HEART FAILURE IN PEDIATRIC AND ADOLESCENT
HYPERTHYROIDISM

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Abstract.

Introduction. Life threatening heart disorders secondary to paediatric and adolescent hyperthyroidism are exceptional.

Aim. We aimed to study cardiothyreosis frequency and outcome in children and adolescents with hyperthyroidism diagnosed between 1980 and 2010.

Material and methods. In this retrospective study we observed 160 clinical and biological hyperthyroidisms in children (≤ 16 years) and adolescents (16-20 years).

Results. Among them four girls aged 3, 16, 17 and 18, without previous familial history of heart diseases, had congestive heart failure (2.5%) without rhythmic troubles. Symptoms of cardiac insufficiency were resistant to digitalis and diuretics, but after anti thyroid drugs, there was an integral restitution of heart function in three cases and a persistent mitral, aortic and tricuspid regurgitation in one case arguing for heart rheumatic disease prior to hyperthyroidism.

Conclusion. Heart failure secondary to thyroid hormones excess is extremely rare before age of 20. Among 160 paediatric and adolescent hyperthyroidisms seen in 30 years, four girls had life threatening congestive cardiac insufficiency (2.5%), but after euthyroidism, heart insufficiency disappeared totally in all cases which pleaded for a direct action of thyroid hormones excess on heart function.

Keywords: reversible congestive heart failure, hyperthyroidism, anti thyroid drugs.

INTRODUCTION

In adulthood, it is well known that hyperthyroidism is a metabolic disorder inducing severe cardiovascular manifestations. The life threatening ones, called cardiothyreosis or thyrotoxic cardiomyopathy, include one or more of these manifestations: congestive heart failure, severe rhythmic disorders, and/or coronary insufficiency. But, in medical literature there are very few reports regarding children who had severe heart complications secondary to thyroid hormones excess. Our aim is to study cardiothyreosis frequency and outcome in children and adolescents with hyperthyroidism diagnosed between 1980 and 2010.

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SUBJECTS AND METHODS

Subjects. 160 clinical and biological pediatric (≤16) and adolescents (≤20) patients with hyperthyroidism were collected to look for heart complications.

Methods

In this retrospective study, all patients had clinical examination and biological exploration. Hormonal assessment was done through radio immune assays from 1980 to 2000, and through chemiluminescence from 2001 to 2010.

Diagnosis of overt hyperthyroidism was based on clinical examination, and an increase in FT3 and/or FT4 with low TSH. Informations collected from medical history, hormonal assessment, thyroid scintigraphy, and thyroid antibodies measurements (thyroid stimulating antibodies or TSab, anti microsomes, and anti thyroglobuline) were used to verify primary overt clinical hyperthyroidism and to classify hyperthyroidism into nosological forms.

Heart exploration was based on clinical examination, electrocardiogram, and chest x rays. Echocardiography was done when heart troubles were suspected.

RESULTS

Among 160 overt hyperthyroidisms observed in 30 years, 04 girls (2.5%) had congestive heart failure without arrhythmia. After anti thyroid drugs intake and normalization of thyroid function, heart insufficiency disappeared in the four cases, but mitral, aortic and tricuspid regurgitation persisted in one case.

OBSERVATIONS

Case No.1: a girl aged 3, was referred by her paediatrician for Graves’ disease with heart failure resistant to digitalis, diuretics and low dose (20mg) of Carbimazol prescribed during 15months. Hyperthyroidism was clinically evident with exophthalmia predominating on the right eye. FT3 and FT4 were high [respectively 8.75 pmol/L (n=2.2-6.2), 34.5 pmol/L (n=8-24)], and TSH was low: 0.05 µU/mL (n=0.10-4). Thyroid scan and ultrasound showed a diffuse goiter. Heart exploration demonstrated mitral leak type IIa IIb, moderate tricuspid leak, dilated left atrium, and pulmonary hypertension. After increasing Carbimazol dose to 45 mg/day and adding a beta-blocker, euthyroidism was achieved and heart function improved, then normalized.

Case No.2: an adolescent girl aged 17 years and 4 months, was referred for the same motive. Her heart medical history began 18 months earlier as she was treated unsuccessfully with diuretics, vasodilators (isosorbide dinitrate) and a converting enzyme inhibitor (Captopril). Her heart frequency was equal to 120 beats per minute and blood pressure = 100 mm/60mm mercury. There was a 3/6 systolic mitral murmur. On electrocardiogram there was a sinus rhythm. Chest x rays exhibited cardiomegaly: cardiothoracic index was equal to 0.59 (fig1). Echocardiography showed a dilated cardiomyopathy with low ejection fraction: 29% (n: ≥60). The shortening fraction was reduced: 10.6% (N ≥ 30), and global contraction was reduced too. Left atrium size was increased: 41 mm. There were mitral
regurgitation grade IIb, and tricuspid leak grade III. On another side, she had an overt hyperthyroidism with mild exophthalmia (right eye = 19 mm and left eye = 20 mm) with bilateral eyelid retraction. Echosonography and thyroid scinti-scan argued for a diffuse goiter. Free T3 was very high = 26.7 pmol/L (n=2-6.2) and TSH very low = 0.05 µU/mL (n=0.10-4). TSab were positive: 39% (n: 0-20). When anti thyroid drugs (Carbimazol: 60 mg) and beta blockers (Propanolol 60 mg) were added to the treatment mentioned above, her free T3 was normalized (3.6 pmol/L), so did her TSH = 0.29. Cardiothoracic index decrease up to 0.50 (fig. 1) and heart frequency decreased too (73 b/mn). Ejection fraction increased up to 55% and shortening fraction was equal to 23%. Left atrium size decreased to 30 mm. Mitral and tricuspid leak became very discrete. After thyroid surgery and correction of transient hypothyroidism, heart function was totally normalized.

**Case No3.** A girl aged 16 was sent to our department in January 1993 for hyperthyroidism, difficult to manage, with short breathing. Signs of hyperthyroidism began when she was fourteen. Carbimazol was prescribed but the treatment was irregular. In her family history there were Graves Basedow disease with vitiligo (mother) and goiters (aunts).

Clinical examination showed a goiter type II, franc hyperthyroidism, right exophthalmia (19 mm vs 15 mm for the left eye) with eyelid retraction, and leg edemas.

Hormonal assessment showed high T4 (276 ng/mL n=47-100) and T3 (10 nmol/mL n = 1.17-2.92) with low TSH (0.06 µU/ml), TS ab = 29% (n=0-20). Thyroid scintigraphy exhibited a large gland with diffuse uptake. On echosonography the right lobe = 62 x 34 x 25 mm, left lobe = 64 x 33 x 25 mm, and thyroid isthmus = 9 mm.

She was treated again with Carbimazol, and beta blockers, but the treatment was again irregular, then she was lost in sight.

She consulted again in February 1999 for the same symptoms. The electrocardiogram showed a sinus rhythm of 150 b/mm. On chest x rays there was a cardiomegaly (cardiothoracic index = 0.62). On heart echosonography, there was a discrete mitral regurgitation (1 b) without pulmonary insufficiency. The cavities were not enlarged. Ejection fraction was normal = 77% (n: ≥ 60), the shortening...
fraction was normal too (38%, n ≥ 30). Leg skin biopsy argued for thyroid dermopathy. After a new prescription of high dose carbimazol and beta blocker to achieve euthyroidism, surgical treatment was decided. Thyroid histology confirmed typical aspect of Graves’ disease. After thyroid substitution, the outcome was excellent.

**Case No. 4.** An adolescent aged 18 with a familial history of high blood pressure and diabetes mellitus was referred for hyperthyroidism with heart failure. She was weighing 47kg for 1.62m (BMI=17kg/m²), hyperthyroidism was franc without goiter and exophthalmia. Free T3 and T4 were very high [respectively 18pmol/mL (n=2-6) and 46pmol/mL n =8-22) and low TSH = 0.016 µU/mL. TS ab=59% (n<12). She had a sinus rhythm equal to 120b/mm. Echocardiography showed a dilated cardiomyopathy with mitral, aortic and tricuspid regurgitations and thickened valves. After 4 months Carbimazol intake, heart insufficiency disappeared, but regurgitations persisted which argued for a rheumatic disorder prior to hyperthyroidism state.

**DISCUSSION**

Cardiovascular complications due to thyroid hormones excess called thyrotoxic heart disease, heart thyrotoxicosis, thyrotoxic cardiomyopathy, tachycardiomyopathy, or cardiothyreosis are usually seen in adults with or without previous heart problems. In paediatric population they are uncommon as very few cases have been reported. When hyperthyroidism is severe, has a long standing or when the heart is previously damaged by congenital or rheumatic disease, heart insufficiency and/or rhythmic troubles occur.

In literature review, congestive heart failure is the most frequent heart abnormality reported in paediatric cases (1-6). This life threatening heart disorder seems to be more frequent in new borns with transient hyperthyroidism (infants born to mothers with Graves’ disease or Hashimoto’s thyroiditis) than in other hyperthyroid children or adolescents (6). Arrhythmias are in the second position. Atrial arrhythmia is reported in some cases (7, 8); atrial flutter is rarer and sometimes difficult to diagnose (9) in children.

To our knowledge asymptomatic monomorphic ventricular tachycardia has been described once by Minegishi (10) in a hyperthyroid boy aged four with multi nodular goiter. Heart ischemia is the rarest disorder. It is observed especially in neonatal hyperthyroidism (11), but can be observed in older children with severe hyperthyroidism.

Regarding hyperthyroidism etiologies, it is well known that in paediatric population Grave—Basedow is the most frequent, the most symptomatic, and the most dangerous disease inducing heart deterioration. But, nodular forms may also be associated to rhythmic troubles (10). Other etiologies can have the same impact on heart function, but they are less common than in adults. Cardiothyreosis mechanism is still discussed, especially when there is a lack of patient’s family history for sudden unexplained death, congenital heart disease, or cardiomyopathy, and
when the affected child has no history of heart disease.

On the basis of literature review, cardiothyreosis mechanisms are numerous and very complex (12). Experimental studies argue for a direct toxic effect of thyroid hormones excess on cardiomyocytes leading to apoptosis and decrease in myocytes’ contraction (13). But, some authors discuss the role of hyper dynamic or high output stress on heart function caused by thyroid hormones excess, as even in the very early stage of cardiothyreosis (also called compensated cardiothyreosis), Cavallo (14) demonstrated an inverse correlation between left ventricular ejection fraction during effort and thyroid hormones (thyroxine and triiodothyronine) serum concentrations. Mitral and/or tricuspid valves prolapse and regurgitation may be another cause, especially in auto immune hyperthyroidism (15). More complex mechanisms such as those involving lipid peroxidation and free radical scavengers are also discussed (16).

For outcome, it seems that in paediatric cases as in adults’, the prognosis of heart lesions depends on the duration and severity of hyperthyroidism, but also on heart function prior to the hyperthyroidism state. So, in young people without a history of heart disease, heart insufficiency secondary to hyperthyroidism is reversible (7, 10-12) as we observed it, but sometimes heart troubles may be lethal (4) especially when hyperthyroidism is misdiagnosed or when heart lesions and pulmonary hypertension are severe.

So, the best way to prevent heart complications secondary to hyperthyroidism in children is to diagnose congenital and rheumatism heart diseases, and to check regularly for hyperthyroidism that may be clinically evident or sub clinical, and even sub biological. If the diagnosis is positive, hyperthyroidism should be treated as early as possible to avoid its life threatening cardiovascular complications.

**In conclusion**, cardiothyreosis is very rare in children and adolescents (2.5%). The reversibility of cardiac insufficiency in children and adolescents under anti thyroid drugs therapy, as we observed it in our cases, emphasizes the importance of an early detection and management of hyperthyroidism in paediatric population.

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