Review

Thyroid Gland Diffuse Lipomatosis: A Case Study and Comprehensive Literature Review

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Review

Thyroid Gland Diffuse Lipomatosis: A Case Study and Comprehensive Literature Review

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Abstract: Diffuse lipomatosis of the thyroid (DLT) is an uncommon condition where mature fat cells infiltrate the thyroid gland, disrupting its normal structure. Although rare, it typically manifests as neck enlargement or symptoms of compression, including breathing difficulties, trouble swallowing, and voice changes, which can complicate diagnosis. This report presents a case of a 61-year-old woman with DLT, who exhibited a multinodular goiter and progressive neck swelling, and examines 53 additional cases from existing literature. The analysis indicates that DLT is frequently misdiagnosed due to its similarities with other thyroid disorders. The precise mechanism underlying its development remains uncertain, but theories include oxygen deprivation in tissues, developmental abnormalities, or disruptions in fat metabolism. Surgical removal is the preferred treatment, especially for patients experiencing symptoms, and has shown favorable long-term outcomes. Additional studies should aim to elucidate the exact cause of DLT and enhance diagnostic precision, particularly in distinguishing it from other fat-containing thyroid lesions such as amyloid goiter and adenolipomas. A deeper understanding of this condition will inform better treatment approaches and enhance patient outcomes for this uncommon but significant thyroid disorder.

Keywords: diffuse lipomatosis; thyroid; amyloid goiter; case report; review

1. Introduction

Diffuse lipomatosis of the thyroid or DLT is characterized by infiltration of the parenchyma of the gland and replacement of the otherwise typical anatomical structure with mature adipose cells. It is not commonly found among other pathological conditions of the thyroid but nonetheless presents an interesting phenomenon. Although the thyroid is closely connected to other mesodermal structures during embryogenesis, contributing to fat deposition in areas around the cervical blood vessels in the subcapsular region of the anterior thyroid region, the presence of significant amounts of adipocytes within the thyroid stroma is rare [1–4]. Diffuse adipose tissue causing enlargement is often found in the thymus, parathyroid glands, pancreas and salivary glands, as a result of atrophy-related parenchymal fatty metaplasia, whereas thyrolipoma is the most common condition in the thyroid [5–7]. Adenolipomas of the thyroid or thyrolipomas are well-circumscribed admixtures of adipose and follicular cells surrounded by a fibrous capsule consisting of a mixed neoplasm that is, mesenchymo-epithelial [4]. Both thyrolipomas and diffuse lipomatosis are benign lesions of the gland, with the latter being more frequently associated with escalating growth clinically manifesting with compression symptoms from nearby organs such as dyspnea, hoarseness, dysphagia, and overall swelling. The enlargement observed in acquired and congenital goiters may also be caused by fat invasion rather than follicular proliferation [8,9]. The exact pathophysiological mechanism responsible for the diffuse nature of the fatty infiltration of the thyroid remains unclear. Here, we present an indigenous case and review the literature on DLT.

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2. Case Report

Our case involves a 61-year-old woman who was referred to our department for a total thyroidectomy. She had been diagnosed with a substernal multinodular goiter two years ago and in the last six months she gradually developed neck swelling, dyspnea, and dysphagia. Her medical history showed that she had chronic renal failure of unknown etiology and had been undergoing hemodialysis for the last year. She was also diagnosed with hypertension, diabetes mellitus and obesity [BMI(Body mass index): 37]. Her thyroid function was normal [TSH (Thyroid Stimulating Hormone): 0.46 pmol/l, FT4 (Free Thyroxine): 20.09 pmol/l, FT3 (Free Triiodothyronine): 3.1 pmol/l)] and she tested negative for serum thyroperoxidase (anti-TPO) and thyroglobulin antibodies (anti-TG). Ultrasonography findings indicated a heterogeneous intrathoracic diffuse goiter and in accordance the CT (Computed Tomography) confirmed the presence of an enlarged gland showing low attenuation and septations. Computed tomography revealed that the thyroid had invaded the entire cervical area and the upper mediastinum compressing the surrounding tissue (Figure 1). Thyroid scintigraphy with Tc^{99m} (Technetium-99m) revealed a low uptake of radioactivity and cold nodules in the lower lobes suggesting the possibility of subacute thyroiditis. The patient underwent total thyroidectomy. The operation lasted for 2 hours and proved to be an arduous challenge. Intraoperatively the thyroid was friable at touch, its capsule was very thin, and the gland was soft-fatty in texture, similar to a lipoma (Figure 2). Following surgery, the patient experienced no complications and was released two days later. Histopathological examination revealed fatty infiltration of the thyroid gland and degeneration of follicles. Immunohistochemical staining for thyroglobulin (TG) and thyroid transcription factor-1 (TTF1) verified the existence of a few colloid-filled thyroid follicles, whereas positive S100 staining demonstrated the preponderance of adipose tissue within the gland. (Figure 3). Therefore, the patient was diagnosed with diffuse thyroid lipomatosis. Two years after surgical treatment, the patient died because of complications associated with kidney failure.

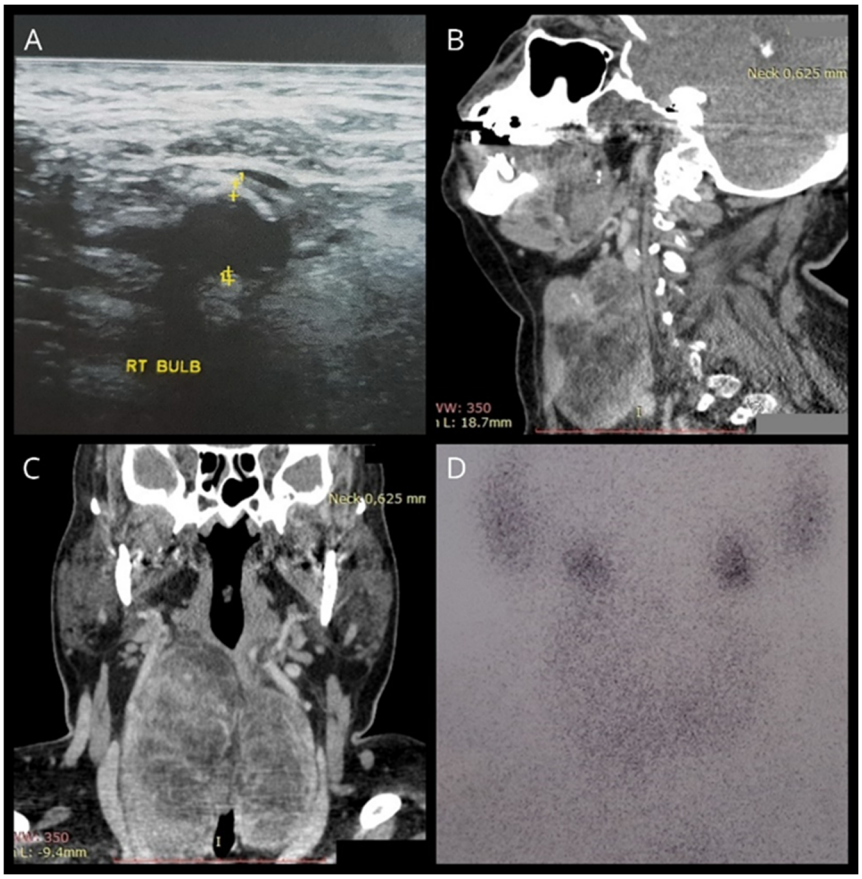

Figure 1. A: Ultrasonography of thyroid showing heterogeneity of parenchyma. **B, C**: CT findings indicating a diffusely enlarged thyroid with hypodense areas and intrathoracic extensions. **D**: Tc^{99m}

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scintigraphy showing heterogeneous uptake of the isotope and cold areas in the lower parts of the gland.

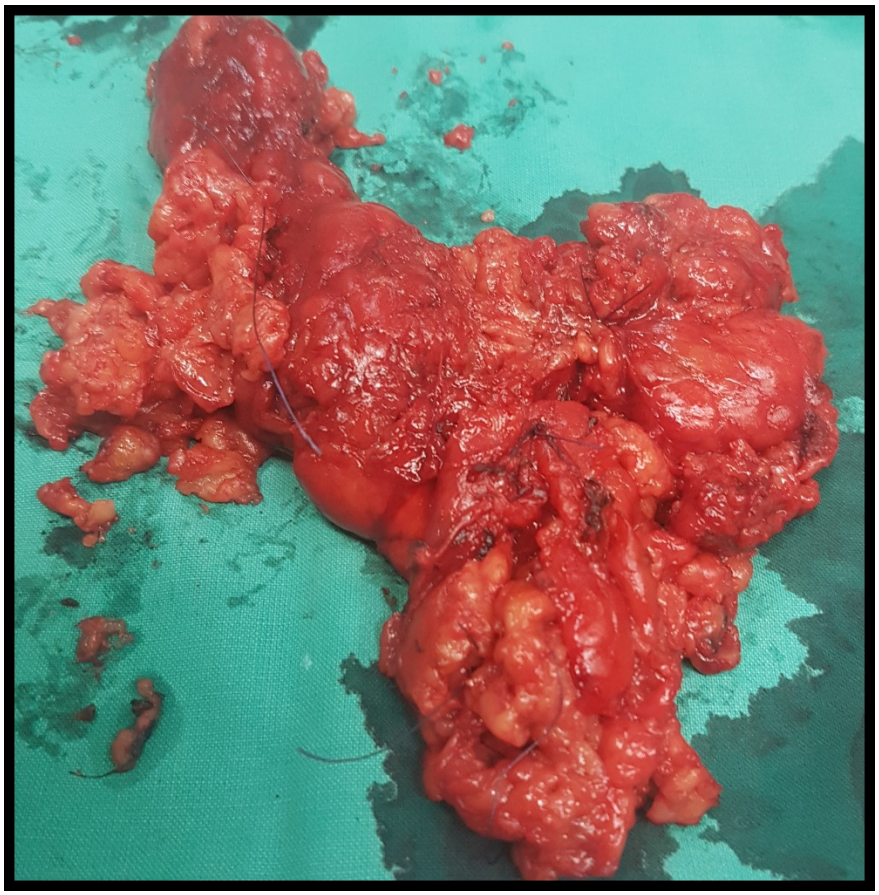

Figure 2. Thyroid specimen after total thyroidectomy.

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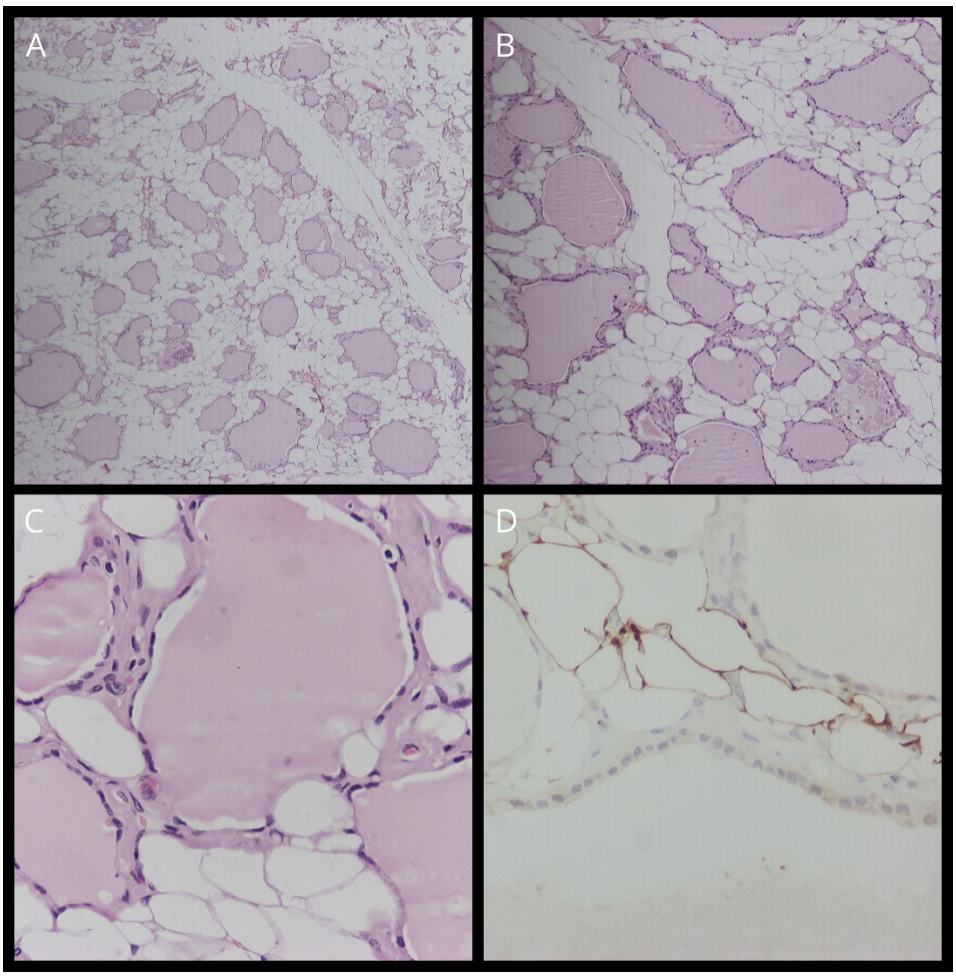

Figure 3. A: Staining with hematoxylin-eosin (H&E) (magnification, x10), **B:** Staining with hematoxylin-eosin (H&E) (magnification, x40), **C:** Staining with hematoxylin-eosin (H&E) (magnification, x100), **D:** TTF-1 staining.

3. Review

The first description of DLT in medical literature was by Dhayagude [10] in 1942. Since then, we have identified another 53 cases of thyroid lipomatosis including our own. Based on our criteria, we identified common characteristics among the above reports including sex, age, symptoms, thyroid function, renal status, initial diagnosis, treatment, histopathological features and follow-up. Nine of the patients (16%) were described by Ge [1], two in 2016 by Bell [11], and more recently 3 cases by Celik [8]. The average age was 50 years (range, 11 - 78 years), and there was no significant sex predilection between male (47%) and female (53%). The most significant clinical feature was local compression (60%), which involved dysphagia, dysphonia/hoarseness, dyspnea, and neck swelling (46.7%), whereas one-third of the patients did not show any symptoms. Thyroid function was uncompromised in most patients (66%), and only a few patients had hypothyroidism (12.7%) or hyperthyroidism (21.3%). What appeared to be of notice was the fact that 40% of patients suffered from renal failure with most of them being affected by secondary amyloidosis. Amyloid goiter is found more frequently in secondary amyloidosis than in primary amyloidosis and is commonly misdiagnosed as a thyroid carcinoma [12]. Many patients were initially diagnosed with goiter (64.6%) either diffuse or multinodular, and one patient reported an amyloid goiter (2.1%), while a diagnosis of DLT was recently proposed in eight reports (16.7%). Among the reports that mentioned a treatment method, total thyroidectomy was the predominant choice (47.9%). Only one patient with a preliminary diagnosis of DLT was discharged without treatment, and partial thyroidectomy was an alternative, especially in patients with unilateral nodular disease. The average thyroid weight was

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232.16 grams (range 15-700 g). All cases revealed that the thyroid was almost entirely composed of mature adipose cells, and in cases of amyloid infiltration, the confirmation consisted of positive Congo red or thioflavin staining. Fat deposits that vary in amount are frequently found in amyloid goiter [7]. Amyloid infiltration was observed in almost half of patients (44.8%). We only included reports in which the gland was almost completely or in most parts infiltrated by fat tissue regardless of amyloid deposition, fibrosis, or lymphocyte aggregates. Only a minority of reports (43.4%) included follow-up information, and most (78.3%) had an uncomplicated post-operative course ranging from 1 day to 12 months. One patient reported respiratory difficulty 3 years after the first evaluation, three others died of complications, two pertaining to renal insufficiency and the other after developing metastases in the residual thyroid lobe. Finally, a DLT case with concurrent secondary amyloidosis was revealed via the patient's autopsy. Table 1 summarizes the characteristics of the DLT in these patients (Table 1).

Table 1. Summary of Thyroid Lipomatosis Case Reports.

Reference	*Sex/ Age*	*Clinical Features*	*Thyroid Function*	*Renal Failure*	*Initial Diagnosis*	*Treatment*	*Thyroid size/weight*	*Pathology*	*Amyloid deposition*	*Follow-up*
10	M/32	Local compression	NS (Not Stated)	No	Diffuse goiter	Excision	10 x 8 x 5.5 cm (R), 8 x 6 x 5.5cm (L)/ 500g	Diffuse infiltration of fibrous-fatty tissue, anomalous follicles, focal fibrosis	NS	NS
35	F/11	No	BMR (Basic metabolic rate) +3% (hyperthyroidism)	No	Diffuse goiter (since birth)	Excision	x5 normal thyroid size	Diffuse fat infiltration alongside small thyroid follicles and lobules with fibrous septa	NS	NS
18	M/15	No	Normal	No	Diffuse goiter (since birth)	Excision	12 x 7 x 4 cm (R), 8 x 5 x 2.5cm (L)/ 253g	Diffuse fat infiltration, small and medium thyroid follicles, stromal edema	NS	NS

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36	M/58	Local compression	Hyperthyroidism	No	Diffuse goiter	Excision	NS	Diffuse fat infiltration surrounding normal follicles, stromal fibrosis, lymphocyte aggregation	NS	NS
37	F/51	No	Normal	No	Diffuse goiter	Excision	NS	Diffuse fat infiltration surrounding normal follicles, stromal fibrosis	NS	NS
38	F/73	No	Normal	No	Diffuse goiter	Excision	NS/120 g	Diffuse fat infiltration around normal follicles, lymphocyte aggregation	NS	NS
39	M/12	No	Normal	No	Right neck mass	Excision	13 x 8 x 6.5cm (R)/415 g	Diffuse fat infiltration surrounding normal thyroid follicles, presence of lymphocytes and fibrous tissue	NS	NS
40	M/26	Neck swelling, hoarseness, dysphagia	Normal	Yes	Cervical mass	Total thyroidectomy	NS	Diffuse infiltration of thyroid by fat	Yes	NS
41	F/77	No	Normal	No	Cervical mass	Excision	NS/700 g	Thyroid follicles	NS	NS

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								surrounded by adipose cells		
42	M/38	Neck swelling	Normal	No	Diffuse enlargement of thyroid	Excision	4 x 3 x 2cm (I), 13 x 7 x 3cm (R), 15 x 9 x 5cm (L)/465g	Mature adipose tissue surrounded the different sized but otherwise normal follicles of the thyroid	No	Well - post-operatively
29	F/58	Neck swelling, dysphagia, hoarseness, hyperthermia	Hypothyroidism	Yes	Diffuse goiter	Total thyroidectomy	9.5 x 7 x 5cm (R), 8 x 6 x 3.5cm (L)/230g	Diffuse fatty infiltration, loss of most thyroid follicles, eosinophilic substance deposition in the hyalinized stroma, lymphocytic thyroiditis	Yes	NS
43	M/64	Enlarged thyroid, dyspnea	Normal	Yes	Diffuse goiter	NS	NS	NS	NS	NS
44	M/45	Neck swelling, respiratory distress	Normal	No	Diffuse thyroid enlargement	Subtotal thyroidectomy	2 x 1.5 x 1cm (I), 9 x 7 x 4cm (R), 9 x 5 x 3.5cm (L), 4 x 3 x 2 (P)/225g	Colloid filled thyroid follicles, fatty infiltration of interfollicular stroma	No	NS
1	F/67	Dysphagia	Normal	Yes	Enlarged nodular left	Left thyroidectomy	7 x 3.5 x 2cm (L)/41g	Thyroid follicles separated by fat,	No	Well- 2 years after

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					thyroid lobe			adipose tissue density varied from 30%-90% of total tissue, fat infiltration in adenomatous nodules		
1	F/59	No	Hypothyroidism	No	Right thyroid mass	Right thyroid lobectomy and isthmusectomy/ left thyroidectomy	7 x 4 x 1.2cm (R+I), 6 x 3 x 1.2cm (L)/56g	Nodular and diffuse pattern of fatty infiltration, presence of a 0.8cm papillary carcinoma	No	Well -6 years after
20	F/40	No	Hyperthyroidism	No	Multinodular goiter	Excision	NS	Colloid filled thyroid follicles of various sizes, replacement of stroma by mature adipose tissue	No	Well - post-operatively
9	M/37	Neck swelling, dyspnea	Normal	Yes	Diffuse thyroid enlargement	Total thyroidectomy	NS/304 g	Widespread deposition of eosinophilic material with scarcity of thyroid follicles, diffuse lipomatosis and amyloidosis	Yes	Well -3rd post-operative day

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								(secondary)		
5	M/62	Neck swelling, dyspnea	Normal	No	Nodular goiter	Near total thyroidectomy	12 x 10 x 6cm (R), 15 x 8 x 6cm(L)/ 285g	Colloid filled thyroid follicles, diffuse infiltration of stroma with mature adipose tissue, scarce lymphocytic infiltration	No	NS
19	M/43	Neck swelling, dyspnea	Normal	Yes	Enlarged thyroid	Total thyroidectomy	6 x 2 x 1cm (I), 7.5 x 6 x 4.5cm (R), 6.5×4.5×2 (L)/160g	Scattered thyroid follicles in a dense mature fat stroma	Yes	NS
45	M/55	Neck swelling, cough	Normal	Yes	Diffuse goiter	Total thyroidectomy	4 x 2 x 1cm (I), 9 x 6 x 4cm (R), 7 x 5 x 2.5cm (L)/ 148g	Infiltration of thyroid by adipose tissue, small amounts of colloid filled follicles remained	Yes	Well post-operatively
22	F/52	No	Normal	NS	Diffuse lipomatosis	NS	NS	NS	NS	Difficulty breathing – 3 years later
46	M/46	NS	Hypothyroidism	No	Cervical mass	Partial thyroidectomy (same procedure at 3 years of age)	NS	Infiltration of thyroid by mature adipocytes. Same results as	No	NS

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								43 years before		
2	F/32	Neck swelling	Hyperthyroidism	No	Toxic multinodular goiter	Total thyroidectomy	11 x 5 x 2cm(total)/88g	Thyroid follicles filled with colloid, diffuse fatty infiltration of stroma	No	NS
3	M/37	Neck swelling	NS	No	Nodular goiter	Total thyroidectomy	5 x 11 x 15 cm (total)/ NS	Thyroid tissue replaced by mature adipocytes, papillary thyroid carcinoma	NS	NS
6	M/47	NS	Hypothyroidism	No	Fatty infiltration of thyroid	Excision	16.5 x 8 x 5.5cm (total)/250g	Atrophic follicles of thyroid alongside mature adipose tissue infiltration, SDHB loss of expression (follicular or adipose cells)	No	NS
8	M/25	NS	Hypothyroidism	NS	NS	NS	NS	Various sizes of thyroid follicles, abundant distribution of mature fat around thyroid tissue	NS	NS
8	F/19	NS	Hypothyroidism	NS	NS	NS	NS	Various sizes of thyroid follicles, abundant distributio	NS	NS

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								n of mature fat around thyroid tissue		
8	M/63	NS	Normal	NS	NS	NS	NS	Preservation of a few thyroid follicles, abundant distribution of mature fat around follicles	NS	NS
47	M/69	Hoarseness, exertional dyspnea	NS	Yes	Diffuse fatty conversion and solid/cystic nodule of thyroid	Right hemithyroidectomy /completion thyroidectomy	NS	Diffuse infiltration of thyroid stroma by mature fat, insular carcinoma	Yes	NS
23	F/67	Neck swelling, respiratory distress	Hyperthyroidism	Yes	Diffuse goiter	Total thyroidectomy	2 x 2cm (I), 12 x 6 x 3.5cm (R), 10 x 5 x 2.5cm (L)/215g	Infiltration of thyroid by mature fat, scarcity of colloid follicles	No	Well-post-operatively
11	F/36	Dyspnea	Normal	Yes	Multinodular goiter	Excision	9.8 x 9.5 x 4.5cm (total)/144g	Replacement of normal thyroid tissue by mature adipocytes except from small remnants of normal colloid filled follicles	Yes	NS
48	M/73	Neck swelling,	Normal	No	Thyroli pomatosis	Near Total	NS	Thyrolipomatosis	NS	NS

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		dyspnea, hoarseness				thyroidectomy				
Present Study	F/61	Neck swelling, dyspnea, dysphagia	Normal	Yes	Diffuse Goiter	Total thyroidectomy	NS	Fatty infiltration of thyroid, degeneration of follicles	NS	Dead – after 3 years (due to kidney failure)
31	F/68	NS	Normal	No	Diffuse goiter	Total thyroidectomy	NS	Fatty infiltration of thyroid, hyperplastic follicles alongside stromal sclerosis and calcification	No	Well- after 3 months
24	F/49	Neck swelling	Subclinical hyperthyroidism	No	Diffuse goiter	Radioiodine ablation (RAI)/ total thyroidectomy	NS	Infiltration of thyroid stroma by fat	NS	Well – post-operatively
30	F/53	Local compression, dysphagia	Normal	Yes	Non-toxic diffuse multinodular goiter	Total thyroidectomy	2.5 x 2 x 1.5cm (I), 5 x 2.5 x 2cm (R), 11 x 7 x 3.5cm (L)/415g	Admixture of adipocytes with follicular cells	NS	NS
28	F/55	Neck swelling, hoarseness	Normal	No	Diffuse goiter	Total thyroidectomy	1.5 x 1cm (I), 5.5 x 3.5 x 3cm (R), 4 x 2.5 x 2.2cm (L)/NS	Replacement of thyroid tissue by mature fat, few distended thyroid follicles	No	Well- post-operatively
49	F/48	Dysphagia	Subclinical hyperthyroidism	Yes	Amyloid Goiter	Total Thyroidectomy	13.5 x 4.5, 6.5 x 3.5 3.5	Adipose metaplasia of	Yes	Well- post-operatively

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							x 2.5 cm/NS	thyroid stroma		
50	M/20	Dysphagia	Normal	No	Follicular nodule	Left hemithyroidectomy	NS	Diffuse fatty infiltration of thyroid	NS	NS
25	M/73	Neck swelling, dyspnea, hoarseness	Normal	No	Diffuse lipomatosis of thyroid	Total thyroidectomy	NS	Diffuse presence of fat cells in the thyroid	No	NS
27	M/72	No	NS	Yes	Diffuse lipomatosis of thyroid	No	NS	NS	NS	NS
21	M/46	Dyspnea, hoarseness, dysphagia	Normal	No	Diffuse goiter	Total thyroidectomy	10.5 x 6.5 x 4.3 (R), 11.1 x 4 x 2.6cm (L)/237g	Normal follicular architecture, fat infiltration of stroma	Yes	Well-post-operatively
32	F/52	No	Normal	No	Goiter/ suspicious nodule	Left hemithyroidectomy	6 x 4 x 2cm (L)/26g	Fatty infiltration of stroma, predominance of adipocytes in most regions	NS	Well – after 6 months
51	M/48	Neck swelling	Normal	Yes	Multinodular goiter	Total thyroidectomy	NS	Diffuse and nodular infiltration of thyroid by adipose cells, scarce thyroid follicles	No	Well-after 12 months
26	M/40	Neck swelling	Normal	No	Thyrolipoma and thymolipoma	Total thyroidectomy	NS	Thyroid follicular cells surrounded by mature	No	Well – after 2 weeks

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								adipocytes		
52	F/69	Neck swelling, dyspnea, dysphagia, hoarseness	Normal	No	Multinodular goiter	Total thyroidectomy	1.5 x 1 x 1cm (I), 6.5 x 5 x 3cm (R), 5 x 3 x 2.5cm (L)/NS	Diffuse infiltration of adipocytes and replacement of normal thyroid follicles	NS	Well – post-operatively
53	F/54	Neck swelling, hoarseness, dysphagia	Normal	Yes	Diffuse lipomatosis of thyroid and follicular neoplasm	Total thyroidectomy	2.6 x 4.5 x 2cm (I), 4.5 x 7.5 x 3.4cm (R), 3.2 x 6.7 x 2.8cm (L)/81g	Papillary thyroid carcinoma, admixture of thyroid follicles with mature adipose tissue	Yes	Dead – after 5 months (urinary tract infection -sepsis)
34	F/57	Dyspnea, dysphagia, local compression	Hyperthyroidism	No	NS	Total thyroidectomy	NS	NS	NS	NS
54	F/60	NS	Hyperthyroidism	Yes	NS	Autopsy	NS	Replacement of normal thyroid follicles by diffuse fat deposits	Yes	Deceased
55	F/44	Tongue mass, dysphagia, weight loss	NS	No	Multinodular goiter	Right hemithyroidectomy	6 x 3.5 x 2cm (R)/15g	Diffuse fat metaplasia of stromal thyroid tissue indicative of thyrolipomatosis	No	Dead – after 5 months (septic shock after metastasis of squamous cell carcinoma of the tongue

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										to the remaining left thyroid lobe)
56	F/78	Neck swelling, dysphagia, hoarseness	Normal	Yes	Multinodular goiter	Total thyroidectomy	22.4 x 8.5 x 5cm/ 300g	Infiltration of the gland by mature adipocytes, a few extended thyroid follicles and a stroma filled with adipocytes and fibrotic tissue	NS	Well – post-operatively
57	F/64	Weight loss, fatigue, enlarged thyroid	Hyperthyroidism	Yes	Diffuse Thyroid Lipomatosis	Methimazole	NS	Benign adipose tissue with entrapped thyroid follicles (biopsy)	Yes	NS
58	F/51	NS	NS	Yes	Multinodular goiter	Total thyroidectomy	9.4 x 6.6 x 5.7cm (R), 8.5 x 5.2 x 4.7cm (L), 2.2 x 1.2 x 1cm (I)/ NS	Lobules of adipocytes with few areas of atrophic thyroid follicles, papillary carcinoma	Yes	Well – after 6 months

4. Discussion

Numerous attempts have been made to explain the etiology of fatty infiltration in the thyroid gland. According to Dhayagude,[10] fat deposits in colloid goiters may arise from the degeneration of follicular tissue due to damage such as hemorrhage, fibrosis, infarction, calcification, or cystic degeneration. Willis [13] in his textbook "The borderland of Embryology and Pathology" describes an adenolipoma explaining that its presence could be a result of the metaplastic formation of fat. In amyloid goiters, it is presumed that adipose tissue is formed from stromal metaplasia of fibroblasts as a result of senile involution or tissue hypoxia [14]. Trites [15] hypothesized that some factor may have affected the primitive foregut during embryogenesis causing the formation of mixed embryonic tumors explaining fatty infiltration in congenital goiters. In various lipomas it has been suggested that a disturbance in lipid metabolism could promote the accumulation of fat tissue [16], whereas others have argued that fat accumulation does not seem to depend on general factors such as obesity [17]. Chevsky et al [18], proposed that adipose tissue might be incorporated into the thyroid during

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embryogenesis along with striated muscle; before the gland capsule is formed. Schroder [4] postulates that DLT is associated with "displaced nests of embryonic structures, calling the entity "choristomatous adiposity". A recent theory that attempts to explain the pathophysiology of the disease suggests that somatic mutations leading to the loss of succinate dehydrogenase-subunit B (SDHB) expression may play a role. Immunohistological staining revealed the loss of this protein in cells from DLT tissue resulting in the deregulation of the mitochondrial respiration process and interference with lipid metabolism. This could result in a decrease in fatty acid oxidation, explaining the attenuation of fat in the gland and the replacement of normal follicles [6]. All of these theories could be plausible because they explain different aspects of infiltration, either regarding its diffuse presence in congenital and acquired goiters or the limitation of fatty deposition in certain regions of the gland.

Imaging techniques are a common diagnostic tool in the investigation of diffuse goiter and are the presumed initial diagnosis in most cases. After extensive investigation, only nine reports assumed that the gland was infiltrated by fat tissue. Ultrasonographic findings most commonly indicate parenchymal heterogeneity [19], gland enlargement and cystic or solid nodules with septations [20–22]. Computed tomography (CT) and fine-needle aspiration (FNA) biopsy are the gold standard for the early diagnosis of disease [20]. The tomographic findings consisted of an enlarged gland with low attenuation (-30 to -70 Hounsfield units) and heterogeneity of the parenchyma with a few areas showing hyperattenuation probably indicating the presence of normal thyroid tissue [20,22–25]. In cases where compressing symptoms were present, invasion of the retropharyngeal space, expansion to the thoracic inlet and compression of nearby organs such as the trachea or esophagus, were found [11,22]. Overall, almost all reports noted a low tomographic density of the thyroid stoma, but it was not low enough to be certain of fatty infiltration [11,24]. MRI (Magnetic Resonance Imaging) is occasionally used to confirm findings of low density in the stroma and increased signals with fat suppression in T1 and T2 sequences [26,27]. Scintigraphy with Tc^{99m} or I^{123} (Iodine-123) showed heterogeneity in radioactive uptake, occasionally indicating the presence of cold nodules [19,28]. Finally, FNA cytology or biopsy was performed in ambivalent cases expressing infiltration of the gland with fatty tissue, either in the background or predominantly. However, clear guidelines for the definitive diagnosis of thyroid lipomatosis are eclipsed, and almost none of the above cases reached a diagnosis until after pathological findings were released [21]. A definitive diagnosis can be achieved after thyroidectomy if the pathological report describes diffuse gland infiltration [11].

The differential diagnoses include non-neoplastic fat-containing lesions such as adenolipoma, DLT, amyloid goiter, lymphocytic thyroiditis, heterotopic nests of adipose cells, parathyroid lipoma, or intrathyroid thymic tissue, and neoplastic lesions such as lipid-rich cell adenoma, liposarcoma, or encapsulated papillary carcinoma. Adenolipoma can be easily differentiated from diffuse lipomatosis by its well-defined, encapsulated appearance along with the simultaneous admixture with proliferated thyroid follicles [19,20,27]. Amyloid goiter is usually found in systemic amyloidosis, either primary or secondary and its pathognomonic characteristic of positive Congo red or crystal violet staining, makes the diagnosis relatively straightforward [5,19]. However, there are cases where both amyloid and fat cell depositions were found in equal amounts or amyloid deposits were scarce amidst a thyroid stroma mainly comprised of fat cells [19]. As there is no certainty regarding the criteria for the differential diagnosis of amyloid goiters with fatty infiltration from thyroid lipomatosis, we only considered cases where there was a clear predominance of fat tissue over amyloid proteins. Accumulation of various amounts of fat cells is a common finding in amyloid goiters because tissue hypoxia caused by a gradual increase in amyloid could drive fibroblasts to differentiate into fat cells as previously stated [29]. Lymphocytic thyroiditis is associated with extensive infiltration of the stroma by lymphocytes, whereas heterotopic nests can be only found in the subcapsular regions of the gland [3,17,20]. The intimate embryologic origin of the thyroid with the parathyroid glands and thymus may be the cause of parathyroid lipomas, with characteristic cytoplasmic glycogen deposits, and ectopic thymic tissue [1,5]. Lipid-rich follicular adenomas can be distinguished by the presence of follicles with aggravated intracytoplasmic lipid formation, circular nuclei, and vesicular morphology [3,30]. Liposarcoma is a rare, aggressive neoplasm that usually

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expands rapidly beyond the thyroid capsule. Finally, there have been a few cases in which papillary carcinoma was found within diffusely enlarged goiters infiltrated with fat. The histopathological features and immunohistochemical profile of the tumor were evident, and adipose cells were occasionally found in small amounts within the stroma [23].

A distinguishing feature of diffuse thyroid lipomatosis is the infiltration and replacement of what would be an otherwise normal thyroid stroma by mature adipose cells [31]. Macroscopically, the gland has a pale yellow-brown color and a soft, and friable texture. In most cases, the gland size exceeded the normal weight (10-20 g), the lobes were enlarged, and when cut, they had a lobular appearance [5,11,23]. Schroder et al [4] noted that the gland may resemble a congenital goiter because of its progressive growth during the first decade of life. Microscopic analysis revealed that mature adipocytes lacking encapsulation had replaced normal thyroid follicles [5,11,14,32]. The fat tissue is lobulated by strands of fibrous tissue. The remaining indigenous cells were clustered in random amounts and were scattered throughout the fatty stroma [14]. The follicles were lined with cuboidal epithelium and exhibited colloid accumulation [23]. Infiltration of fat with scarce lymphocytes was observed in a few cases, whereas deposition of pink unshaped material was found around the remnants of the follicular tissue [5,11]. Only in instances of systemic amyloidosis was this discovery described; in these cases, the amyloid A protein was identified through immunohistochemical staining and validated by apple-green birefringence during polarized microscopy using Congo red staining [11]. Papillary carcinoma coincided with DLT in three cases and was described as a localized group of follicles; surrounded by fat, with oval cells and enlarged ground glass nuclei. Immunohistochemical positivity for thyroglobulin and TTF-1 confirmed the diagnosis [3,33].

Total thyroidectomy via a transverse horizontal cervical incision appears to be an appropriate therapeutic option for patients with symptomatic swelling [30]. Caution should be exercised in view of the softness and friability of the thyroid gland to avoid extensive intra-operative bleeding. Mobilization of the gland should be performed meticulously; with minimal traction during detachment and identification of the adjacent laryngeal nerves and parathyroid glands [20]. Left hemithyroidectomy was performed under FNA guidance. Subsequent histopathological evaluation confirmed a diagnosis of diffuse thyroid lipomatosis. Biopsy samples may have been obtained from areas with scarce or no fat content [32]. Our review summarizes that there should be a surgical attempt to assuage the patient only in cases in which compression symptoms are present. If the patient is asymptomatic and DLT is confirmed via imaging techniques or biopsy, the patient should be discharged, and follow-up will be advised in the next few months to re-estimate the extent of the disease [27]. Owing to the underlying pathophysiological mechanisms of the disease, in cases where DLT is confirmed before or during surgery, the potential presence of ectopic thyroid tissue should be investigated [34]. Finally in cases with thyroid swelling and hyperactivity indicated from scintigraphy, a CT scan should be ordered to examine the consistency of the gland and in view of a possible DLT diagnosis, radioiodine ablation therapy can be dismissed altogether and replaced directly by total thyroidectomy [24].

5. Conclusions

Diffuse lipomatosis of the thyroid gland is a rare but fascinating condition that involves replacement of normal thyroid tissue with fatty infiltration. Our review of the literature and presentation of a case report highlight the clinical features, diagnostic challenges, and treatment options associated with this condition. Our results indicate that surgical intervention should be considered in symptomatic patients as it has been shown to lead to positive long-term results in most cases. Further research is needed to better understand the underlying mechanisms of DLT, which will enable the development of more accurate diagnostic and therapeutic approaches and improve patient outcomes.

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