adjunctive molecular techniques were not used.

Cytologic criteria for HT were the presence of mature and stimulated lymphocytes and a variable amount of follicular and/or Hürthle cells. Cytologic criteria for PC were the presence of papillary and/or follicular structures and characteristic nuclear features (finely granular chromatin and nuclear cytoplasmic inclusions). The criterion for HT and PC coexistence was the presence of both cytologic diagnoses at the same time (Fig. 1).

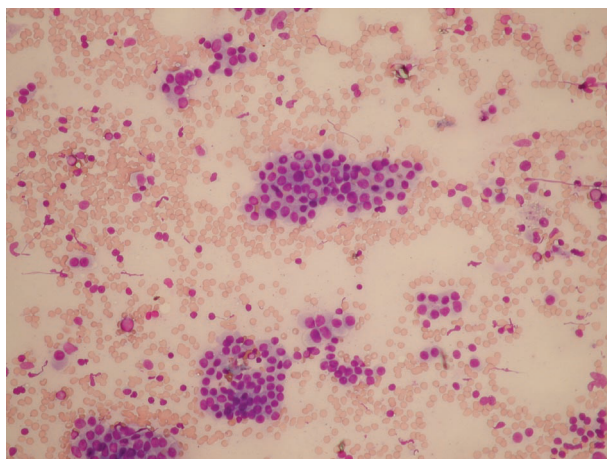


Fig. 1. Coexistence of papillary carcinoma and Hashimoto's thyroiditis (May-Grünwald-Giemsa, X400).

We evaluated the prevalence of HT and of PC in all patients undergoing FNAC; the prevalence of coexisting HT and PC in all patients undergoing FNAC; the prevalence of PC in patients with FNAC diagnosis of HT; and the prevalence of HT in patients with FNAC diagnosis of PC. The potential association between the presence of PC and HT in cytologic material was assessed by use of χ^2 -test. The differences were considered significant at $p < 0.01$.

Table 1. Prevalence of papillary carcinoma (PC) and Hashimoto's thyroiditis (HT) in fine needle aspiration cytology reports

Cytologic diagnosis	Number of patients (%)
HT	2114 (20.12)
HT + PC	42 (0.40)
PC	227 (2.16)
Other	8125 (77.32)
Total	10508 (100)

Results

The sensitivity, specificity, false negative rate and false positive rate for FNAC were 99.7%, 92.7%, 0.1% and 3.9%, respectively. HT was found in 2156 (20.5%) of 10508 patients with FNAC diagnosis, 89 (4.1%) male and 2068 (95.9%) female patients, mean age 48 (range 3-85) years. PC was found in 269 (2.6%) of 10508 patients with FNAC diagnosis, 33 (12.3%) male and 236 (87.7%) female patients, mean age 51 (range 14-85) years. Coexistent HT and PC were recorded in 42 (0.4%) of all patients undergoing FNAC, one (2.4%) male patient and 41 (97.6%) female patients, mean age 50 (range 19-72) years (Table 1).

Table 2. Association between papillary carcinoma (PC) and Hashimoto's thyroiditis (HT) in fine needle aspiration cytology reports

Cytologic diagnosis	HT present	HT absent	Total
PC present	42	227	269
PC absent	2114	8125	10239
Total	2156	8352	10508

χ^2 -test: $p = 0.0522$

Among 2156 patients with FNAC diagnosis of HT, the prevalence of PC was 1.9%, which is lower than the prevalence of PC in other patients without HT (2.7%). Among 269 patients with FNAC diagnosis of PC, the prevalence of HT was 15.6%, which is lower than the prevalence of HT in other patients without PC (20.6%). There was no statistically significant difference ($p = 0.0522$) between the presence of PC in patients with HT and the presence of PC in other patients undergoing FNAC (Table 2).

Discussion

The association of HT and thyroid cancer (particularly PC) has been suggested mostly on the basis of retrospective analyses of surgical series. Hirabayashi and Lindsay⁵ report an increased prevalence (22.5%) of thyroid cancer in thyroids affected by HT when compared with glands without HT (2.4%). Okayasu *et al.*¹³ provided clear evidence for the prevalence of lymphocytic infiltration to be higher in patients with PC than in patients with adenomatous goiter or follicular adenoma. Ott *et al.*¹⁰ have reported a 32% incidence of thyroid

carcinoma in patients with HT⁸. Cipolla *et al.*¹⁵ found an association with HT in 26.7% of PC subjects. Singh *et al.*¹⁸ found the prevalence of HT to be significantly higher in patients with PC (odds ratio, 1.89; 95% CI, 1.02-3.50). In a retrospective study of patients that underwent initial thyroidectomy for PC, Kebebew *et al.*²⁰ report on 30% of patients with PC to have coexisting chronic lymphocytic thyroiditis. Repplinger *et al.*²¹ have reported that HT is associated with an increased risk of developing PC. Female patients with HT undergoing thyroidectomy are by 30% more likely to have PC.

Contrary, some other authors failed to show any significant increase in the incidence of thyroid cancer in patients with HT. Intidhar Labidy *et al.*¹⁴ found incidence thyroid cancer associated with highly selected population of HT patients in 14.1% of cases. Crile⁶ reports that observation of 373 patients with struma lymphomatosa diagnosed by FNAC failed to reveal a single instance of carcinoma of the thyroid. Matsubayashi *et al.*¹² and Kashima *et al.*¹¹ did not find correlation between HT and PC but they report that lymphocytic infiltration surrounding the tumor or inside the tumor in PC might be of use as a means for predicting a favorable prognosis. Segal *et al.*⁷ report that in 7 cases of HT occurring in association with carcinoma there was no evidence suggesting that thyroid carcinoma originated from the proliferating epithelium of HT. They suggest that thyroid carcinoma stimulates the development of HT in some patients, and that the presence of the autoimmune inflammatory reaction and circulating antibodies retards the growth and dissemination of thyroid carcinoma. Similarly, in a retrospective study of 859 patients with PC that underwent thyroid operation, McConahey *et al.*⁹ found the death from thyroid cancer to be highly associated with the absence of HT.

Our findings obtained in a large series of unselected patients that underwent thyroid FNAC showed a low rate (0.4%) of PC and HT coexistence. We found no statistically significant difference ($p=0.0522$) in the prevalence of PC in patients with HT when compared with the prevalence of PC in other patients undergoing FNAC. Our results obtained in a large series of 10508 unselected patients showed that there was no statistically significant association between the presence of HT and the presence of PC in cytologic material, allowing for a conclusion that the relationship between HT and PC reported in patients that had undergone thyroidectomy may be a subject of a selection bias.

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Sažetak

ISTODOBNA PRISUTNOST PAPILARNOG KARCINOMA I HASHIMOTOVOG TIREOIDITISA

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Cilj ove studije bio je utvrditi incidenciju istodobne prisutnosti papilarnog karcinoma i Hashimotova tireoiditisa u citološkim uzorcima. Prikupljeni su citološki nalazi za 10.508 bolesnika podvrgnutih ultrazvučnoj citološkoj punkciji štitnjače tankom iglom (FNAC). Hashimotov tireoiditis je utvrđen kod 2156 (20,5%), a papilarni karcinom kod 269 (2,6%) od tih 10.508 bolesnika, dok je 42 (0,4%) bolesnika imalo i papilarni karcinom i Hashimotov tireoiditis. U bolesnika s Hashimotovim tireoiditisom učestalost papilarnog karcinoma bila je 1,9%, a među bolesnicima s papilarnim karcinomom učestalost Hashimotova tireoiditisa bila je 15,6%. Kod bolesnika podvrgnutih FNAC nije bilo statistički značajne povezanosti između prisutnosti papilarnog karcinoma i Hashimotova tireoiditisa ($p=0,0522$). Dakle, u citološkom materijalu velikog niza bolesnika utvrđena je incidencija istodobne prisutnosti papilarnog karcinoma i Hashimotova tireoiditisa od 0,4%. U citološkim uzorcima nije utvrđena statistički značajna povezanost između Hashimotova tireoiditisa i papilarnog karcinoma.

Cljučne riječi: Novotvorine štitnjače – citologija; Novotvorine štitnjače – kirurgija; Karcinom, papilarni – citologija; Tireoiditis, autoimuni – patologija; Tireidektomija