

Endocrine Imaging

Title: Severe Graves' Orbitopathy occurring in a patient with thyroid hemiagenesis.

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TEXT:

A 64-year old woman was addressed to the endocrinology clinics, following the observation of **subclinical hypothyroidism and** positive anti-TPO auto-antibodies, (TSH levels 6.28 uUI/ml). Ultrasound examination showed **a diffusely enlarged heterogeneous hypoechoic right lobe, with two micronodules (3 and 7 mm) and** the absence of the left thyroid lobe... The patient started levothyroxine (L-T4) replacement therapy (50 µg/day), remaining euthyroid for almost four years. In August 2014, she presented **tiredness, tremors and palpitations** with markedly increased free thyroid hormone and suppressed TSH levels. L-T4 therapy was discontinued, with no clinical improvement. **On September 2014**, the laboratory findings confirmed the persistence of thyrotoxicosis. The ⁹⁹Tc scintiscan showed increased uptake in the right thyroid lobe, suggesting the diagnosis of Graves' disease which was corroborated by the demonstration of highly positive (46.2UI/L) TSH receptor antibodies (TRAb), measured using a 2nd generation TRAK human lumitest (Thermofisher, AG, Henningsdorf/ Berlin, Germany; normal value <1.8 U/L). Consequently, the patient started methimazole (MMI) treatment (30 mg/day). **On November 2014**, Graves' Orbitopathy (GO) with symptomatic vertical diplopia appeared, requiring 8^ prisms for correction of constant diplopia. The Nuclear Magnetic Imaging of the orbits showed thickening of extra-ocular muscles (medial and inferior right rectus and bilaterally superior recti). Further follow-up showed rapid progression of the GO, with deterioration of vertical diplopia. The ophthalmological assessment, according to the EUGOGO guidelines (1) demonstrated bilateral active GO with spontaneous orbital pain, chemosis, lid edema and hyperemia resulting in a clinical activity score (CAS) of 5/10. The patient presented also constant diplopia, a proptosis of 23.5/22 mm and significant worsening of eye motility. The severity NOSPECS score was 2B3A4B5060. The persistence of hyperthyroidism (TSH 0.01 mU/L, FT₄ 22.3 pmol/l and FT₃ 10.1 pmol/l) and elevated TRAb levels (41.4 U/L) required an increase of MMI to 40 mg/day. High doses of intravenous methylprednisolone (**IVMP**) were also administered once a week for 12 weeks (six pulses of 830 mg followed by six more pulses of 415 mg with a cumulative dose 7.5 g) **from**

January to March 2015. Six weeks after completing corticosteroid treatment, the patient was re-examined, GO resulted inactive (CAS 2/10). Monthly follow up showed progressive improvement of both inflammatory manifestations and eye motility. Euthyroidism was maintained, under escalating MMI dose which was discontinued on September 2015. GO persisted inactive, with only inconstant diplopia, a CAS of 1/10 and a severity NOSPECS score 2A3A405060GO. The patient could eventually resume her daily activities, including bicycle riding (February 2016). The patient remained euthyroid during the remaining follow-up (TSH 2.86 uUI/ml and undetectable TRAb on January 2018).

Thyroid hemiagenesis is rare, with a prevalence estimated to 0.2% at systematic ultrasound screening (2). Its association with Graves' disease is exceptional and only 21 patients have been previously reported in the literature (3). Interestingly, spontaneous conversion from hyperthyroidism to hypothyroidism or long-term remission has been previously reported in two cases. A third case, unresponsive to oral steroids underwent orbital decompression. Notably, the present report illustrates the second documented case of GO successfully treated with IVMP administration in thyroid hemiagenesis.

References

1. Bartalena L, Baldeschi L, Boboridis K, Eckstein A, Kahaly GJ, Marcocci C, Perros P, Salvi M, Wiersinga WM; European Group on Graves' Orbitopathy (EUGOGO), The 2016 European Thyroid Association/European Group on Graves' Orbitopathy Guidelines for the Management of Graves' Orbitopathy. *Eur Thyroid J.* 5:9-26 (2016).
2. Shabana W, Delange F, Freson M, Osteaux M, De Schepper J, Prevalence of thyroid hemiagenesis: ultrasound screening in normal children. *Eur J Pediatr* 159:456–458 (2000).
3. Ozgen AG, Saygili F, Kabalak T, Thyroid hemiagenesis associated with Graves' disease and Graves' ophthalmopathy: case report. *Thyroid* 14:75-77 (2004)

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The Authors declare no conflict of interest.

No approval by the ethical committee was required.

The informed patient's consent was obtained.

The ophthalmological assessment of the patient was performed at Graves' Orbitopathy Center, Endocrinology, Fondazione Ca' Granda IRCCS, University of Milan, Milan, Italy.

Legend to the Figure

Figure 1 clinical assessment of the patient

Panel A: Ultrasound examination demonstrating the absence of the left thyroid lobe and the presence of a diffusely enlarged heterogeneous hypoechoic right lobe.

Panel B: ^{99m}Tc Thyroid scan confirming an increased uptake of the right thyroid lobe.

Panel C: MRI imaging of the orbit, showing thickening of extra-ocular muscles (medial and inferior right rectus and bilaterally superior recti)

Panel D: Orthoptic evaluation. Eye motility was calculated as the sum of ductions in each eye and the asymmetry as the difference of the ductions between the two eyes, measured in degrees. The dashed line represents the mean results of normal controls, the gray area the ductions measured in the patient. Total Motility Score (TMS) was calculated as the sum of ductions in each eye and a bi-ocular TMS (in gray) as the sum of both eyes TMS. The Asymmetry Ratio (in black), was calculated as the differences of the ductions between the two eyes divided by the mean Asymmetry Ratio measured in normal controls. IVMP treatment was able to improve right eye motility leading to a reduction of diplopia.