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Monoarthritis Due to Metimazole in an Adolescent with Graves Basedow Disease

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Abstract

Hyperthyroidism (HT) is rare in pediatrics (5% of HT) and the most common cause is Graves-Basedow Disease (GBD). The first-line treatment is synthetic antithyroid drugs (ATD). The associated adverse effects are usually mild and frequent. In a few cases, severe effects such as severe polyarthritis occur, leading to its suspension. The clinical case of a 10-year-old patient with symptoms of thyrotoxicosis and grade II diffuse goiter is presented. The analysis highlights: suppressed TSH (Thyroid stimulating hormone) and elevated thyroid hormones tetraiodothyronine (T4) and triiodothyronine (T3). With the presentation of GBD, treatment was started with Methimazole (MTZ) and atenolol. Twenty-one days after the start of treatment, the patient developed an urticarial rash, pain, and functional impotence in the right hip. Ultrasound showed effusion compatible with arthritis. Infectious and inflammatory causes were ruled out. With a possible diagnosis of monoarthritic secondary to treatment with methimazole, it is suspended. Two weeks later the patient regained walking without pain. Radioiodine (15 mCi) was performed as definitive treatment without complications. Polyarthritis as an adverse effect of ATD use is known as "antithyroid arthritis syndrome." It occurs in 1 to 2% of patients. To date, monoarthritic has not been described as an adverse effect in pediatrics. Correct control of symptoms and immediate definitive treatment is necessary.

Introduction

Hyperthyroidism (HT) is rare in children, corresponding to 5% of all HT. In childhood, Graves Basedow Disease (GBD) is the first cause (90%) and usually occurs between 11 and 15 years of age [1]. Treatment must be early due to the deleterious effects of thyroid hormones on different organs [2]. Synthetic antithyroid drugs such as Methimazole (MTZ) are the first line of treatment [2,3].

Adverse effects associated with antithyroid drugs are infrequent and usually mild, these are: urticaria, skin rash, gastrointestinal. In rare cases, serious complications such as severe polyarthritis appear, leading to the need to suspend treatment. They usually occur in the first 8 weeks after starting treatment, but sometimes even several years later [4].

Only a few case reports have described polyarthritis as an adverse effect of MTZ in children, but not in the form of monoarthritic [5]. The case of a pediatric patient who developed hip monoarthritic during treatment with MTZ is presented. Radioiodine was proposed as a definitive treatment.

Case Presentation

A 10-year-old male with a personal history of asthma and mild intellectual deficit with no notable family history. He was admitted to the Pereira Rossell Hospital Center for an emergency with symptoms of 8 months of evolution: restlessness, difficulty in attention and polyphagia. He presents figures of high blood pressure and weight loss of 6 kg in 1 year. He denied dyspnea, dysphagia, or any stressful life events.

The physical examination highlights: Weight: 28 kg. Height: 140 cm. BMI 14 kg/m^2 (Figure 1).

Ocular: bilateral proptosis, no elements of infiltrative orbitopathy or activity.

Neck: Diffuse grade II goiter (WHO Classification). CV: rr, 120 cpm, BP 120/60 mmHg (systolic BP greater than p95 for age and sex and less than p99, diastolic BP less than p90).

PNM: Fine distal tremor and hyperreflexia of all four limbs.

From the laboratory, the following stand out: elevated thyroid hormones (Figure 2) and elevated antithyroid antibodies (Table 1). Ultrasound showed diffusely enlarged thyroid gland, volume of 14cc.

With hyperthyroidism due to GBD, methimazole was started at 1.5 mg/kg/day (40 mg/day) and atenolol 50 mg/day.

Twenty-one days after the start of treatment, he developed an urticarial rash, pain, and functional impotence of the right lower limb with prostration. Osteoarticular examination: great decrease in range of mobility of the right hip. No involvement of other joints, fever, or fluid elements. Hip x-ray reports: no alterations; and ultrasound of the right hip: an echogenic effusion with 3mm thickening of the capsule. The complementary tests are displayed in Table 1. Positive antinuclear antibodies stand out. Infectious and inflammatory causes were ruled out.

With a possible diagnosis of monoarthritic secondary to treatment with methimazole it was suspended and ketoprofen was started to control pain. Two weeks after suspension, the patient regained ambulation without pain. Tachycardia and elevated thyroid hormones were observed, and symptomatic treatment was performed (Figure 2).

Radioiodine (15 mCi) was performed as definitive treatment without complications. Hypothyroidism sets in, so treatment with levothyroxine is started (Figure 2).

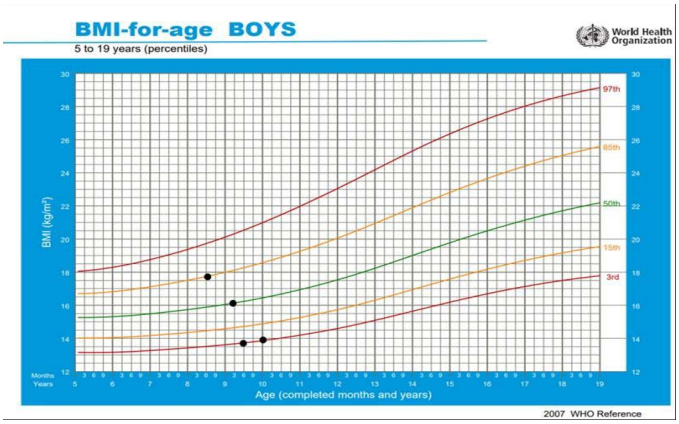
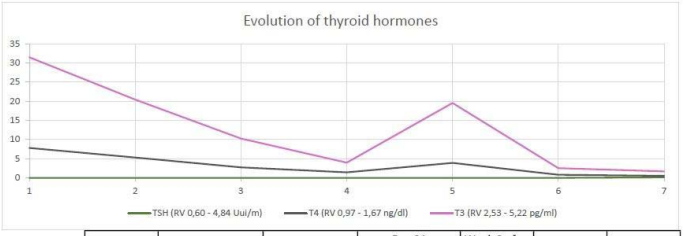


Figure 1: Body Mass Index (BMI) for Age

The Curve Shows the Evolution of BMI for the Patient's Age from 8 Years and 6 Months to the Current age.



	At diagnosis	Day 5 of methimazole	Day 15 of methimazole	Day 21 (methimazole suppression starts)	Week 2 after methimazole suppression	Day 15 after radioiodine	Day 20 after radioiodine
TSH (RV 0,60 - 4,84 Uui/m)	< 0,01	< 0,01	< 0,01	< 0,01	< 0,01	< 0,01	0,14
T4 (RV 0,97 - 1,67 ng/dl)	7,77	5,28	2,7	1,41	3,86	0,78	0,51
T3 (RV 2,53 - 5,22 pg/ml)	31,42	20,39	10,23	3,95	19,52	2,5	1,67

Figure 2: Evolution of Thyroid Hormones

The graph shows the evolution of thyroid hormones from the moment of diagnosis where suppressed TSH and elevated FT4 and FT3 are observed. After treatment with MTZ, a progressive decrease in FT4 and FT3 is observed until reaching normalization (day 21 of MTZ). Then, with the suspension of MTZ, we observed a new increase in thyroid hormones FT4 and FT3, which subsequently decreased again after treatment with Radioiodine. It can be seen in the graph that 15 days after definitive treatment the patient was hypothyroid. Note that TSH remained suppressed.

Table 1: Antithyroid Antibodies and Tests for Etiology of Hip Arthritis

Anti-thyroglobulin antibodies	213 UI/ml	(RV 0 – 37 UI/ml)
Anti-thyroperoxidase antibodies	86 UI/ml	(RV 0 – 18 UI/ml)
Erythrocyte sedimentation rate (ESV)	58 mm/h	(RV 0-20 mm/h)
Procalcitonin (PCT)	0,13 ng/ml	(RV < 2 ng/ml)
C-reactive protein (CRP)	7,6 mg/L	(RV < 20 mg/L)
C3 Plugin	126 mg/dl	(RV 75- 127 mg/dl)
C4 Plugin	11,4 mg/dl	(RV 18-47 mg/dl)
Rheumatoid factor	10,5 UI/ml	(RV 0 – 20 UI/mL)
Antinuclear antibodies	Homogeneous pattern. Positive, title 1/80	
Anti-neutrophil cytoplasmic antibodies	Negative.	

Discussion

The treatment of choice for GBD in pediatrics is synthetic antithyroid drugs (ATD). Adverse effects associated with MTZ occur in 1-15% [4]. Skin rush and gastrointestinal symptoms are mild and frequent, mostly well tolerated and easily treatable [6].

Polyarthritis as an adverse effect of ATD use is known as "antithyroid arthritis syndrome": myalgia, polyarthritis, fever, and rash. It occurs between 1 to 2% [5,7]. It is important to distinguish polyarthritis caused by MTZ from mild arthralgias which are a minor adverse effect [8]. However, its appearance requires rapid cessation of ATD, as this symptom could develop into severe transient migratory polyarthritis [5].

To date, monoarthritis has not been described as an adverse effect in pediatrics; but in this patient it manifested in a disabling manner that led to the suspension of MTZ. It is essential to rule out differential diagnoses such as infectious and inflammatory arthritis.

The incidence of positive ANA in patients with autoimmune thyroid disease is 20%-45%, significantly higher than in the general population [9]. Despite the positivity of these in our patient, inflammatory arthritis was not considered as a cause of hip arthritis given the lack of clinical diagnostic criteria such as, for example, its evolution time. It cannot be ruled out that in the future the patient will present any of these entities given the high prevalence of connective tissue diseases in patients with autoimmune thyroid diseases [9].

Radioiodine or surgery are considered as definitive therapeutic options in case of not tolerating or responding to ATDs [2]. Radioiodine was proposed with prior control of thyrotoxicosis symptoms with excellent results and without complications.

Conclusions

Arthritis due to ATD is extremely rare, close monitoring of treatment is essential to detect possible adverse effects that can be potentially serious. Correct control of symptoms and immediate definitive treatment is necessary.

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