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# Recurrent thyroid eye disease: a case series

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## Abstract

***Aim:*** **To report recurrent thyroid eye disease, which is unusual because the condition is considered a monophasic disease and recurrence is rarely reported.**

***Method:*** **A retrospective case note review was carried out on all patients who had attended the thyroid eye disease clinic in our hospital. Six patients with recurrence of their disease were identified. One case is presented in detail and the clinical findings of 5 similar cases are documented.**

***Results:*** **Of the 6 patients, 5 were female. The average age at time of diagnosis with thyroid eye disease was 47 years and at the time of recurrence was 56 years. All were managed conservatively at their first presentation but 4 patients required radiotherapy to control the recurrence. Three patients required squint surgery after their disease reactivated. The most common operation for strabismus was an inferior rectus recession.**

***Conclusions:*** **Thyroid eye disease is considered to be a monophasic autoimmune disease with an initial active phase of progressive deterioration followed by a static phase with gradual improvement over the years. The cases presented show that the natural history of the disease does not always follow this conventional pattern and this is an important consideration when planning future management.**

**Key words:** Monophasic, Natural history, Recurrence, Thyroid eye disease

## Introduction

This report describes in detail the recurrence of active thyroid eye disease in a 47-year-old woman (case 1) and documents the findings of 5 similar cases (cases 2–6).

## Case report

Case 1 was diagnosed with a diffuse toxic goitre at the age of 25 years, 6 months after the birth of her second child. She was treated with carbimazole for 3 years before having a subtotal thyroidectomy. This achieved a euthyroid state for 2 years, after which thyroxine replacement therapy was required for hypothyroidism.

Whilst expecting her third child (age 29 years), the patient developed thyroid eye disease. She presented with a 3 mm left proptosis and lid retraction. The patient developed exposure keratopathy in the left eye, which was initially treated conservatively with lubricants but which later required surgery to relieve both upper and lower lid retraction.

Ten years later, the patient developed increasing proptosis of both eyes and began to experience vertical diplopia when reading. Orthoptic assessment revealed a left hypertropia of $2^{\Delta}$ in downgaze. The patient could read without diplopia by holding reading material in an upright position and therefore Fresnel prisms were not required. A CT scan confirmed the presence of proptosis and revealed enlargement of the left superior and lateral recti. Thyroid function tests at the time were normal. Bilateral orbital decompressions were performed due to the threat of worsening exposure keratitis. Following decompression surgery, the patient developed a left hypertropia of $20^{\Delta}$ for near and distance with vertical diplopia, which was relieved with a $14^{\Delta}$ base-down Fresnel prism left eye.

Six months later, when the disease was thought to be stable, further surgery was carried out in the form of bilateral scleral graft insertions into the lids and, 2 years later, extraocular muscle surgery to relieve the diplopia . Pre-operative orthoptic examination revealed a left hypertropia measuring approximately $45^{\Delta}$. There was gross restriction of the right eye on elevation and restriction of the left eye on depression. Surgery to recess the left superior rectus and right inferior rectus was performed using adjustable sutures. Post-operatively, the deviation had reversed to a variable right hypertropia of $1–6^{\Delta}$ with diplopia, which was relieved with a $5^{\Delta}$ base-down prism right eye. Over the next 18 months, the patient's condition stabilised with a right hypertropia of $5^{\Delta}$. The patient was discharged from the eye clinic, with a $2^{\Delta}$ base-down prism incorporated into her right spectacle lens.

At the age of 51 years the patient returned to the ophthalmology department complaining of diplopia and a red right eye. She was found to have a right hypertropia of $10^{\Delta}$ and clinical activity score[1]* (CAS) at the time suggested active thyroid eye disease in the right eye (CAS right eye 5, left eye 0). This was confirmed on magnetic resonance imaging with STIR sequences,

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*The Mourits score provides an indication of disease activity, and is based on the well-known signs of inflammation: pain, redness, swelling and impaired function.[1] One point is given for each of the following signs and symptoms: orbital pain or pain during ocular movements, redness (eyelid or conjunctiva), swelling (proptosis, lid oedema, chemosis or caruncle swelling), limitation of ocular movements, and visual impairment. Of a total of 10 points, patients with a score of three or above are considered to have active disease.

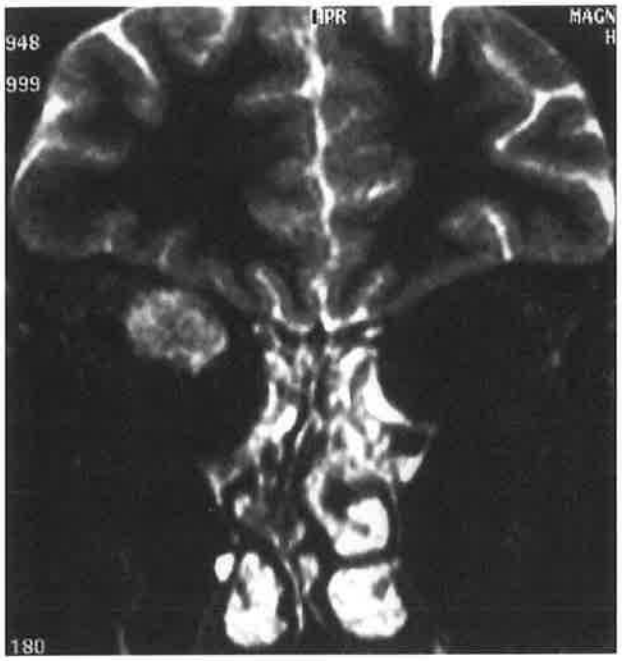


**Fig. 1.** Magnetic resonance imaging with STIR sequence showing a grossly enlarged, actively inflamed superior rectus muscle.

which showed a marked thickening and enhancement of the right superior rectus muscle (Fig. 1). Biochemical investigation at the time revealed stable thyroid function tests. The patient had a course of radiotherapy to both orbits, with good effect. Clinical activity score after treatment was 1 in either eye.

Due to limitation of depression of the right eye the patient continued to experience troublesome diplopia in the primary and reading positions (Fig. 2). A year later, when the condition was stable, a right superior rectus recession was performed. This reduced the right hypertropia from $18^{\Delta}$ to $4^{\Delta}$, improved the uniocular fields of fixation and enlarged the area of binocular single vision. To date, the patient has maintained single vision with a $3\frac{1}{2}^{\Delta}$ base-down prism incorporated into her right spectacle lens (Fig. 3).

The clinical findings of 5 similar cases with recurrence of thyroid eye disease (cases 2–6) are presented in Table 1. All were managed conservatively at their first presentation but 4 patients required radiotherapy to control the recurrence. Three patients required squint surgery after their disease reactivated. The most common operation for strabismus was an inferior rectus recession.

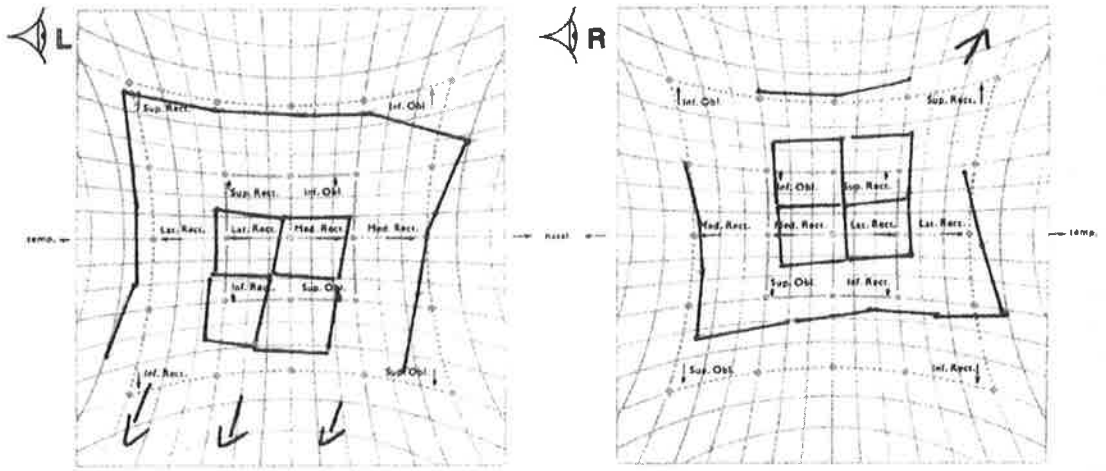


**Fig. 2.** Hess chart before strabismus surgery.

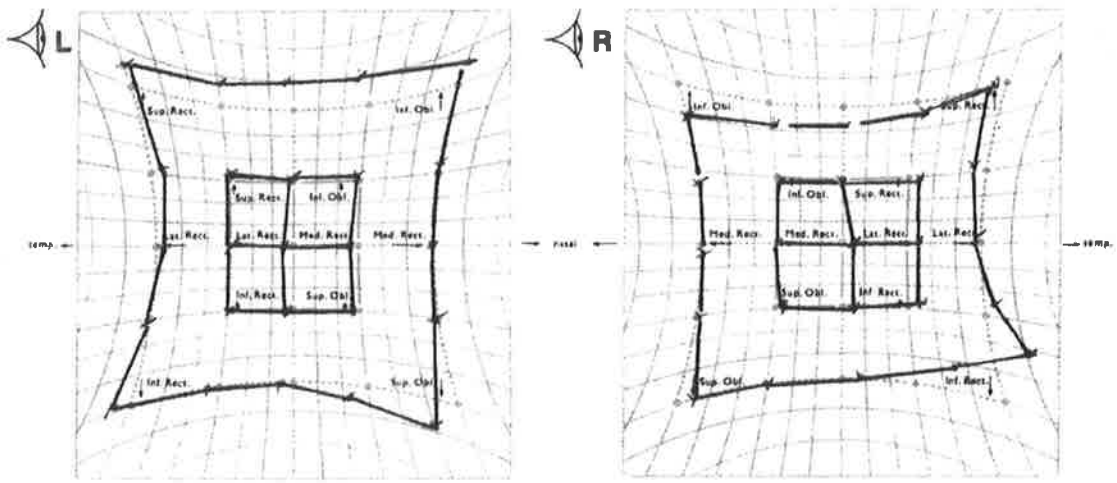


**Fig. 3.** Hess chart after strabismus surgery.

**Table 1.** Clinical details of patients with recurrent thyroid eye disease

| | Case number | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | 6 |
| Sex | Female | Female | Female | Female | Male | Female |
| Age at diagnosis of thyroid eye disease | 29 | 57 | 50 | 55 | 53 | 39 |
| Age at recurrence | 51 | 80 | 54 | 58 | 55 | 42 |
| Thyroid function at recurrence | Stable | Stable | Stable | Stable | Hyperthyroid | Stable |
| Signs at presentation | Lid retraction<br>Proptosis | Lid retraction<br>Proptosis | Lid retraction<br>Proptosis<br>Strabismus | Lid retraction<br>Proptosis | Proptosis<br>Optic neuropathy<br>Strabismus | Proptosis<br>Strabismus<br>Soft tissue involvement |
| Treatment at presentation | Conservative | Conservative | Conservative | Conservative | Oral steroids | Conservative |
| Signs at recurrence | Soft tissue involvement<br>Strabismus | Soft tissue involvement<br>Proptosis | Soft tissue involvement | Strabismus | Soft tissue involvement<br>Proptosis | Proptosis<br>Strabismus |
| Treatment at recurrence | Radiotherapy | Radiotherapy | Radiotherapy | Conservative | Radiotherapy<br>Oral steroids | Conservative |
| Lid surgery | Yes | Yes | No | Yes | Yes | No |
| Orbital decompression | Yes | No | Yes | No | Yes | No |
| Strabismus surgery | Yes | No | Yes | Yes | Yes | Yes |
| Type of strabismus surgery | (L) SR–/(R) IR–<br>(R) SR– | None | (L) IR– | (L) IR– | (R) IR–/ (R) MR– | (R) IR– |

(R), right eye; (L), left eye; SR, superior rectus recession; IR, inferior rectus recession; MR, medial rectus recession.

## Comment

Case 1 experienced a recurrence of thyroid eye disease, which affected the right eye, 22 years after initially presenting with the disease affecting the left eye. The 5 similar cases of recurrence suggest that reactivation of the disease may be more common than previously thought.

Thyroid eye disease is an inflammatory autoimmune condition of unknown aetiology. The natural history of the disease was first described by Rundle in the 1940s (Fig. 4) and involves an active inflammatory phase followed by a static phase, followed by a period of relative inactivity when the disease is thought to have become 'burnt out'.[2–4] Return to normal is rare. Although many patients follow this pattern of monophasic disease activity, there are a small but significant number who do not.

Reactivation of thyroid eye disease is not commonly described but is a recognised phenomenon,[5,6] suggesting that the disease may take on a biphasic or even multiphasic course. The timescale of disease activity was very variable amongst the 6 patients reported. Cases 1 and 2 clearly demonstrated late reactivation, with up to 20 years between presentations. Cases 3 to 6 demonstrated a much shorter time interval between recurrences and it is uncertain whether these are true recurrences or simply exacerbations during the active phase of the disease. However, these cases were asymptomatic and had documented inactive disease between presentations, suggesting renewed activity at the time of recurrence.

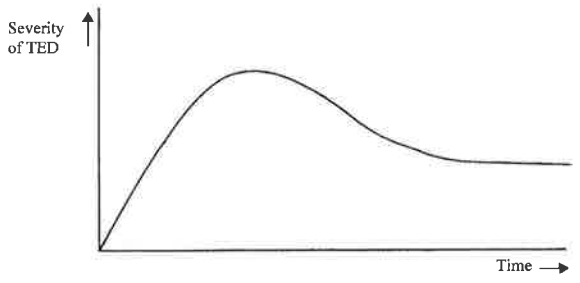


**Fig. 4.** 'Rundle's curve' showing the usual progression of thyroid eye disease (TED).

In some instances of unilateral thyroid eye disease, as in cases 1 and 5, recurrence on the other side may develop. In case 6 recurrence occurred in the same eye, whilst in cases 2, 3 and 4 the disease appeared to be initially unilateral and on recurrence was bilateral. Thyroid eye disease is usually considered a bilateral condition but is often asymmetrical. Where one eye may appear to be inactive, subclinical symptoms and signs may be present and the ophthalmopathy may develop during the course of the disease.

The pathogenesis of thyroid eye disease is unknown but is thought to involve an immune-mediated process.[7,8] Inflammatory cells infiltrate soft tissues and extraocular muscles of the orbit. Fibroblasts secrete glycosaminoglycans that attract fluid into the retro-orbital space leading to peri-orbital swelling, proptosis and extraocular muscle swelling. Chronic inflammation leads to fibrosis and a restrictive myopathy. Patients vary with regard to presentation of the disease and orthoptic findings. Strabismus is thought to occur in approximately 15% of all patients with thyroid eye disease[9] and such patients form a significant part of an orthoptist's workload.

Despite recent progress in the understanding of the disease, treatment is often not entirely satisfactory.[10] During the active phase and in mild cases, local therapeutic measures such as artificial tears and ointment, lid taping at night and prisms can control symptoms. In severe forms of the active disease more aggressive immunomodulation may be required, such as high-dose steroid and/or orbital radiotherapy. During the 'burnt out' stage of the disease, which is normally considered to be at least a 6 month period of inactivity,

rehabilitative surgery to the eyelids, orbits or extraocular muscles may be desirable. In this context, it is worth bearing in mind that recurrent thyroid eye disease may be more common than previously reported, as this will have prognostic implications for the patient about to undergo such surgery.

## Conclusion

Thyroid eye disease usually remains quiescent after the active phase, although we should be aware that in some patients the disease could recur. Orthoptists play a vital role in assessing these patients and in determining appropriate management of any motility dysfunction. It remains a clinical challenge to predict the course and outcome for each individual patient.

## References

1. Mourits MP, Koornneef L, Wiersinga WM. Clinical criteria for the assessment of disease activity in Graves' ophthalmopathy: a novel approach. *Br J Ophthalmol* 1989; **73:** 639–644.
2. Rundle FF, Hales IB. Ocular changes in Graves' disease: a long term follow up study. *Q J Med* 1960; **29:** 113–126.
3. Perros P, Crombie A, Kendall-Taylor P. Natural history of thyroid associated ophthalmopathy. *Clin Endocrinol* 1995; **42:** 45–50.
4. Perros P, Kendall-Taylor P. Natural history of thyroid eye disease. *Thyroid* 1998; **8:** 423–425.
5. Kalmann R, Mourits M. Late recurrence of unilateral Graves orbitopathy on the contralateral side. *Am J Ophthalmol* 2002; **113:** 727–729.
6. Selva D, Chen C, King G. Late reactivation of thyroid orbitopathy. *Clin Exp Ophthalmol* 2004; **32:** 46–50.
7. Heufelder AE. Pathogenesis of ophthalmopathy in autoimmune thyroid disease. *Rev Endocr Metab Disord* 2000; **1:** 87–95.
8. Bahn RS, Heufelder AE. Pathogenesis of Graves' ophthalmopathy. *N Engl J Med* 1993; **329:** 1468–1475.
9. Skov CM, Mazow ML. Managing strabismus in endocrine eye disease. *Can J Ophthalmol* 1984; **19:** 269–274.
10. Bartalena L, Pinchera A, Marcocci C. Management of Graves' ophthalmopathy: reality and perspectives. *Endocr Rev* 2000; **21:** 168–199.