Rare disease

Extranodal marginal zone B cell lymphoma of MALT type with extensive plasma cell differentiation in a man with Hashimoto's thyroiditis

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Summary

Primary thyroid gland lymphomas are uncommon tumours that occur in the setting of lymphocytic thyroiditis or Hashimoto's disease in almost all cases. Rarely these tumours show extensive plasmacytic differentiation. In these conditions, a distinction between an inflammatory thyroid infiltrate and extramedullary plasmacytoma may be extremely difficult and precise criteria and ancillary techniques are necessary for a correct diagnosis. The authors report a case of mucosa associated lymphoid tissue (MALT) lymphoma of the thyroid gland in a 69-year-old Iranian man with Hashimoto's thyroiditis which was diagnosed by means of immunohistochemical stains. This case demonstrates that histology may not distinguish between extramedullary plasmacytoma and MALT lymphoma of the thyroid gland and the use of immunohistochemical staining stains were essential to prove definite diagnosis.

BACKGROUND

Malignant lymphoma may involve the thyroid as part of systemic lymphoma (secondary lymphoma) or may arise primary in the thyroid.¹ Approximately 20% of patients dying of generalised malignant lymphoma will show thyroid involvement at autopsy. Thyroid replacement is rarely extensive enough to produce clinical hypothyroidism.^{1 2} Of all thyroid malignancies, 1% to 3.5% are malignant lymphoma. Primary malignant lymphoma of the thyroid usually arises in an immunologically abnormal gland, usually are affected by chronic lymphocytic thyroiditis.^{3 4} Marginal zone lymphoma represents a distinct subtype of B-cell, non-Hodgkin lymphoma with a defined morphological and immunohistochemical staining (IHC) profile. It most often arises in association with mucosa associated lymphoid tissue (MALT), hence the alternative designation of MALToma. The histological pattern can be nodular or diffuse, often with reactive lymphoid follicles, with an infiltrate of centrocyte like cells which may also show plasmacytoid differentiation.⁵ The gastrointestinal tract is the most affected site, comprising 50% of all MALT lymphoma cases. However, it has been infrequently described in many other extranodal sites, including lung, head and neck, ocular adnexa, skin, breast and thyroid gland.^{6–10} MALT lymphoma of the thyroid gland is uncommon, comprising only approximately 4% of all extranodal MALT lymphoma and commonly arises in a setting of Hashimoto's thyroiditis or lymphocytic thyroiditis.^{11 12} This article describes an unusual case of thyroid MALT lymphoma with a striking plasmacytic differentiation.

CASE PRESENTATION

A 69-year-old Iranian male presented in the out-patient clinic with an 18 month history of swelling in front of neck. No history of pressure symptoms or weight loss was present. There was no significant family history. Clinical examination

revealed a smooth swelling involving especially right lobe of the thyroid. It was firm in consistency. There was no retrosternal extension. No cervical lymphadenopathy was noted. No sign of hypo or hyperthyroidism was present.

INVESTIGATIONS

Laboratory investigation revealed an erythrocyte sedimentation rate which was 50 mm/h. Thyroid hormonal assay was normal and antithyroid microsomal antibodies were undetectable. Sonography revealed thyroid enlargement that was prominent in the right lobe, a 5 cm nodule with mixed echo was seen in the right lobe of the thyroid gland. The patient refused fine needle aspiration. Neck CT scan without contrast showed thyroid enlargement, mainly right lobe that shifted the trachea to the left side (figure 1). Calcification was not seen. Because of progressive enlargement, several weeks later, he underwent right thyroid lobectomy. The patient had an uneventful post-operative recovery. Gross examination of the resected right lobe revealed a greyish brown vaguely nodular mass measuring 6×3×3 cm which was partially encapsulated. On sectioning, the cut surface was greyish and vaguely nodular. Microscopic examination was performed on paraffin-embedded sections stained with H&E. The thyroid parenchyma was diffusely replaced by dense plasmacytoid cells. Reactive lymphoid follicles with well-circumscribed germinal centres and mantle zones were scattered. However, small to medium size lymphocytes surrounding normal thyroid epithelium and oxyphilic cell metaplasia were also evident (figure 2). These histologic features raised suspicion of extramedullary plasmacytoma of the thyroid in the presence of Hashimoto's thyroiditis. IHC studies performed on formalin-fixed, paraffin embedded tissue block with a panel of monoclonal antibodies directed against different cluster of differentiation (CD) antigens and neoplastic cells

Figure 1 Neck CT scan without contrast showed thyroid enlargement, mainly right lobe that shifted the trachea to the left side.

were positive for CD138, CD20 (figure 3), bcl2 and negative for CD10, CD23, k β 3, CD5 and cyclin D1. Ki67 staining showed less than 15% proliferative activity in tumour cells. Final diagnosis was extranodal marginal zone B cell lymphoma of MALT type with extensive plasma cell differentiation in a man with Hashimoto's thyroiditis.

DIFFERENTIAL DIAGNOSIS

Rarely MALT lymphomas of the thyroid gland show extensive plasmacytic differentiation. In these conditions, a distinction between an inflammatory thyroid infiltrate and extramedullary plasmacytoma may be extremely difficult and precise criteria and ancillary techniques are necessary for a correct diagnosis.

TREATMENT

Clinical staging was completed and the patient was in stage IA(E), therefore radiation therapy (36 Gy) was started.

OUTCOME AND FOLLOW-UP

He is still under out-patient follow-up without any evidence of recurrence for 2 months. Post-treatment CT scan shows no evidence of residual tumour (figure 4).

DISCUSSION

Since introduction of the concept of MALT type lymphoma by Isaacson and Wright in 1983 various extranodal locations (including thyroid) have been described. The thyroid gland contains no native lymphoid tissue. Intrathyroid lymphoid tissue occurred in various pathologic conditions but more evidently in the course of autoimmune disease,

notably chronic autoimmune thyroiditis (Hashimoto's thyroiditis).^{3 13} Histologically, the acquired lymphoid tissue can evolve to lymphoma including MALT-lymphoma¹⁴ but exact mechanisms causing malignant transformation is not yet clear. It seems that the evolution from Hashimoto thyroiditis to MALT lymphoma occurs in 0.5% of the patients.³ One study showed that at least 70% of primary non-Hodgkin's lymphoma of the thyroid gland demonstrated findings suggestive of transformation and 53% of them progressed from Hashimoto thyroiditis through MALT lymphoma and finally to diffuse large B cell lymphoma.¹⁵ Most cases occur in adult with a median age of 61 and slight female preponderance. Our patient was a 69-year-old Iranian male. The most striking clinical feature in this patient's presentation was progressive non-tender enlargement of the thyroid. This is a characteristic feature of thyroid lymphoma.¹⁶ Compressive symptoms which seen in up to 30% of patients, were absent in our patient. Also the finding of undetectable antithyroid microsomal antibodies is unusual in patient with Hashimoto's thyroiditis. The presented case did not show antimicrosomal antibody. Extranodal marginal zone B cell lymphoma of MALT comprises morphologically heterogeneous small B cells, including marginal zone (centrocyte like) cells, cells resembling monocytoid cells and scattered immunoblast and centroblast like cells. Plasma cell differentiation is seen in a proportion of the cases.¹² In this case, microscopic examination revealed extensive plasma cell infiltration in the presence of Hashimoto's disease and raised suspicion of extramedullary plasmacytoma. Extranodal plasmacytoma of the thyroid is uncommon.^{17 18} Some cases complicate Hashimoto's thyroiditis,¹⁹ but plasmacytoma

Figure 2 Sheets of plasma cells infiltrate thyroid follicles.

Figure 3 Immunostaining for cluster of differentiation (CD) 20 shows the neoplastic cells are positive for CD 20.

differs from MALToma in showing a monotonous population of plasma cells and lacking immunoreactivity for CD 20. Plasmacytoid cells in the presented case show immunoreactivity for CD 20. On the other hand, plasmacytoma of the thyroid has alternatively interpreted as an extreme form of extranodal marginal zone B cell lymphoma with

striking plasma cell differentiation in view of its similar clinical behaviour.²⁰ In addition, in the interfollicular variant of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), pseudofollicles can surround reactive lymphoid follicles, mimicking a marginal zone pattern. Recognising the cellular composition of the pseudofollicles

Figure 4 Post-treatment CT scan shows no evidence of residual tumour.

supports CLL/SLL over a diagnosis of marginal zone lymphoma. Immunophenotyping is helpful, as most cases of marginal zone lymphoma are CD5 negative. It should be noted that in contrast to lymphoplasmacytic lymphoma, extranodal marginal zone lymphoma of MALT arises as extranodal sites and a minority of cases involve the bone marrow, therefore the location of disease usually resolves this potential differential diagnosis. In addition, most MALT lymphomas are not associated with IgM paraprotein.²¹ Marginal zone lymphomas of the thyroid gland are indolent tumours that tend to remain localised in the thyroid for a long time before dissemination occurs, similar to their gastric or salivary gland counterpart. Treatment of thyroid lymphomas may involve the different modalities of surgery, radiation therapy and chemotherapy. After a surgical procedure, postoperative radiation therapy of the neck and superior mediastinum to a minimum dose of 45 to 50 Gy should be adequate for local control of disease for most tumours. For tumours with adverse prognostic factors, such as large bulk, fixation, extracapsular extension, or retrosternal extension, Tupchong *et al.* recommended the addition of chemotherapy because of the high risk of distant disease and local failure.²² The prognosis is excellent but worsened when complicated by large cell transformation.²³

Learning points

- ▶ MALT lymphoma of the thyroid gland is uncommon, comprising only approximately 4% of all extranodal MALT lymphoma.
- ▶ It commonly arises in a setting of Hashimoto's thyroiditis or lymphocytic thyroiditis.
- ▶ The possibility of low-grade MALT lymphoma should be suspected in a case of thyroid swelling with predominant plasma cell infiltration.
- ▶ Ancillary studies especially IHC stains are of great help in categorisation of such cases and their differentiation from other simulating conditions such as extramedullary plasmacytoma.

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Patient consent Obtained.

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