ISSN: 2572-407x

Ho MHT, et al. Int Arch Endocrinol Clin Res 2026, 11:041
DOI: 10.23937/2572-407X.151041
Volume 12 | Issue 1
Open Access

International Archives of Endocrinology Clinical Research

CASE REPORT

A Girl with Incidental Finding of Elevated Triiodothyronine then Concurrent Overt Graves Disease and Myasthenia Gravis

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Abstract

Graves disease in children typically presents with suppressed thyroid-stimulating hormone (TSH) and elevated free thyroxine (FT4) and triiodothyronine (FT3). Isolated raised FT3 is not commonly quoted as an early feature of evolving Graves disease. Graves disease is known to be associated with myasthenia gravis. There is, however, little literature on the temporal relationship between the onset of the two diseases. We report the case of a 14-year-old Chinese girl with incidental isolated FT3 elevation, initially minimally symptomatic, who subsequently developed overt thyrotoxicosis and concurrent ocular myasthenia gravis. Treatment with propylthiouracil and pyridostigmine led to normalization of thyroid function and improvement of ptosis. This case highlights the importance of recognizing isolated FT3 elevation as a potential early sign of evolving Graves disease and underscores the need for vigilance regarding associated autoimmune conditions.

Keywords

Graves disease, Myasthenia gravis

Introduction

Graves thyrotoxicosis is commonly presented with suppressed thyroid stimulating hormone (TSH) and elevated and free thyroxine (FT4) and triiodothyronine (FT3) [1]. However, some individuals with Graves disease may have normal FT4 levels but high FT3 levels, a condition known as T3 toxicosis, which can be seen upon diagnosis or during relapses in the course of the disease [2]. This disease entity in the paediatric population is not frequently described [3].

The association of Graves disease and other autoimmune disorders is well recognized [4]. The concurrence of Graves disease and myasthenia gravis is particularly well recognized in the Asian population [5] and is more common in women under the age of 50 years [6]. However, there is little literature on the temporal relationship of the onset of the two diseases.

This case report illustrates a girl with Graves disease who initially had minimally-symptomatic triiodothyronine toxicosis (T3 toxicosis), then presented with overt thyrotoxicosis and concurrent onset of myasthenia gravis.

Case Description

A 14-year-old Chinese girl with good past health was found to have raised free FT3 level of 10.4pmolL (3.53-6.45) when she received her first body health checkup. Her TSH [4.66mIU/L (0.3-50) and FT4 [12.01pmol/L (11.9-21.6)] were normal. At that time, she was not aware of any symptoms of hyperthyroidism nor any eye complaints. She was referred to a paediatric specialist clinic. Five weeks later, prior to the clinic appointment, she noted sudden onset of right eyelid drooping and therefore attended the Accident and Emergency Department of our hospital. Concurrently, she also reported new onset palpitations and agitation. On retrospect, she recalled having had mild hand tremors and heat intolerance for around a year, but all along there had been no diarrhoea or menstrual disturbances. She did not report any other neurological symptoms. She did not have any recent infective or febrile illnesses.

Her maternal aunt had Graves disease and was on anti-thyroid drugs. Her paternal aunt also had history

Citation: Ho MHT, Wong WY, Chak WK, et al. (2026) A Girl with Incidental Finding of Elevated Triiodothyronine then Concurrent Overt Graves Disease and Myasthenia Gravis. Int Arch Endocrinol Clin Res 12:041. doi.org/10.23937/2572-407X.151041

Received : March 07, 2026, **Accepted:** April 4, 2026: **Published:** April 7, 2026

of thyroid disease but the details could not be retrieved.

On examination, her growth parameters were 160.8cm in height (50th-75th centile) and 57.5 kg in weight (75th-91st centile). Her heart rate was 114 beats per minute and regular, and her blood pressure was 137/87 mmHg. She had right eye partial ptosis with fatiguability. She also had slight proptosis over the left eye (Figure 1). There was no lid lag, lid retraction or chemosis. The extra-ocular eye movement was normal and she reported no diplopia. The other neurological examination was normal. There was no evidence of proximal muscle weakness or peripheral muscle fatiguability. The reflexes were normal. She had a moderate diffuse goitre. There was no thyroid bruit or retrosternal extension of the goitre. She was also noted to have resting hand tremor and sweaty palms. Bedside peak flow rate did not show any respiratory compromise.

Her laboratory findings were consistent with myasthenia gravis and Graves disease.Her FT4 level was >64.4 pmol/L (8.6-15.7), FT3 was >20 pmol/L (3.6-5.7) and TSH was <0.01 mIU/L (0.47-3.63). She had raised anti-thyroid-stimulating hormone receptor antibody [38.8IU/L (>1)] and anti-thyroid peroxidase antibody [>350IU/ml (<50)]. Her anti-thyroglobulin was normal [84.7IU/ml (<100)]. She had a positive acetylcholine receptor antibody at 3.21nmol/L (<0.45 nmol/L). Nerve conduction velocity was normal over four limbs. However, repetitive nerve stimulation showed decremental response of 24% which indicated myasthenia gravis. Tensilon test was positive and right eye ptosis decreased after 2mg Tensilon was given (Figure 2).

Screening of other autoantibodies were performed. Her anti-nuclear antibody (ANA) titre was raised at a level of 160, with homogenous and speckled pattern. Other autoimmune antibodies including anti-islet cell, anti-glutamic acid decarboxylase 65-kilodalton isoform (anti-GAD65), anti-insulinoma-associated antigen 2 (anti-IA2), anti-adrenal antibodies were negative. She was started on carbimazole 15 mg twice a day. However, she developed allergic reaction 1-2 weeks after starting the medication, presenting as urticarial rash. She was switched to propylthiouracil 100mg twice a day and it was well tolerated. At the same time, she was also started on pyridostigmine, initially with a small dose of 30 mg three times a day and gradually titrated up.

Figure 1: Right eye partial ptosis and left eye slight proptosis.

Figure 2: Response after Tensilon given.

She reported improved right eye ptosis after starting the medication. The thyroid function normalized. She was receiving surveillance for other autoimmune disease, and she displayed no signs or symptoms of lupus or other autoimmune diseases.

Discussion

Graves thyrotoxicosis is commonly presented with suppressed TSH and elevated FT4 and FT3 [7]. Patients could be identified to have subclinical hyperthyroidism due to evolving Graves disease or other thyroid disease if they have low TSH, normal FT4 and FT3 [8]. Isolated raised FT3 is not commonly quoted as an early feature of evolving Graves disease. Our patient was identified to have raised FT3 incidentally when she was at a minimally symptomatic phase of early Graves disease.

Five weeks later upon presentation at the Accident and Emergency department when she developed overt thyrotoxic symptoms, her biochemical profile had also evolved to the more classical profile of Graves disease. Her minimal symptoms in the initial isolated T3-toxicosis phase was consistent with the reports that the majority of T3 toxicosis in Graves disease had mild clinical toxic reaction only, possibly because the level of only one of the two metabolically active thyroid hormones is elevated [9]. This case illustrated that a minimally-symptomatic isolated raised FT3 could be an early manifestation of Graves disease.

The early diagnosis of myasthenia gravis in our patient was made because of the physician's awareness of the association of Graves disease and myasthenia gravis. Autoimmune thyroid disease is known to be associated with myasthenia gravis. The pathophysiology is proposed to be due to cross-reactivity against epitopes or auto-antigens shared by the thyroid and eye muscles [10]. Ptosis is not an expected symptom of thyroid ophthalmopathy. Therefore, if a patient with Graves disease presents with ptosis, concurrence of myasthenia gravis should be considered [11].

There is little literature on the temporal relationship between the onset of the two diseases. Simultaneous onset of Graves disease and ocular myasthenia gravis have been reported but it was in the context of post-COVID infection in an adult patient [12]. Limited similar reports have been made in the paediatric population. Our patient had simultaneous onset of overt Graves disease and myasthenia gravis. An underlying auto-dysregulation could explain the concurrence of both diseases, but a trigger could not be identified in this case.

Patients with Graves disease are also known to have increased frequency of other autoimmune endocrine diseases (eg, diabetes mellitus, celiac disease [13] and primary adrenal insufficiency) and non-endocrine autoimmune disorders (eg, vitiligo, systemic lupus erythematosus, rheumatoid arthritis, thrombocytopenic purpura, and pernicious anemia). In our case, monitoring of signs and symptoms of other autoimmune disease and biochemical screening of other auto-antibodies were performed. Her ANA titre was elevated at 160 but she displayed no signs or symptoms of other autoimmune diseases or lupus. She is receiving regular monitoring for any other autoimmune diseases.

Conclusion

We report the case of a 14-year-old Chinese girl with incidental isolated FT3 elevation, initially minimally symptomatic, who subsequently developed overt thyrotoxicosis and concurrent ocular myasthenia gravis. This case highlights the importance of recognizing isolated FT3 elevation as a potential early sign of evolving Graves disease and underscores the need for vigilance regarding associated autoimmune conditions.

Disclosures

None declared.

Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient's relatives or guardians.

Funding

No pubic or commercial funding.

Contribution

All authors were involved equally in the diagnosis and management of this patient and manuscript submission.

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