Proptosis as First Presentation of Graves' Disease

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Abstract

Graves’ disease is usually diagnosed as a syndrome of clinical and biochemical features including ophthalmopathy (TAO); the latter occurring in up to 50% of patients with the syndrome. The incidence of TAO is higher in females than in males, as with the parent syndrome (16:2.9 cases per 100 000 people annually). Onset is later in males, who also tend to have more severe cases and poorer prognosis. A 34 year-old male patient initially presented at the Eye Clinic with a three-month history of right-sided proptosis. Main findings were right proptosis of 3 mm, with no lid retraction or lag, nor impairment of vision. He was subsequently referred to the Endocrinology Clinic; there he was diagnosed with Graves’ disease and placed on antithyroid medication. Ocular manifestations may be the first signs of Graves’ disease, as occurred with this patient.

Keywords: Proptosis; Graves’ disease; Thyroid associated ophthalmopathy; Radioiodine

Introduction

Graves’ disease (GD) is usually diagnosed as a syndrome of clinical and biochemical features including ophthalmopathy (TAO); the latter occurring in up to 50% of patients with the syndrome [1,2].

The incidence of TAO is higher in females than in males, as with the parent syndrome (16:2.9 cases per 100 000 people annually) [3]. Onset is later in males, who also tend to have more severe cases and poorer prognosis [4]. Five to ten per cent of patients may present with euthyroid ophthalmopathy, also referred to as ‘ophthalmic Graves’ disease’ [5].

Case Report

A 34 year-old male patient initially presented at the Eye Clinic with a three-month history of right-sided proptosis. Main findings were right proptosis of 3 mm, with no lid retraction or lag, nor impairment of vision.

Thyroid function tests revealed primary hyperthyroidism. He was thus referred to the Endocrinology Clinic, where he was diagnosed with GD and was placed on oral carbimazole and propranolol.

In 16 additions, a goitre was detected; whose ultrasonographic thyroid volume was 43 cm$^3$. In 17 the right lobe measured 30.9 x 48.7 x 35.2 mm, while the left measured 25.4 x 45.2 x 18 28.7 mm. Despite this, ophthalmopathy worsened. He developed epiphora, and right-sided proptosis, progressed to become bilateral (right more than left). Hyperthyroidism also remained recalcitrant to antithyroid medication; his most recent doses of antithyroid medication are oral carbimazole 15 mg twice daily (Table 1) and propranolol 40 mg once daily.

The patient found out about radioiodine therapy and opted for it, preferring it to surgery. On presentation at our Unit, main examination findings were bilateral proptosis (worse in the right eye) NOSPECS Class III (Figure 1). However, previously detected goitre was no longer visible nor palpable. His Tc-99m pertechnetate thyroid scan is as shown in Figure 2. He was counselled regarding radioactive iodine (RAI) therapy under steroid cover (Figure 3).

Table 1: Thyroid function tests performed at first presentation in Thyroid Clinic (TC), and on follow-up visit, both done while patient was still on carbimazole.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Initial test at presentation</th>
<th>Reference range</th>
<th>Follow-up test on carbimazole</th>
<th>Reference range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>0.2 mIU/L</td>
<td>0.5–6.5 mIU/L</td>
<td>&lt;0.005 mIU/L</td>
<td>0.27–4.2 mIU/L</td>
</tr>
<tr>
<td>FT4</td>
<td>283 nmol/L</td>
<td>65–175 nmol/L</td>
<td>17.5 pmol/L</td>
<td>12–22 pmol/L</td>
</tr>
<tr>
<td>FT3</td>
<td>3.7 nmol/L</td>
<td>1.0–3.25 nmol/L</td>
<td>5.5 pmol/L</td>
<td>3.9–6.7 pmol/L</td>
</tr>
</tbody>
</table>

TSH: Thyroid-Stimulating Hormone; FT4: Free Thyroxine; FT3: Free Triiodothyronine

The patient found out about radioiodine therapy and opted for it, preferring it to surgery. On presentation at our Unit, main examination findings were bilateral proptosis (worse in the right eye) NOSPECS Class III (Figure 1). However, previously detected goitre was no longer visible nor palpable. His Tc-99m pertechnetate thyroid scan is as shown in Figure 2. He was counselled regarding radioactive iodine (RAI) therapy under steroid cover (Figure 3).

Figure 1: Clinical photograph of bilateral proptosis seen in this patient at his first presentation in our Thyroid Clinic.
Discussion

TAO is said to be the most common disease affecting the orbit [6]. It is a complex autoimmune process related to orbital autoantigens such as thyroid-stimulating hormone receptor (TSHR), calsequestrin, collagen XIII, flavoprotein, and insulin-like growth factor-1 (IGF-1) [7,8]. Smoking is an established risk factor, which increases the risk of developing TAO significantly [1-9]. Smoking also increases the risk of its exacerbation following RAI [10]. Other risk factors for TAO are female gender (reflecting increased incidence of GD in women), and RAI therapy, as well as hypothyroidism following treatment with RAI. Male gender and older age were cited in other instances [11-13]. Our patient had no history of smoking. Moreover, a small study has showed that patients with GD who had undergone total thyroidectomy with or without treatment with RAI were much improved compared to those treated with antithyroid drugs (ATDs) [14].

As demonstrated in this case of interest, TAO may precede detection of Graves’ disease in 10 to 20 per cent of patients [11,12]. The most frequent sign in TAO is eyelid retraction, which affects almost all (90–98%) of patients [15,16]. TAO is the most common cause of bilateral or unilateral proptosis [1,17]. Typically, proptosis in TAO is bilateral, but may be asymmetrical, as was seen in our patient [18]. Severe ophthalmopathy occurs in approximately 3–5% of cases [19]. Proptosis or epiphora as a presentation of TAO has been described [20]. Most commonly, TAO has an active, inflammatory clinical phase, which lasts for 18–24 months followed by a plateau and a fibrotic stage. The stable phase is marked by stability of clinical symptoms although signs and symptoms of congestive orbitopathy can persist [21].

Patients with TAO may be investigated using imaging modalities such as orbital ultrasound (USS), computed tomography (CT), magnetic resonance imaging (MRI) or scintigraphy. In cases of clinically unilateral TAO, CT detects subclinical enlargement of the extraocular muscles on the contralateral side in 50% of patients [14]. Subclinical orbital alterations may be seen on USS or on CT in up to 79% of patients [22]. Uptake on single-photon emission computed tomography (SPECT) may help predict response to therapy [23]. Management of TAO requires achieving and maintaining euthyroidism and may be conservative in less severe cases, using corticosteroids. More advanced orbitopathy will benefit from surgery. Non-steroidal anti-inflammatory agents have also been tried with success in a small study [24].

Conclusion

Proptosis may be the first indicator of Graves’ disease, which does not always present classically. TAO as a cause of proptosis or epiphora may not be readily discerned yet remains one of the differential diagnoses to consider. This report serves to increase the clinical index of suspicion for such cases. Management of TAO may be conservative or surgical, for more severe cases. RAI is also an option but may worsen the condition.

References


