

Case Report: A Rare Association of Diffuse Thyroid Lipomatosis with Amyloid Deposition

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Established Facts

- Diffuse thyroid lipomatosis is a rare histopathological condition of unknown etiology, characterized by diffuse fatty infiltration of the thyroid.
- This condition can result in diffuse goiter with compressive symptoms.

Novel Insights

- This is one of the few reported cases of diffuse lipomatosis with coexisting deposition of amyloid in the thyroid gland.

Keywords

Diffuse thyroid lipomatosis · Amyloid goiter

Abstract

Diffuse thyroid lipomatosis is a rare histopathological condition of unknown etiology, characterized by diffuse fatty infiltration of the thyroid stroma, which can result in diffuse goiter with compressive symptoms. We report a case of a 46-year-old man with 1-year history of progressive goiter enlargement with compressive symptoms. Imaging studies re-

vealed multiple coalescent nodules. The patient underwent surgery, and the microscopic appearance revealed a diffuse infiltration of thyroid stroma by mature adipose tissue with associated amyloid deposition. A final diagnosis of diffuse lipomatosis of the thyroid gland was established. This patient represents one of the few reported cases of diffuse lipomatosis with coexisting deposition of amyloid protein of the thyroid gland and contributes to the better understanding of this extremely rare condition.

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Introduction

Diffuse thyroid lipomatosis is a histopathological condition of unknown etiology characterized by extensive diffuse fatty infiltration of the thyroid stroma. In some rare cases, it has been associated with the deposition of amyloid in the thyroid gland [1, 2]. This condition can lead to the enlargement of the gland and can result in compressive symptoms [1]. Extensive adipose tissue in the thyroid gland can be found in a broad spectrum of conditions, from malignant lesions (thyroid carcinomas) to benign conditions (such as Graves' disease) [2, 3]. Diffuse thyroid lipomatosis (or thyrolipomatosis) and thyrolipoma (adenolipoma) are part of the benign spectrum of lesions of the thyroid gland. The diffuse form is even less common than thyrolipoma and is characterized by mature adipose tissue deposition without evidence of encapsulation [4]. On the other hand, amyloid goiter results from the deposition of insoluble proteins due to its abnormal folding process and also can lead to the deposition of adipose tissue within the thyroid gland [5, 6]. A case of diffuse thyroid lipomatosis with coexistent deposition of amyloid protein is presented.

Case Presentation

We report the case of a 46-year-old man with a history of bronchiectasis with multiple episodes of viral and bacterial respiratory infections since he was 19 years old, chronic otitis media, pansinusitis, and infertility due to idiopathic hypogonadotropic hypogonadism. The patient referred a history of consanguinity (2 grandparents are brothers, and his parents are first-degree cousins). He has 2 children, both born after medically assisted reproduction, diagnosed with severe immunodeficiency with frequent respiratory and central nervous system infections. The patient presented with a 2-year history of progressive weight loss (<10% of total body weight) associated with fatigue to mild effort. Physical examination showed a lobulated diffuse thyroid enlargement and multiple inflammatory lymph nodules in the lateral compartments of the neck. Routine blood tests were normal, including cell blood count, renal function, proteinogram, beta-2 microglobulin, immunoglobulins, and C-reactive protein. The sedimentation rate was 35 (normal range 0–22 mm/h).

Thyroid function tests were within normal range with free T4 1.46 pg/dL (NR 0.90–1.70), free T3 3.3 pg/mL (NR 2.0–4.5), and TSH 1.35 μ UI/mL (NR 0.30–4.20). Serum anti-thyroperoxidase and anti-thyroglobulin antibodies as well as serum calcitonin levels were undetectable. Two months later, neck ultrasound (US) scan revealed thyroid enlargement with a right thyroid lobe of 65 \times 32 \times 34 mm and a left lobe of 64 \times 31 \times 28 mm with iso-hypoechogenic and solid nodules with 18 mm and 15 mm in the right and left lobes, respectively, without cervical lymphadenopathy. FNA was performed in both nodules, which showed colloid goiter. The CT scan revealed a diffuse enlarged thyroid with areas of low-



Fig. 1. CT scan showing diffuse thyroid enlargement with hypodense areas.

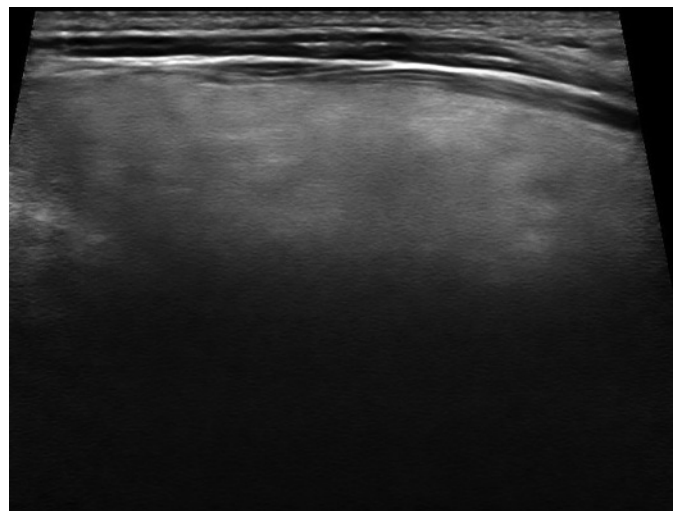


Fig. 2. Thyroid ultrasound: the thyroid left lobe showing diffuse hyperechogenicity.

er density than the remaining parenchyma (Fig. 1). The trachea was slightly deviated to the left side without compression. No cervical or mediastinal suspicious lymph nodes were detected. Twelve months later, the goiter enlarged, and he developed symptoms of dyspnea, dysphonia, and dysphagia. Neck US revealed coalescent iso-hyperechogenic nodules in the thyroid gland, the largest with 20 mm (Fig. 2), and FNA was repeated in this nodule with the diagnosis of a follicular lesion of undetermined significance, showing scarce cellularity, abundant colloid, macrophages, and some follicular cells with nuclear alterations (slight nuclear increase, clear chromatin, membrane irregularity, and grooves).

Fig. 3. a Histologically, there was infiltration of thyroid stroma by mature adipose tissue (black arrow). **b** Interstitial amyloid deposition stained with Congo red (black arrow) showing apple-green birefringence under polarized light (yellow arrow).

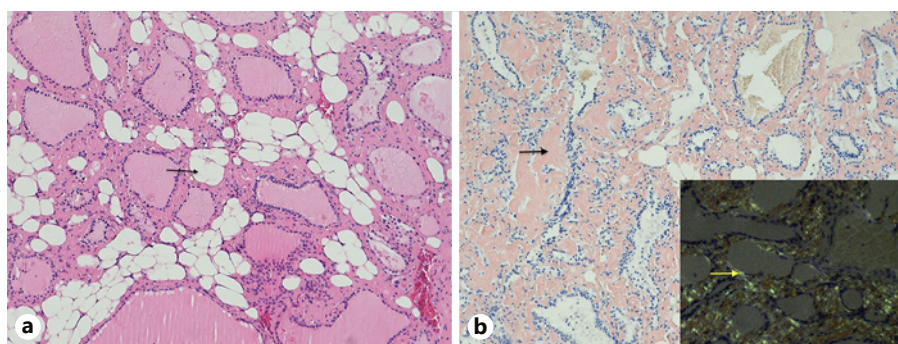


Table 1. Patient characteristics and imaging findings for the cases of diffuse thyroid lipomatosis and amyloid deposition reported in the English literature

| Cases of diffuse thyroid lipomatosis and amyloid deposition reported | | | | | | |
|--|------------------------|-------------------------------------|--|---|---|---|
| study, year | age, sex | thyroid function/signs and symptoms | medical history | fine-needle aspiration results | histologic features | |
| 1 | Gonulalan et al. [2] | 43, male | Normal thyroid function Goiter and compressive symptoms | Chronic kidney disease due to amyloidosis type A | Colloidal cyst | Thyroid weight 160 g. Sparse thyroid follicles in dense lipoid stroma. Amyloid positive |
| 2 | Jaques and Stearns [5] | 55, male | Normal thyroid function Goiter enlargement for 2 years without compressive symptoms | Crohn's disease Amyloidosis type A | Droplets of fat | Thyroid weight 148 g. Extensive infiltration of the gland by adipose tissue. Amyloid positive |
| 3 | Bell et al. [7] | 36, female | Normal thyroid function Goiter for 2 years with compressive symptoms | Rheumatoid arthritis Amyloidosis type A Renal transplant | Nodular hyperplasia | Thyroid weight 144 g. Normal thyroid tissue was replaced by mature adipose tissue except for a small remnant of medium-size normal thyroid follicles. Amyloid positive |
| 4 | Loh et al. [8] | 67, male | Normal thyroid function Thyroid nodule with compressive symptoms | Chronic kidney disease Follicular and insular thyroid carcinoma Bronchiectasis | Nondiagnostic | Follicular carcinoma, showing signs of lymphovascular invasion. Staining favored AA-type amyloidosis |
| 5 | Bacan et al. [9] | 47, male | Unavailable | Ankylosing spondylitis Kidney deposition of amyloid type A Bronchiectasis | Amorphous acellular material | Amorphous acellular material with apple green birefringence with Congo red under polarized light and positive staining with amyloid A immunohistochemistry |
| 6 | Bacan et al. [9] | 34, female | Unavailable | Familial Mediterranean fever Chronic renal failure due to amyloidosis type A Bronchiectasis | Unavailable | Unavailable |
| 7 | Present case (2020) | 46, male | Normal thyroid function Progressive goiter with compressive symptoms | Infertility Sinusitis Bronchiectasis | Colloidal cyst and follicular lesion of undetermined significance | Thyroid weight 237 g. Follicles covered by follicular cells, some with clear chromatin and grooves, perifollicular and perivascular extensive eosinophilic stroma consisting of mature adipose tissue. There was no cell atypia, and focal follicular atrophy was present |

A total thyroidectomy was performed without surgical complications. The macroscopic appearance of the resected thyroid showed a bosselated, homogenous 237-g thyroid with yellow and hemorrhagic areas, without visible nodules. The left lobe measured 111 × 40 × 26 mm and the right lobe 105 × 65 × 43 mm. Microscopic examination of multiple sections revealed normal follicular architecture, with normal appearing follicular cells. There was fatty infiltration of the perifollicular and perivascular stroma, with extracellular deposition of an amorphous eosinophilic material, consistent with amyloid. There was apple-green birefringence of Congo red-stained slides under polarized light, confirming the presence of amyloid protein (Fig. 3). A final diagnosis of diffuse lipomatosis of the thyroid gland with amyloid deposition was established. There was no evidence of systemic amyloidosis. Abdominal fat and bone marrow biopsies revealed no pathological alterations. ¹⁸F-DG-PET scan presented a faint lung uptake probably related to the bronchiectasis. The electrocardiogram and echocardiogram showed no abnormalities. Alpha-1 antitrypsin deficiency, familial Mediterranean fever, inflammatory bowel disease, cystic fibrosis, and idiopathic pulmonary fibrosis were also ruled out. The patient remains asymptomatic under treatment with levothyroxine.

Discussion

This case represents one of few published cases of diffuse thyroid lipomatosis. With the keywords “diffuse thyroid lipomatosis,” “thyrolipoma,” and “thyrolipomatosis” in the PubMed, we could find only 39 case reports and only 6 also had concomitant amyloid deposition (Table 1). These patients usually presented with normal thyroid function and severe compressive symptoms [2, 3, 7, 8, 10]. Bakan et al. [9] and Loh et al. [8] described 3 patients with coexistent bronchiectasis as in our patient (Table 1) [11]. Amyloid deposition can also lead to massive goiters and be associated with variable amounts of adipose tissue within the thyroid gland; however, the majority of the cases of diffuse thyroid lipomatosis do not have significant amyloid content [5, 6].

The patient and his children have an unclear immunodeficiency disorder with severe and recurrent infections, which is still under investigation. Although it is consensual that amyloid deposition can occur as a reaction to systemic disease, such as a chronic inflammatory disease or a chronic infection, the pathophysiology underlying the association between amyloidosis and fat tissue deposition (especially in a massive way) remains to be elucidated. One possibility is capillary injury induced by amyloid, which leads to ischemia and subsequent metaplasia of stromal fibroblasts [5, 6, 10]. In addition, adipose tissue proliferation within the thyroid has been associated by some authors with disturbed embryogenesis [3, 4]. To the

best of our knowledge, this case represents one of the few patients reported with diffuse thyroid lipomatosis with coexistent deposition of amyloid. Despite its rarity, thyroid lipomatosis should be considered in the differential diagnosis of a patient presenting with a goiter, and the clinician must be aware of the possibility of underlying systemic diseases.

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Statement of Ethics

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and the Helsinki Declaration of the World Medical Association. The authors declare that the manuscript, complete or in parts, does not infringe any copyright and does not violate any privacy rights. The authors declare that no experiments were performed on humans or animals for this investigation. The authors state that the subject has given his written informed consent to publish his case, including publication of images.

Conflict of Interest Statement

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Author Contributions

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Data Availability Statement

The authors confirm the data supporting the findings of this case report are available within the article. Raw data that support the findings of this case report are also available from the corresponding author, upon reasonable request.

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