

Simultaneous papillary carcinoma and mucosa-associated lymphoid tissue (MALT) lymphoma of the thyroid; a case report

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Abstract

Primary lymphoma of the thyroid is an uncommon malignancy, whereas papillary thyroid carcinoma is the most common thyroid malignancy. Both have an association with Hashimoto's thyroiditis. We discuss a case of an 83 year old male who presented with a large neck swelling, which subsequently proved to be a primary thyroid lymphoma (extra-nodal marginal zone) with concurrent papillary thyroid carcinoma. These tumours manifested on a background of Hashimoto's thyroiditis. To date there have only been 13 other cases of joint papillary thyroid carcinoma and thyroid lymphoma within the literature. Our case report adds to this by discussing diagnosis, histopathological features and pitfalls in early detection.

Keywords autoimmune thyroiditis; Hashimoto's thyroiditis; MALT lymphoma; papillary thyroid carcinoma; thyroid

Background

Primary lymphoma of the thyroid is an uncommon malignancy, accounting for 0.6–5% of thyroid malignancies, and women are more commonly affected, in the 6th decade.^{1,2} The most common primary thyroid lymphoma is diffuse large B-cell, which may arise from mucosa-associated lymphoid tissue lymphomas (MALT), and in some instances the two malignancies may be mixed.²

Papillary thyroid carcinoma is usually the least aggressive and most common of thyroid carcinomas, with a 211% increase in incidence rates in the USA between 1975 and 2013.³ Some authors have suggested that this increase is due to improved diagnostics and over-diagnosis of small tumours which would otherwise likely remain indolent.^{4,5} Despite this, there has been an increase in the USA of thyroid-cancer related mortality since 1994 (an increase of approximately 1.1% per year), and this

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trend mirrors the fact that there has also been an increase in the incidence of advanced stage papillary thyroid carcinoma.³

Hashimoto's thyroiditis is associated with both papillary thyroid carcinoma and primary thyroid lymphomas.^{6,7} Hashimoto's thyroiditis is a term synonymously used for autoimmune thyroiditis, and the disease is caused by a predominantly T-cell mediated autoimmunity.⁸

Case report

An 83 year old male presented to ENT with a swelling of the right neck in 2015. The serum TSH level was elevated and the serum free T4 level was low. An ultrasound scan of the neck was undertaken, which showed an enlarged right thyroid lobe containing a deep hyperechoic, partially calcified nodule. The nodule was BTA (British Thyroid Association) classification U3 and a fine needle aspiration (FNA) biopsy was performed.

The FNA showed classical features of papillary thyroid carcinoma such as nuclear grooves, inclusions and clearing. Background inflammatory cells and macrophages were also seen. The cell block confirmed the diagnosis of papillary thyroid carcinoma and a total thyroidectomy was arranged.

The operation was complicated due to scarring from previous surgery undertaken on the left thyroid at a private hospital, where a subtotal hemithyroidectomy was undertaken many years previously. The histology reports for this were not available for review, but no malignancy was identified at that time. Due to the scarring, the thyroid was excised in two pieces.

A solitary focus of classical papillary thyroid carcinoma was identified in the right lobe, measuring 18 mm in maximum size (Figure 1). No lymphovascular invasion, extrathyroidal extension or anaplastic features were seen. The background thyroid demonstrated areas of atrophy and fibrosis with focal reactive changes consistent with a Hashimoto's thyroiditis (Figure 2). However, in addition there was a prominent, diffuse infiltration of small to medium sized B-cell lymphocytes across both lobes (confirmed with CD20 and CD3 immunohistochemistry), with loss of germinal centres (Figure 3). The lymphoid infiltrate extended beyond the thyroid and into adjacent fibro-fatty connective tissues, indicating an infiltrative and invasive nature. Kappa restriction was identified using kappa and lambda light chain immunohistochemistry. Four level 6 lymph nodes were

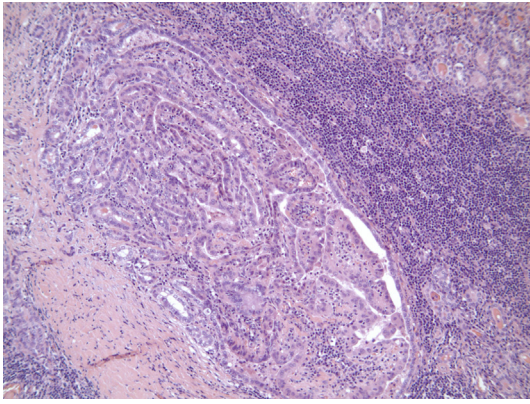


Figure 1 Papillary thyroid carcinoma, with a classical papillary architecture and nuclear features such as grooves and clearing. Haematoxylin and eosin, x10 magnification.

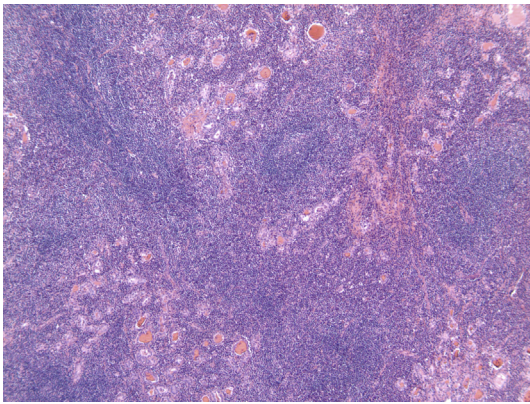


Figure 2 Hashimoto's thyroiditis, displaying germinal centres, atrophic thyroid follicles and oncocytic change. Haematoxylin and eosin, x 5 magnification.

included in the resection and no evidence of metastatic papillary thyroid carcinoma was seen. There was no evidence of lymphoma in the lymph nodes, and this was confirmed with immunohistochemistry for CD3, CD20, CD21 and CD23. The diagnosis of papillary thyroid carcinoma with concurrent extra-nodal marginal zone lymphoma was made and the case referred to the local haematological malignancy diagnostic service (HMDS).

HMDS confirmed the diagnosis of an extra-nodal marginal zone lymphoma through molecular studies, immunohistochemistry and morphology. Their molecular studies included polymerase chain reactions to confirm clonal re-arrangements within the lesional B-cells on a polyclonal background. These were performed using DNA extracted from the paraffin-embedded tissue using IgH FR1 and FR2 binding sites (both of which were present). DH-JH and IgK Vκ/intr-kde were undertaken to assess heavy chain and light chain clonality.

The patient remains disease-free and under review. No chemoimmunotherapy or radiotherapy treatment has been given. Follow up scans have revealed no recurrent disease, and despite the difficult surgery, no remnant thyroid tissue has been identified. The patient has suffered a left recurrent laryngeal nerve injury and their right vocal cord is compensating.

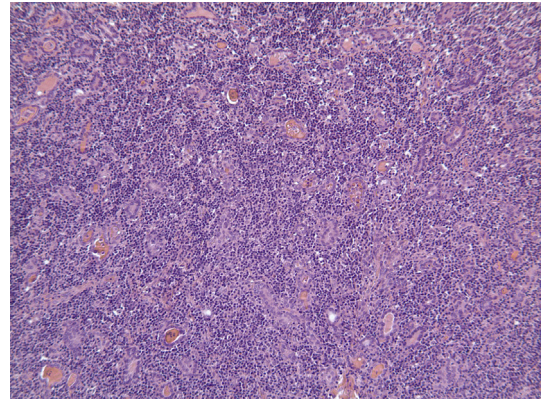


Figure 3 Diffuse infiltration of small to medium-sized B-cells, with loss of germinal centres. Haematoxylin and eosin, x10 magnification.

Discussion

To date, there have been 13 case reports of co-existing papillary carcinoma and lymphoma of the thyroid,^{9–15} four of which were included in a case series with other primary thyroid lymphomas.¹⁶ The case by Reid-Nicholson¹⁰ was not a primary lymphoma of the thyroid, as the papillary thyroid carcinoma had been infiltrated by a pre-existing chronic lymphocytic leukaemia/small lymphocytic lymphoma. All of the 12 remaining primary thyroid lymphoma cases with concurrent papillary thyroid carcinoma included either a diffuse large B cell lymphoma, MALT lymphoma or a mixed MALT/Diffuse large B cell lymphoma. This pattern fits with current epidemiological data with regards to primary lymphomas of the thyroid,² and our case is no exception to this. Occasional T-cell lymphomas of the thyroid are reported in the literature (none associated with Hashimoto's thyroiditis). However, these cases are usually in areas where HTLV-1 is endemic.¹⁷

Of the remaining 12 primary lymphoma cases within the literature, all patients had Hashimoto's thyroiditis, similar to the case presented herein, with the exception of the cases by Cheng et al. and Chen et al., where it is not clear whether the patient had Hashimoto's thyroiditis.^{13,14} Including our case, the male to female ratio of primary thyroid lymphoma with concurrent papillary thyroid carcinoma is 2:11. Our case is more unusual as the papillary thyroid carcinoma and primary thyroid lymphoma occurred in a male patient, the only other case being within the series by Lam et al.¹⁶ Across the cases in the literature and our own case, the mean age of the patient at diagnosis is 58 years, with a range of 25–84, and our patient fits towards the upper end of the range.

Hashimoto's thyroiditis is a known risk factor for developing primary thyroid lymphoma, with up to a 67-fold increase in risk within this subgroup of patients.⁶ Hashimoto's thyroiditis is also considered to be a risk factor for papillary thyroid carcinoma, though this is more contentious.⁷ As both malignancies share a potential risk factor in the form of autoimmune thyroiditis, it is not unfeasible for both a primary lymphoma and papillary thyroid carcinoma to arise concurrently. As such, the possibility of both papillary thyroid carcinoma and a primary lymphoma being present when Hashimoto's thyroiditis is present needs to remain in the forefront of the mind of the pathologist, radiologist and surgical team.

In a large review by McLeod and Cooper,⁸ there was no specific conclusion as to whether the incidence of Hashimoto's thyroiditis was increasing, so the trend of increasing papillary thyroid carcinoma may be independent of the incidence of Hashimoto's thyroiditis. The review did however confirm an increased incidence of Hashimoto's thyroiditis in women compared to men and that the disease becomes more common with age, which again is mirrored by the demographics seen in patients with concurrent primary thyroid lymphomas and papillary thyroid carcinomas.

Lymphomas of the thyroid may be difficult to diagnose alone from an FNA, where they can mimic Hashimoto's thyroiditis, or (as in this case) arise from background autoimmune disease. Therefore in cases where there is rapid enlargement of the thyroid with FNA features of a lymphocytic thyroiditis, the possibility of a lymphoma of the thyroid needs to be considered, and surgeons need to be aware of the limitations in thyroid FNAs in making a diagnosis of primary thyroid lymphoma versus a primary lymphoma.¹⁸

Hirokawa et al.,¹⁹ discuss the sensitivity and specificity of FNA cytology, ultrasound and flow cytometry in cases of thyroid lymphomas and found that of 75 'lymphoma-suspected cases' that flow cytometry provided the best sensitivity and specificity for lymphoma diagnosis. They also suggest a diagnostic algorithm for suspected lymphoma cases, determining diagnostic resection vs monitor. However, further prospective work will be needed to justify the use of this algorithm in practice.

Conclusion

Papillary thyroid carcinoma with concurrent primary lymphoma remains a rare occurrence. Due to the joint risk factor of Hashimoto's thyroiditis, it is possible for the two entities to arise together on the background of autoimmune disease.

Due to the increasing incidence of papillary thyroid carcinoma, and the shared association with Hashimoto's thyroiditis, concurrent primary thyroid lymphomas and papillary thyroid carcinomas are likely to become more common. Because of this, it is imperative that members of the clinical team – pathologists, radiologists and surgeons – are aware of this clinical vignette to ensure patients are diagnosed and treated correctly. ◆

Self-assessment questions

1. The most common primary thyroid lymphoma is

- a) Marginal Zone Lymphoma
- b) Diffuse Large B-cell Lymphoma
- c) Mantle Cell Lymphoma
- d) Hodgkins Lymphoma
- e) Small Lymphocytic lymphoma

Answer: B

2. Primary thyroid lymphoma accounts for what percentage of thyroid malignancies?

- a) 5–7%
- b) 0.1–0.5%
- c) 0.6–5%
- d) 8–15%
- e) 16–20%

Answer: C

3. Which of these statements is true?

- a) Patients with Hashimoto's thyroiditis have a 67-fold increased risk of developing papillary thyroid carcinoma
- b) There has been a decrease in the incidence of advanced stage papillary thyroid carcinoma
- c) There has been a 175% increase in the incidence of papillary thyroid carcinoma from 1975 to 2013
- d) There has been a 1.1% increase per year since 1994 of thyroid-cancer related mortality
- e) Concurrent papillary thyroid carcinoma and primary lymphoma of the thyroid is more commonly seen in males

Answer: D

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