Dual Thyroid Ectopia with Graves' Disease: a Case Report and a Review of the Literature

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Abstract Ectopic thyroid or thyroid ectopia is a rare developmental anomaly with the prevalence of 1 per 100,000–300,000 population. Even rarer, such an anomaly manifests as dual thyroid ectopia. To our best knowledge, only one case has been reported on dual thyroid ectopia with Graves' disease in the English literature. We present here a case of dual thyroid ectopia complicated by Graves' disease, whereby the diagnosis was rendered through judicious use of various diagnostic modalities coupled with a close clinical follow-up. In this case, therapeutic consideration should be personalized with proper informed consent of the patient.

Keywords Dual thyroid ectopia · Dual ectopic thyroid · Graves' disease · ^{99m}Tc -pertechnetate thyroid scintigraphy

Introduction

Ectopic thyroid or thyroid ectopia is a rare developmental anomaly. Even rarer, such an anomaly manifests as dual thyroid ectopia. To our best knowledge, only one case has been reported on dual thyroid ectopia with Graves' disease

in the English-language literature [1]. We report here a case of dual thyroid ectopia complicated by Graves' disease.

Case Report

A 25-year-old woman presented with a long-standing mass at the base of the tongue (Fig. 1). Neck computed tomography (CT) revealed two homogenous enhancing masses, one at the base of the tongue and another at the midline of the neck, anterior to the cricoid cartilage (Fig. 2). Orthotopic thyroid gland was absent (Fig. 3). In addition, she was hyperthyroid biochemically (thyroid stimulating hormone [TSH]: undetected [reference range, 0.350–4.940], free thyroxine [T4]: 29.44 pmol/l [reference range, 9.01–19.05] and had a high level of anti-thyroid microsomal antibody (268.86 IU/ml [reference range, < 120]). Anti-thyroglobulin antibody and anti-nuclear antibody were negative. To control thyrotoxicosis, propylthiouracil was administered and tapered down gradually over 15 months until euthyroid state was achieved (TSH 0.468 mIU/l, free T4 13.89 pmol/l). During this period, the size of the mass in the tongue remained static. A ^{99m}Tc -pertechnetate thyroid scintigraphy was also performed when the hyperthyroidism was subdued into subclinical hyperthyroid state (TSH 0.26 mIU/l, free T4 16.6 pmol/l). Two foci of increased uptake in the neck corresponding to the masses seen in the CT were noted (Fig. 4). These findings established the presence of ectopic lingual and subhyoid thyroid glands. In addition, hyperfunction of these lesions was implied by the high lesion-to-background ratio (17 [reference range, 5–10]). For better control of the disease, radioactive iodine therapy was considered during the active intervention. The patient, however, made an informed decision to opt for conservative management after due risks and benefits of each therapy were explained. The patient was closely followed-up. Five months after withdrawal of propylthiouracil, she remained euthyroid.

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Fig. 1 A midline mass at the base of the tongue

Discussion

Thyroid ectopia (TE) is a rare developmental anomaly with a prevalence of 1 per 100,000–300,000 population [2]. Even rarer, such an anomaly manifests as dual thyroid ectopia (DTE) [3]. This unusual congenital aberration is a result from abnormal caudal migration of the thyroid tissue during embryogenesis. In the case of DTE, lingual and sublingual were the most common first sites, and subhyoid followed by suprahyoid were the most common sites of a second ectopic thyroid [3]. Although thyroid dysgenesis including TE is usually sporadic, genetic mutations in the thyroid-related transcription factors TITF1/NKX2-1, PAX8, HHEX, and FOXE1 have been identified [4]. Patients with TE usually present with local obstructive symptoms (such as progressive dyspnoea, stridor or dysphagia) or asymptomatic swelling in the base of the tongue or anterior neck. It is commonly associated with hypothyroidism but rarely with hyperthyroidism [5–7].

On the other hand, in cases of thyrotoxicosis, the clinical features alone would suffice to make the diagnosis of

Fig. 2 CT with intravenous contrast showing two homogenous enhancing masses with distinct margin localized at the base of tongue and anterior to the cricoid cartilage (*arrow*)

Fig. 3 CT with intravenous contrast showing absent of thyroid gland in the normal position

Graves' disease. However, in the absence of key features of Graves' disease, such as thyroid bruit, pretibial myxoedema and acropachy, it is difficult to make an accurate diagnosis. In particular, the differentiation between Graves' disease and initial hyperthyroid state of Hashimoto's disease (hashitoxicosis) is always difficult. Both diseases may have similar presenting symptoms, raised free thyroxine and anti-thyroid autoantibody markers. For example, the prevalence of autoantibodies to the thyroid microsomal antigen/thyroid peroxidase in Graves' disease and Hashimoto's disease is high, about 74% and 99% respectively [8]. Although Graves' disease is usually characterized by raised anti-thyroid receptor antibody (TRAb) [9] (about 60–70% of cases), patients with hashitoxicosis may also have elevated TRAb [10]. Application of TRAb in clinical decision-making in such a situation remains controversial; instead, a radioactive iodine uptake is favoured in a recent guideline [11]. The use of TRAb assay may have a role in predicting the outcome of Grave's disease after medication withdrawal [12, 13]. However, there is not enough evidence to suggest that the duration of treatment should be justified by the changes in the TRAb titre [14, 15].

The classical finding of diffuse enlargement of thyroid gland in Graves' disease by ultrasonography or CT may not

Fig. 4 ^{99m}Tc -pertechnetate thyroid scintigraphy showing two focal areas of abnormal radiotracer uptake in lingual (*arrow*) and subhyoid regions (*dotted arrow*) with no evidence of radiotracer uptake in the region of normal functioning thyroid

be seen, let alone in ectopic gland. The natural histories of these diseases might provide clues to the diagnosis but this requires close follow-up. The duration of hashitoxicosis varies and it usually resolves within 6 months [16]. Whereas the duration of remission in medically treated Graves' disease is usually longer, about 12–18 months [17].

A radioisotope thyroid scan plays significant dual roles in dissolving these challenging situations. Firstly, for TE, the anomaly is usually suspected when a midline mass is detected by ultrasoundography or CT in the absence of orthotopic thyroid. Its thyroid origin could therefore be determined by a radioisotope thyroid scan [18]. Secondly, the status of thyroid function could be glimpsed through the radioisotope thyroid uptake scan [19]. This offers a better delineation between Graves' disease and Hashimoto's disease, especially in the initial hyperthyroid state. Increased uptake would be expected in Graves' disease compared with in Hashimoto's disease [20].

This current case demonstrates dual thyroid ectopia complicated by Graves' disease, whereby a radioisotope thyroid scan was of great help. The DTE was first suspected with the neck CT findings. The possibility of Graves' disease complicating these ectopias was then considered given the initial hyperthyroid state with positive anti-thyroid microsomal antibody. The use of ^{99m}Tc -pertechnetate thyroid scintigraphy not only confirmed the DTE but also the hyperfunction of these ectopias, as indicated by high intensity of these ectopias compared with that in both salivary glands [19, 21, 22]. High lesion-to-background ratio was also demonstrated. In this case, prophylthiouracil was administered to control thyrotoxicosis. Similar to that of Graves' disease, the treatment response was achieved after a substantial long tapering period. The presence of relatively long duration of disease process (hyperthyroidism), positive autoantibody and notably, strong scintigraphic evidence of hyperfunctioning glands clinches the diagnosis of Graves' disease. Histology confirmation is unnecessary.

Furthermore, this case poses several dilemmas in the therapeutic approach. Regarding Graves' disease, the treatment depends on institutional guidelines. Medical therapy or radioactive iodine (RAI) therapy is the mainstay of treatment. Patients in Australia, Europe, Japan and most of the countries are more likely than their North American counterparts to receive an initial course of medical therapy prior to the consideration of RAI therapy. Due to surgical risk, thyroidectomy, either partial or total, is indicated for large goiter causing obstructive symptom or malignancy is suspected.

Regarding TE, treatment is unnecessary unless the patient is symptomatic. RAI therapy or surgical removal with long-term recombinant L-thyroxine replacement therapy remains the mainstay of treatment. In general, the advantages of RAI therapy include non-invasive procedure, ability

to achieve euthyroid status and ability to diminish the size of the mass [19–21]. The surgical option may be considered when the mass is large, there is the presence of local symptoms, suspicion of malignant transformation or contraindication to RAI in pregnancy or young children [2, 16]. However, the choice of therapy varies according to the patient's age, co-morbidity, size of mass, thyroid functional status, presence of local symptom, national policy, physician's preference and patient's acceptance of the treatment modality. Some authors recommended complete surgical removal of the ectopic gland in view of the risk of malignant transformation [16]. However, the question as to whether there is a cancer risk in DTE complicated by Graves' disease remains unknown. In general, Graves' disease is rarely complicated by malignancy [17, 18].

In this case, a wide range of the therapeutic options, such as medical therapy, RAI therapy, surgical therapy, close clinical observation and a combination of these therapeutic modalities, could be considered [11, 13, 15, 23]. Due to the rarity of this case, there is no known best option. Therefore, each treatment option must be weighed between the risks and benefits. RAI therapy remains an open choice in this situation, whereby Graves' disease and TE could be simultaneously controlled via this modality. However, of paramount importance, informed consent of the patient to the treatment plan should be given priority.

In summary, we present here a case of dual thyroid ectopia complicated by Graves' disease, whereby the diagnosis was rendered through judicious use of various diagnostic modalities coupled with a close clinical follow-up. This case was successfully managed via medical therapy followed by close observation. However, RAI therapy remains an open option and therapeutic consideration should be personalized with proper informed consent of the patient.

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