

# ENDGAMES

## CASE REPORT

# Airway obstruction after the development of Hashimoto's thyroiditis

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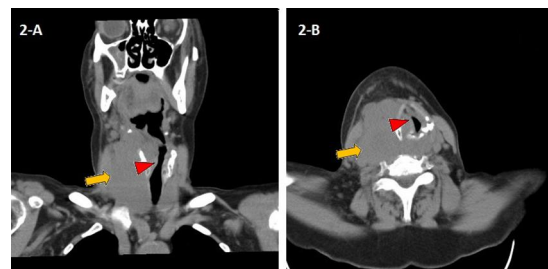
A 67 year old white woman presented to her family doctor in January 2013 with a small asymptomatic thyroid swelling. Her serum thyroid stimulating hormone (TSH) concentration was high (37 mIU/L; reference range 0.5-4.5) and serum free thyroxine was low (5.4 pmol/L; 10-21), consistent with a hypothyroid state. However, she had no clinical features of hypothyroidism. Ultrasonography of the neck showed diffuse hypoechoic enlargement of the thyroid gland, with no retrosternal extension. Her serum anti-thyroid peroxidase (anti-TPO) value was also high (>600 kU/L; <35 kU/L). These features were suggestive of autoimmune (Hashimoto's) thyroiditis. She was advised to take thyroxine tablets (100 µg) daily, and after two months her neck swelling reduced in size and her serum TSH concentration normalised (1.2 mIU/L).

However, four months later she noticed a rapid increase in neck swelling associated with dysphagia for solid foods, hoarseness of voice, and difficulty with breathing, for which she attended the emergency department of our hospital. She was a non-smoker and her medical history included hypertension, for which she was prescribed amlodipine. At that time she was still taking thyroxine and her TSH concentration was normal (2.6 mIU/L).

On examination she had inspiratory stridor, with a respiratory rate of 25 breaths/min and an oxygen saturation of 94% in room air. A large neck mass (10 cm) was visible, predominantly on the right side (fig 1). Her systems examinations were normal and she had no palpable lymphadenopathy. Computed tomography of the neck showed enlargement of the right lobe of the thyroid gland, with narrowing of the larynx at the level of the piriform sinuses (fig 2).



**Fig 1** Patient showing a large neck mass, predominantly on the right side



**Fig 2** Computed tomogram of the neck showing enlargement of the right lobe of the thyroid gland (yellow arrow), with narrowing of the larynx at the level of the piriform sinuses (red arrowhead)

## Questions

- 1 What was the differential diagnosis of the thyroid swelling when she initially presented?
- 2 How would you investigate a patient with thyroid swelling?
- 3 What are the possible causes of the large neck mass at her second presentation, and the most likely diagnosis?
- 4 What investigations would you perform at that stage to obtain a diagnosis?

5 How should the patient be managed?

## Answers

### 1 What was the differential diagnosis of thyroid swelling when she initially presented?

#### Short answer

Thyroid swelling (goitre) can be caused by a variety of benign or malignant conditions. The most common cause of thyroid swelling worldwide is iodine deficiency goitre.

#### Long answer

The causes of thyroid swelling are iodine deficiency (diffuse or nodular goitre), toxic and non-toxic nodular goitre, autoimmune (Hashimoto's) thyroiditis, Graves' disease, follicular adenoma, subacute thyroiditis, and thyroid cancer.<sup>1</sup> Thyroid swelling can also occur in IgG4 thyroiditis, which is a newly recognised entity representing IgG4 related disease of the thyroid gland.<sup>2</sup> Patients with thyroid swellings may show clinical or biochemical features (or both) of hypothyroidism or hyperthyroidism. Although the most common cause of thyroid swelling worldwide is iodine deficiency, Hashimoto's thyroiditis is more common in Western countries, where iodine deficiency is less prevalent.<sup>1</sup>

### 2 How would you investigate a patient with thyroid swelling?

#### Short answer

Thyroid function tests, thyroid antibody tests, and imaging of the neck are necessary investigations. Fine needle aspiration cytology should also be considered for the diagnosis of benign and malignant thyroid disorders.

#### Long answer

Serum TSH measurements are used to assess thyroid function. A normal TSH concentration denotes a euthyroid state, making the measurement of free thyroxine and free triiodothyronine unnecessary. If TSH is high, a free thyroxine assay should be performed to differentiate between subclinical hypothyroidism (high TSH and normal free thyroxine) and clinical hypothyroidism (high TSH and low free thyroxine). If TSH is low, then free thyroxine and free triiodothyronine assays are indicated to identify subclinical hyperthyroidism and clinical hyperthyroidism, including triiodothyronine toxicosis. Anti-TPO autoantibodies are present in about 90% and 75% of patients with Hashimoto's thyroiditis and Graves' disease, respectively, and the measurement of these antibodies is useful in the differential diagnosis of thyroid swelling.<sup>3</sup> Ultrasonography helps to assess the size, consistency, and nodularity of the goitre and is useful for guiding biopsies. If there are symptoms of neck compression, computed tomography or magnetic resonance imaging help to assess the extent of the goitre and its effect on nearby structures in the neck. Fine needle aspiration cytology is a cost effective method for evaluation of thyroid nodules and is recommended in patients with a solitary or dominant thyroid nodule larger than 1 cm.<sup>4</sup>

### 3 What are the possible causes of the large neck mass at her second presentation, and the most likely diagnosis?

#### Short answer

Airway obstruction can be caused by benign and malignant tumours of the thyroid gland, as well as haemorrhage into a

thyroid nodule. Neck tumours of non-thyroid origin can also compromise the airway. Because our patient was diagnosed earlier as having Hashimoto's thyroiditis, a thyroid tumour is the most likely cause.

#### Long answer

Benign thyroid swellings such as thyroid adenoma, thyroid abscess, Riedel's thyroiditis, subacute thyroiditis, IgG4 thyroiditis, Hashimoto's thyroiditis and Graves' disease can lead to airway obstruction.<sup>1</sup> Although rare, spontaneous haemorrhage into a thyroid nodule can also cause rapid enlargement of the neck swelling and lead to life threatening airway obstruction.<sup>5</sup> Malignant thyroid tumours that can cause rapid airway obstruction are poorly differentiated or anaplastic thyroid carcinoma; lymphoma; and metastatic tumours of the thyroid from the breast, lung, kidney, and colon. Thyroid tumours secondary to melanoma and leiomyosarcoma can also cause airway obstruction,<sup>6</sup> as can non-thyroid tumours of the head and neck.

In patients with Hashimoto's thyroiditis, the most likely cause of a rapid increase in the size of the thyroid swelling is the development of a primary thyroid lymphoma. The risk of primary thyroid lymphoma is about 60 times higher in patients with Hashimoto's thyroiditis than in the general population.<sup>7</sup> Severe airway compromise occurs in about 25% of patients with thyroid lymphoma, commonly in high grade lymphoma variants.<sup>8</sup> Hashimoto's thyroiditis is also associated with a significantly higher risk of papillary thyroid carcinoma, which is attributed to the raised serum TSH concentrations secondary to hypothyroidism.<sup>9</sup>

### 4 What investigations would you perform at that stage to obtain a diagnosis?

#### Short answer

Emergency computed tomography of the neck and fine needle aspiration cytology or core biopsy from the mass are essential for diagnosis.

#### Long answer

In a patient with a large neck mass and airway compromise, a malignant tumour is highly likely, so urgent diagnosis and treatment are needed to prevent life threatening complications. Computed tomography or magnetic resonance imaging is used to measure the size and extent of the goitre and to study the effect on nearby structures in the neck and the extent of airway compromise. If airway obstruction as a result of the large neck mass is suspected, spirometry with flow volume loop measurement can be useful. Fine needle aspiration cytology or core biopsy (or both) from the neck mass will help in the histopathological diagnosis.

It is often difficult to make a diagnosis of thyroid lymphoma on the basis of cytological findings (fine needle aspiration cytology) alone. However, in conjunction with the results of flow cytometric analysis, it is possible to make a quick preliminary diagnosis of non-Hodgkin's lymphoma (B cell or T cell subtype).<sup>10</sup> Histopathological and immunohistochemical studies are often needed because prognosis and treatment options vary according to the histological subtype of the tumour. Hence a large bore needle biopsy or excisional biopsy is often required.<sup>8</sup> For the staging of non-Hodgkin's lymphoma, a bone marrow biopsy and computed tomography of the neck, chest, abdomen, and pelvis are essential. Fluorodeoxyglucose positron emission tomography (FDG-PET) scanning is useful for detecting regional

and distant disease at initial diagnosis and to monitor therapeutic response.<sup>11</sup> Primary thyroid lymphoma can affect the thyroid gland alone or along with adjacent cervical lymph nodes. Diffuse large B cell lymphoma (DLBCL) is the most common histological subtype (70-80%) of thyroid lymphoma, followed by extranodal marginal zone lymphoma.<sup>12</sup>

## 5 How should the patient be managed?

### Short answer

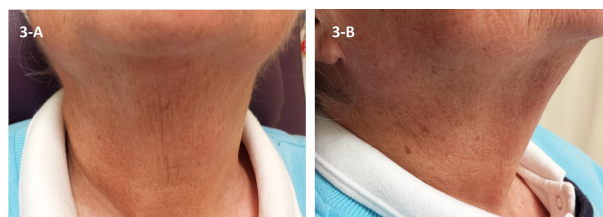
The management of patients with thyroid lymphoma and airway compromise includes management of ABC (airway, breathing, and circulation) and urgent administration of multiagent chemotherapy or radiotherapy.

### Long answer

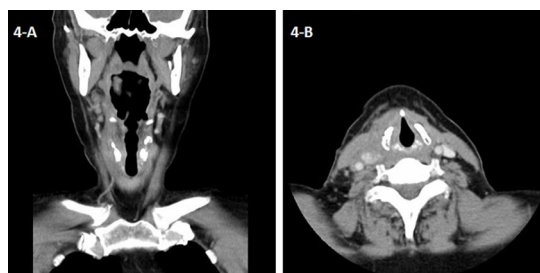
Patients with thyroid lymphoma and airway compromise should be managed in an intensive care unit and monitored closely. Emergency tracheostomy or cardiorespiratory support may be needed if the airway obstruction worsens. A multiagent chemotherapy regimen incorporating high dose steroids such as CHOP-R (cyclophosphamide, vincristine, doxorubicin, prednisolone, and rituximab) is indicated in the management of such patients. In general, high grade lymphomas such as DLBCL reduce in size within hours after initiation of chemotherapy, and this can circumvent the need for tracheostomy. The rapid reduction in size is attributed to the effect of high dose steroids. Because steroids and chemotherapeutic drugs can rapidly alter the histopathology of the tumour, tissue biopsy should be performed before such drugs are started.<sup>8</sup> Patients with low grade primary thyroid lymphoma, such as extranodal marginal zone lymphoma or follicular lymphoma, can be effectively treated with local radiotherapy alone. However, for DLBCL of the thyroid, the survival rates are highest with multiagent chemotherapy followed by local radiotherapy.<sup>13</sup> Unlike in other thyroid tumours, thyroidectomy and tracheostomy are not routinely indicated in thyroid lymphoma except for treating life threatening airway obstruction.<sup>14</sup>

## Patient outcome

Our patient was diagnosed as having primary thyroid lymphoma, DLBCL subtype, stage IE using the Ann-Arbor classification. Multiagent chemotherapy containing high dose prednisolone (CHOP-R regimen) was administered immediately after the diagnosis. Within 72 hours of starting chemotherapy the stridor resolved completely. Her neck swelling disappeared completely after seven days and she was discharged home (fig 3). Her voice returned to normal after two weeks. A repeat computed tomogram performed two weeks after the first cycle of chemotherapy showed a marked reduction in tumour size and complete resolution of the airway narrowing (fig 4). She underwent four cycles of CHOP-R chemotherapy with a 21 day interval and no complications. Follow-up positron emission tomography showed that the lymphoma was in complete remission, and radiotherapy of the involved fields in the neck was planned after the chemotherapy cycles were completed.



**Fig 3** Complete disappearance of neck swelling after seven days of multiagent chemotherapy



**Fig 4** Repeat computed tomogram performed two weeks after the first cycle of chemotherapy showing a marked reduction in tumour size and complete resolution of the airway narrowing

With current treatment modalities, the prognosis of primary thyroid lymphoma is generally excellent, with high long term survival and cure rates.<sup>13</sup>

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Patient consent obtained.

- Ross D. Diagnostic approach to and treatment of goiter in adults. In: Cooper D, ed. *UptoDate* 2013. www.uptodate.com/home.
- Kakudo K, Li Y, Taniguchi E, Mori I, Ozaki T, Nishihara E, et al. IgG4-related disease of the thyroid glands. *Endocr J* 2012;59:273-81.
- Mariotti S, Caturegli P, Piccolo P, Barbesino G, Pinchera A. Antithyroid peroxidase autoantibodies in thyroid diseases. *J Clin Endocrinol Metab* 1990;71:661-9.
- American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer, Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 2009;19:1167-214.
- Lee JK, Lee DH, Cho SW, Lim SC. Acute airway obstruction by spontaneous hemorrhage into thyroid nodule. *Indian J Otolaryngol Head Neck Surg* 2011;63:387-9.
- Wood K, Vini L, Harmer C. Metastases to the thyroid gland: the Royal Marsden experience. *Eur J Surg Oncol* 2004;30:583-8.
- Pedersen RK, Pedersen NT. Primary non-Hodgkin's lymphoma of the thyroid gland: a population based study. *Histopathology* 1996;28:25-32.
- Friedberg SJ, Freedman AW, Tuttle RM. Thyroid lymphoma. In: Ross D, ed. *UptoDate* 2012. www.uptodate.com/home.
- Zhang L, Li H, Ji QH, Zhu YX, Wang ZY, Wang Y, et al. The clinical features of papillary thyroid cancer in Hashimoto's thyroiditis patients from an area with a high prevalence of Hashimoto's disease. *BMC Cancer* 2012;12:610.
- Van den Bruel A, Drijkoningen M, Oyen R, Vanfleteren E, Bouillon R. Diagnostic fine-needle aspiration cytology and immunocytochemistry analysis of a primary thyroid lymphoma presenting as an anatomic emergency. *Thyroid* 2002;12:169-73.
- Stein SA, Wartofsky L. Primary thyroid lymphoma: a clinical review. *J Clin Endocrinol Metab* 2013;98:3131-8.
- DiBlase SJ, Grigsby PW, Guo C, Lin HS, Wasserman TH. Outcome analysis for stage IE and IIE thyroid lymphoma. *Am J Clin Oncol* 2004;27:178-84.
- Walsh S, Lowery AJ, Evoy D, McDermott EW, Prichard RS. Thyroid lymphoma: recent advances in diagnosis and optimal management strategies. *Oncologist* 2013;18:994-1003.
- Klyachkin ML, Schwartz RW, Cibull M, Munn RK, Regine WF, Kenady DE, et al. Thyroid lymphoma: is there a role for surgery? *Am Surg* 1998;64:234-8.

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