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Case Report

Benign on cytology, malignant on histopathology: Coexistence of Hashimoto's thyroiditis with Papillary carcinoma of thyroid

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Abstract

Papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT) are common diseases in clinical practice. Hashimoto's thyroiditis is the most common autoimmune thyroid disease and the most common cause of hypothyroidism. It is characterized by diffuse lymphocyte infiltration, fibrosis, and parenchymal atrophy. Papillary thyroid carcinoma is the most common malignant neoplasm of the thyroid. There is a high prevalence of association between HT and PTC. FNAB is useful for diagnosing PTC in patients with HT associated thyroid lesions. The presence of HT in patients with PTC was associated with disease presentation at an earlier stage, less aggressive clinical course and better outcome. Here we have presented a case of hashimoto's thyroiditis with papillary thyroid carcinoma in a 37 years old female who came with complaints of swelling in front of neck. Cytology and radiology showed features of HT but, on histopathology it was diagnosed as HT with PTC.

Key words

Benign, Malignant, Autoimmune, Hashimoto's thyroiditis, Papillary thyroid carcinoma, Cytology, Histopathology.

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Introduction

Hashimoto's thyroiditis (HT) is the most common autoimmune thyroid disease and the most common cause of hypothyroidism [1]. Hakaru Hashimoto, a Japanese surgeon and pathologist, first described this condition in 1912. It is characterized by diffuse lymphocyte infiltration, fibrosis, and parenchymal atrophy. Thyroid autoimmune diseases are more commonly expressed in women when compared to men, and such trend is even more obvious in the post-menopausal period [1]. Papillary thyroid carcinoma (PTC) is the most common malignant neoplasm of the thyroid accounting for 70 % to 80 % of thyroid cancers [2]. There is a high prevalence of association between HT and PTC. The presence of HT in patients with PTC was associated with disease presentation at an earlier stage, less aggressive clinical course and better outcome [3]. Here, we have presented such a case of Hashimoto's thyroiditis with Papillary thyroid carcinoma in a 37 years old female patient.

Case report

A 37 years old female patient came to our hospital with complaints of swelling in front of neck since 1 year. She had no other significant clinical history. On examination, there was a moderate diffuse enlargement of the thyroid gland, which was moving with deglutition. There were no symptoms of hypo or hyperthyroidism. Routine blood investigations revealed slightly low T3 and T4 levels with mild elevation of TSH levels. Ultrasonography and cytology showed features of hashimoto's thyroiditis. **(Photo – 1, Photo - 2)** There was an elevation of the anti-thyroid peroxidase antibodies. Due to cosmetic reasons patient underwent subtotal thyroidectomy.

Grossly, we received a nodule of thyroid measuring 2.5 x 2 cm. Cut section showed solid meaty appearance. Microscopy, sections showed predominantly areas showing features of hashimoto's thyroiditis **(Photo – 3, Photo - 4)** with few foci showing tumor tissue with papillary architecture and central fibrovascular core. Individual cells were oval, overlapping and overcrowding with clear nucleus; intranuclear inclusion and grooves. **(Photo – 5, Photo - 6)**

Photo – 1: Clusters of thyroid follicular cells with hurthle cell change. (Low power)

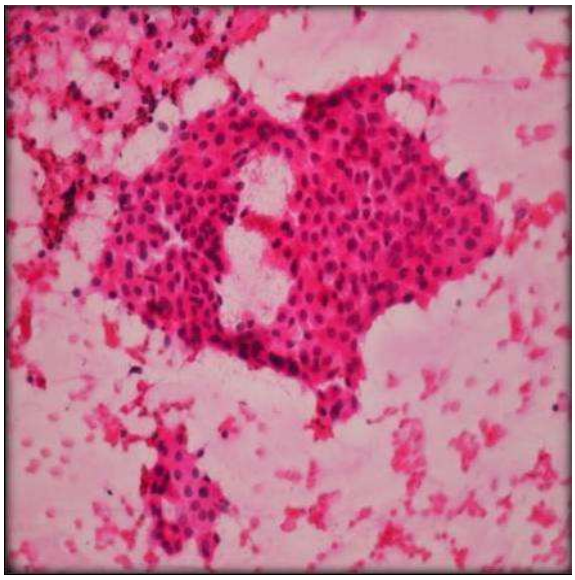

Photo – 2: Clusters of thyroid follicular cells with hurthle cell change. (High power)

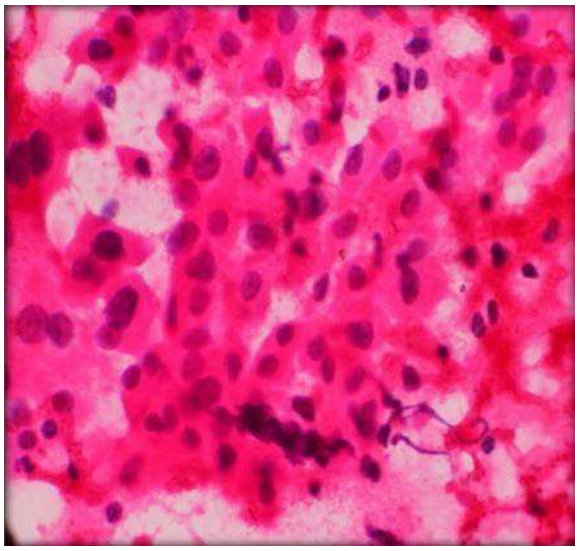

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Photo – 3: Features of hashimoto's thyroiditis with lymphoid aggregates. (Low power)

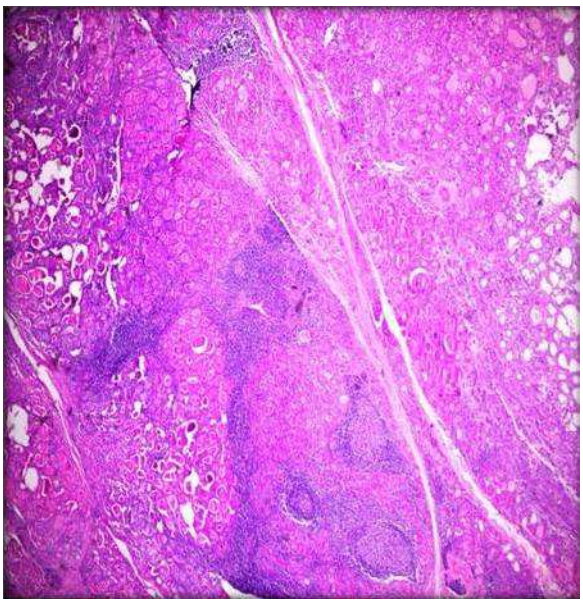
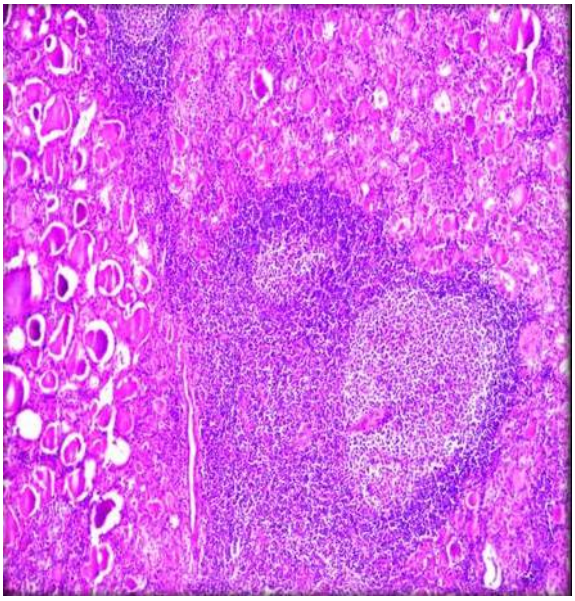


Photo – 4: Features of hashimoto's thyroiditis with lymphoid aggregates. (High power)



Discussion

Papillary thyroid carcinoma (PTC) and Hashimoto's thyroiditis (HT) are common diseases in clinical practice. HT is the most prevalent autoimmune disease and one of the most common endocrine diseases [3]. The disease occurs in 0.3–1.5 per 1000 individuals worldwide and is more predominant in females with gender prevalence ratios of 5 to 20: 1 [4, 5]. Pathogenesis strongly indicates an autoimmune background, associated with T-helper lymphocyte (CD4+) activation by class II human leukocyte antigen cells [5]. Ninety percent of the cases have high anti-thyroid peroxidase and anti-thyroglobulin antibody titres. The cause of HT is thought to be a combination of genetic susceptibility and environmental factors. Papillary thyroid carcinoma (PTC) is the most common malignant neoplasm of the thyroid accounting for 70 % to 80 % of thyroid malignancies [4]. The risk factors for PTC, including radiation exposure, insufficient iodine intake, hormonal factors, and family history. The association between PTC and HT was first described in 1955 by Dailey, et al [6]. Clinically HT presents with diffuse enlargement of the thyroid gland with low levels of serum T3 and T4. Sonographic findings of diffuse HT include decreased echogenicity, heterogeneity, hypervascularity, and presence of hypo echoic micro nodules with echogenic rim. It is characterized by diffuse lymphocyte infiltration, fibrosis, and parenchymal atrophy. Definitive diagnosis depends on the clinical examination, hormone levels and cytology but histopathology is confirmatory [4]. Our case presented as hashimoto's thyroiditis clinically, radiologically and cytologically but on histopathology, there was an evidence of papillary carcinoma along with HT. The gold standard for diagnosis of papillary thyroid carcinoma is conventional histology, the essential element being the characteristic nuclear features, regardless of papillary structures. The nuclear changes include nuclear overlapping, elongated ground glass nuclei with grooves and pseudo inclusions are characteristic. Immunoexpression of high molecular weight cytokeratins, S100 protein and HBME-1 helps to identify papillary thyroid carcinoma [7]. FNAB is useful for diagnosing PTC

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in patients with HT associated thyroid lesions, with a sensitivity of more than 90% [4, 8]. It is important to distinguish between diffuse and focal lymphocytic infiltration around the tumor.

Photo – 5: Papillary arrangement of tumor tissue.

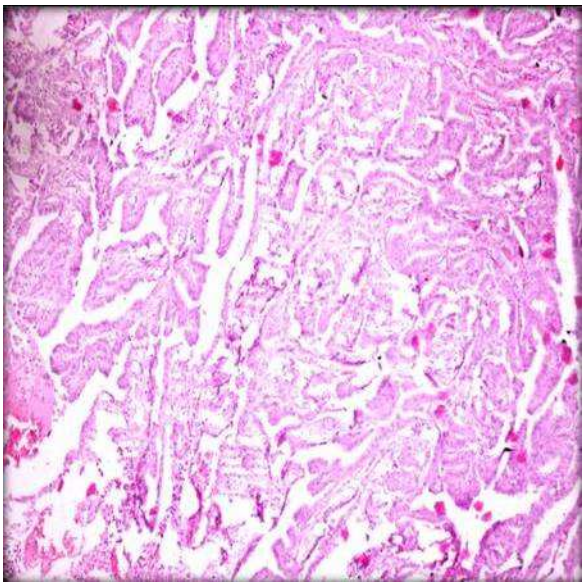
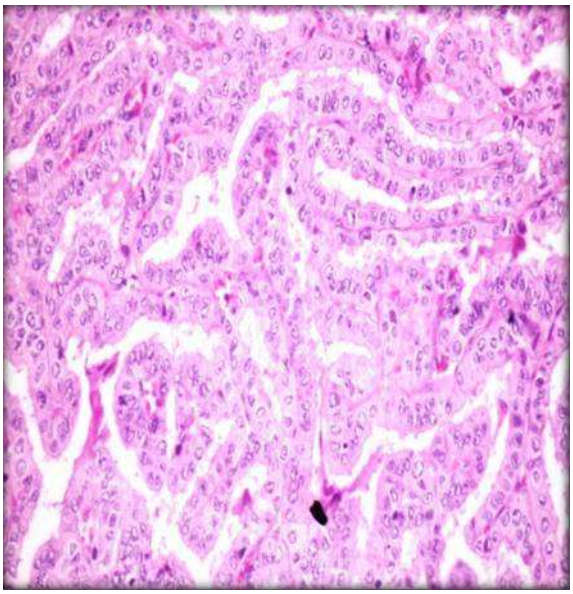


Photo – 6: Nuclear features of papillary thyroid carcinoma



HT was defined as diffuse lymphocytic infiltration, rather than peritumoral lymphocytic infiltration alone. The inflammatory response may cause DNA damage through formation of reactive oxygen species, resulting in mutations that eventually lead to the development of PTC [4]. The frequency of HT in PTCs was about 23%, ranging from 5 to 85%. The varying incidence rates of HT in PTC may be due to several factors such as different diagnostic criteria for HT, various surgical procedures, and heterogeneous patient characteristics [9]. Several studied demonstrated that serum TSH levels might play an important role. Thus, when considering whether HT is a risk factor for PTC, it is important to evaluate the serum TSH level. HT and PTC is that elevated levels of TSH found in hypothyroid patients with HT stimulate follicular epithelial proliferation, thereby promoting the development of papillary carcinoma.

It remains unclear whether HT predisposes patients to develop PTC or HT is an incidental finding with concurrent PTC, or HT is a part of the host tumor response system. However, PTC with concurrent HT is associated with female gender, young age, less aggressive disease such as small tumor size, less frequent capsular invasion and nodal metastasis, and better prognosis [3, 4, 5, 9].

Conversely, several authors identified a few biomolecular markers, including RET/PTC rearrangements, p63 protein, and loss of heterozygosity of hOGG1, that are potentially involved in neoplastic transformation from HT to PTC [1, 4, 7, 8, 9, 10]. Recently, genome-wide association studies (GWAS) and carefully designed candidate gene approaches have determined that the FOXE1 genetic variant, which is downstream of the TSH-cAMP pathway, is the suspected risk factor for follicular cell derived thyroid cancer [10]. However, many studies showed a clear association between both the conditions still there are controversies,

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which require further research for definite criteria.

Conclusion

HT and PTC are the common conditions occurring in thyroid. Several studies demonstrated an association between both the conditions due to overlapping morphological, immunohistochemical and molecular features. PTC with concurrent HT is associated with female gender, young age, less aggressive disease such as small tumor size, less frequent capsular invasion and nodal metastasis, and better prognosis. Careful observation and follow up of HT patients is recommended, especially those with nodular variants to exclude PTC.

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