

# Clinical profiles of thyroid dermatopathy: a dermato-endocrinology minireview

## Abstract

**Background:** Thyroid disorders sometimes have extra-thyroidal manifestations. Hyperthyroidism is a clinical syndrome resulting from excessive secretion of thyroid hormones. The commonest cause is Graves' disease. About 0.5 – 4.3% of patients with Graves' disease have an infiltrative dermatopathy called thyroid dermatopathy. It is due to excessive deposition of glycosaminoglycans from activated fibroblasts. Skin fibroblasts are activated by thyroid stimulating hormone receptor antibodies and the whole process is initiated by T lymphocytes. Thyroid dermatopathy is rarely also found in other thyroid disorders such as Hashimoto thyroiditis.

The diffuse non-pitting oedema variant is the commonest clinical presentation. Other variants include the nodular, plaque, mixed and elephantiasis types. The main concerns of the patients usually are cosmetic, discomfort and difficulty in wearing shoes. Thyroid dermatopathy usually presents after the diagnosis of Graves diseases but it may present together or sometime after. Rarely, thyroid dermatopathy presents before the diagnosis of Graves' disease is made. Apart from the shin and feet, other sites that can be affected include arms, forearms, back, thighs, pinna and nose.

**Conclusion:** The management is multidisciplinary, involving Dermatologists and Endocrinologists. Usually, controlling the thyroid dysfunction does not translate into regression of the skin lesion. However, many patients have their thyroid dermatopathy regressing spontaneously while others usually require local therapy. Other therapeutic options include systemic therapy such as pentoxifylline, compressive physiotherapy and surgery.

**Keywords:** thyroid dermatopathy, clinical profile, dermato-endocrinology perspective

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## Introduction

The thyroid gland is a butterfly-shaped endocrine organ located in the neck. It produces thyroid hormones which regulate metabolic activities in the body. Hyperthyroidism is a clinical syndrome caused by excessive production and secretion of the thyroid hormones. The commonly reported clinical features are heat intolerance, anxiety, excessive sweating, palpitation, fatigue, hyperdefaecation and menstrual disturbance.<sup>1</sup> Graves' disease, an autoimmune disorder, is the commonest cause of hyperthyroidism.<sup>2</sup> Occasionally, it affects other organs such as the eyes and the skin. Thyroid dermatopathy, sometimes called pretibial myxedema, is found in about 0.5 - 4.3% of patients with Graves' disease.<sup>3</sup> It is an infiltrative dermatopathy diagnosed in the presence of typical symptoms and signs, biochemical evidence of thyroid dysfunction or evidence of the characteristic autoimmune markers as well as pathological findings in the skin.<sup>3</sup> It manifests in various ways, affecting the skin of different parts of the body.

## Pathogenesis

In genetically predisposed individuals, thyroid dermatopathy results from an immunological cross-reaction occurring in the skin where thyroid stimulating hormone (TSH) receptor antibodies stimulate the fibroblasts in the connective tissue of the skin.<sup>4</sup> In vitro studies have demonstrated that fibroblasts in the skin and orbit express TSH receptors on their cell surface.<sup>5</sup>

Activation of the fibroblasts make them overproduce glycosaminoglycans leading to fluid retention in the connective tissue of the skin. The antigen-antibody response is initiated by the activation of T lymphocytes. Other factors such as localized trauma and venous stasis have also been suggested to contribute to the development of thyroid dermatopathy.

Histopathologically, reduced collagen fibres, extensive mucin deposition, reduced elastic tissue and oedema are the characteristic findings.<sup>3</sup> Other rarely documented pathological features include hyperkeratosis, acanthosis and papillomatosis.<sup>3</sup> The pathogenesis is summarized in Figure 1 below.

## Risk factors

Risk factors for the development of thyroid dermatopathy are not known. However, some researchers have suggested that previous radioiodine therapy, smoking, thyroid hormonal imbalance as well as the presence of Graves' orbitopathy could predispose an individual to developing thyroid dermatopathy.<sup>6,7</sup>

## Sites of thyroid dermatopathy

The term 'pretibial myxoedema' is less favored to thyroid dermatopathy because the skin lesions are found in many other areas apart from the pretibial area. The common sites documented in the literature<sup>3</sup> and their frequency are illustrated in Table 1 below. The reasons for lower limb predilection of thyroid dermatopathy are not

known. Some hypotheses include gravitational forces and more fibroblasts concentration.<sup>3</sup>

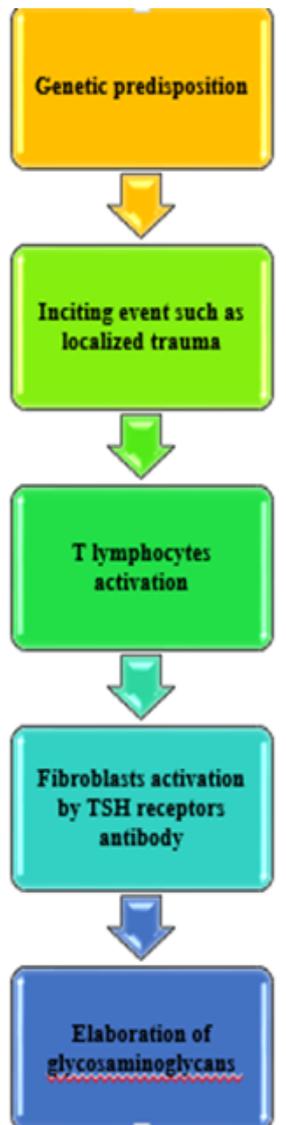


Figure 1 Pathogenesis of thyroid dermatopathy.

Table 1 Sites of thyroid dermatopathy and their frequencies

Sites	Frequency
Pretibial Only	94%
Pretibial + Feet	4%
Pretibial + Upper Extremities	<1%
Arms	<1%
Preradial Forearms	<1%
Upper Back	<1%
Shoulder	<1%
Pinnae	<0.5%
Nose	<0.01
Thigh	<0.01

### Clinical presentation of thyroid dermatopathy

Thyroid dermatopathy is found mostly in Graves’ disease but it has also been documented in patients with Hashimoto thyroiditis, atrophic thyroiditis and in euthyroid individuals.<sup>6</sup> It is also more frequently seen in females compared to males. This may be due to the fact that autoimmune thyroid disorders are generally more common in females.<sup>3</sup> The main reasons for presentation include cosmetic, discomfort and difficulty in wearing shoes.

The temporal profile of thyroid dermatopathy in relation with Graves’ disease is variable. Usually, it occurs after the diagnosis of Graves’ disease but it may predate diagnosis of Graves’ disease and they may present concurrently.<sup>3</sup> Often, it occurs after the onset of Graves’ orbitopathy, another manifestation of Graves’ disease with similar pathophysiology. Thyroid dermatopathy needs to be differentiated from lichen planus, stasis dermatitis, lichen simplex chronicus and necrobiosislipoidica. So, a review by a Dermatologist is crucial in the management of thyroid dermatopathy. Figure 2 below shows a picture of thyroid dermatopathy in a black patient.

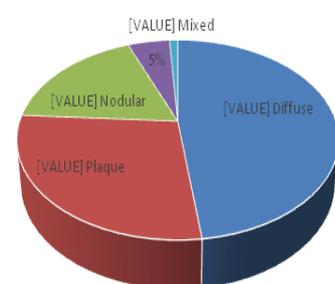


Figure 2 Thyroid dermatopathy.

### Types of thyroid dermatopathy

Thyroid dermatopathy presents in various forms. The various clinical variants are discussed briefly below Figure 3 below illustrates the clinical variants of thyroid dermatopathy and their frequencies. This is based on the findings of a retrospective study conducted by Sabanova et al.<sup>8</sup>

Prevalence of thyroid dermatopathy variants



■ Diffuse ■ Plaque ■ Nodular ■ Elephantiasis ■ Mixed

Figure 3 Thyroid dermatopathy variants and their frequencies.<sup>8</sup>

Diffuse thyroid dermopathy variant usually presents as non-pitting oedema. It is the commonest variant and is characterized by induration of the skin giving the classical 'peau d' orange' sign.<sup>3</sup> In some patients, in addition to the peau d'orange sign, they also have diffuse hyperpigmented papules. Other variants are nodular and diffuse plaque types. Rarely, patients present with mixed nodular and plaque type. The elephantiasis variant, which presents like the late stage of lymphatic filariasis, has also been documented.<sup>8</sup> This is often accompanied by significant functional disability.

Complications of thyroid dermopathy include psychological distress, superimposed bacterial infection, recurrence and entrapment neuropathy causing foot drop.<sup>3</sup>

### Treatment of thyroid dermopathy

Treatment of thyroid dermopathy requires a collaborative effort from the Endocrinologist and the Dermatologist. The treatment is often challenging with many patients requiring months before regression begins but they mostly regress eventually.<sup>4</sup> Studies have shown that control of the thyroid dysfunction may not necessarily lead to the regression of thyroid dermopathy.<sup>2</sup> Topical steroids, and in some instances intralesional steroid, with or without occlusion, have been tried with some moderate response. In some severe variants, compressive physiotherapy as well as surgery have been adopted as therapeutic options in the management of thyroid dermopathy. Newer therapies include the use of pentoxifylline and somatostatin analogues to reduce the elaboration of glycosaminoglycans. However there is paucity of data on the outcomes of these modalities. In resistant cases, intravenous globulins have been employed. Also plasmapheresis has been tried, as documented in the literature.<sup>3</sup>

### Prognosis

Largely, the prognosis is good. A study done by Schwartz et al, looking at the long term outcome of thyroid dermopathy, reported that close to half of the patients in the series regressed spontaneously, without requiring any intervention.<sup>4</sup> Majority of the patients requiring therapy had only topical steroids or intralesional steroids and most of them significantly respond to therapy in form of partial or complete regression.

### Conclusion

Thyroid dermopathy is an infiltrative dermopathy due to accumulation of glycosaminoglycans deposited by skin fibroblasts

activated by TSH receptor stimulating antibodies. They are found in less than 5% of Graves' disease. The commonest presentation is diffuse non-pitting oedema. Other variants include nodular, plaques, elephantiasis and the mixed types. The most common sites involved are the pretibial area and feet while other sites such as upper limbs, back and thighs are rarely involved. Thyroid dermopathy resolves spontaneously in many patients. Local therapy is the most commonly employed modality and management requires inputs from the Dermatologist and the Endocrinologist.

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### Conflicts of interest

The author declares that there are no conflicts of interest.

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