The importance of annual screening of thyroid function among the pediatric patients with Down syndrome - case report

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Abstract

Down syndrome (21 trisomy) is a genetic disorder caused by the presence of an extra chromosome. Thyroid disorders occurs frequently (8-18%) among pediatric patients with Down syndrome. To prevent them, it is necessary to perform a range of investigations that are part of annual screening of each person diagnosed with Down syndrome.

In this article we report the association of Down syndrome and an acquired severe hypothyroidism due to autoimmune thyroiditis in a 7 years-old female patient.

Keywords: Down syndrome, hypothyroidism, child, autoimmunity

Introduction

Down syndrome (DS) is the most common genetic cause of intellectual disability and different conditions including autoimmunity diseases [1] are associated with DS as well as thyroid dysfunction. The hypothyroidism has subclinical symptoms that can be above all difficult to identify in patients with intellectual disabilities. Moreover the symptoms of hypothyroidism superpose with DS symptoms include impair intellectual, decrease linear growth, dentition abnormality, decreased physical activity and dry skin [2].

Case report

The authors of this article report the case of a 7 year-old female patient, known at 7 month

of age in 3rd Department of "Sf. Maria" Pediatric Hospital of Iasi diagnosed with Down syndrome that has returned to regular appointments. In November 2013, the patient comes to our clinic accusing excessive weight gain (6 kg in the last 3 months) and chronic constipation (1 stool in 6 days). At the physical examination (Figure 1) we observed: height = 106 cm, weight = 29 kg, BMI = 25.80 kg/m², symmetrical and infiltrated facies, harsh and dry aril, discrete pharyngeal congestion mucosa, overly adipose tissue on the waist abdomen, thorax and limbs. circumference (Wc) = 80 cm, polyadenopathy less than 1 cm, normotonic, weakness and hypokinetic muscular system. nasal obstruction, partially offset by an oral noisy breathing, nasal voice, hoarseness, excessive appetite, globular abdomen, umbilical hernia, slowed intestinal transit and retard in psychomotor development with IQ= 50.

The laboratory investigations reveled inflammatory syndrome (ESR= 20 mm/1h and CRP (semi-quantitative agglutination) high than 6 mg/l), thrombocytopenia (PLT=

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 $87 \times 10^3/\mu$ L), hepatic-cytolysis syndrome (ALT= 59 U/L, AST= 49 U/L), dyslipidemia (Total cholesterol= 267 mg/dl, HDL-cholesterol= 41.5 mg/dL, LDL-cholesterol= 205.6 mg/dl, triglycerides= 198 mg/dl). Total serum protein= 76.73 g/l, albumin= 41 g/L, Alpha 1= 1.8 g/L, Alpha 2= 7,9 g/L, Beta 1= 7,7 g/L, Beta 2= 2,1 g/L, Gamma= 16,2 g/L.



Fig.1. The physical examination of the patient

Otolaryngological and cardiological examination were performed which revealed values under normal parameters. The EKG described sinus rhythm 77/min, AQRS= 60° , PQ= 0.12 sec, much flattened T waves in all derivations, QT= 0.38 sec (elongate).

Imagistic investigations were also performed, the thyroid ultrasound showed right thyroid lobe (RTL)= 8.4/ 6.8 /15.1 mm, left thyroid lobe (LTL)= 7.4/6.2/12.2 mm (total volume=0.60 ml) intense hypoechogenic structure with hypervascularization in Doppler mode, abdominal ultrasound revealed liver steatosis, gastric stasis and massive colon gas.

Considering the child condition we needed a genetic examination that described generalized obesity, short stature, cranio-facial dysmorphia and set the diagnosis of DS, a psychological examination that observed moderate delay in psychomotor and language, trends anxiety. After the examination, it was recommended to be global stimulated throw physical and intellectual activities.

Other test was required to screening of thyroid function, diabetes mellitus and celiac disease and reveled an autoimmune thyroiditis with severe hypothyroidism with thyroid peroxidase antibodies (TPOA) = 679,19,5 UI/mL (NV = less than 50 UI/mL) , thyroid stimulating hormone (TSH) = 508,5 (NV= $0,27-4,20 \mu$ U/mL), free thyroxine (fT4) = 0,20 (NV= 0,93-1,70 ng/dL), IgG/IgA transglutaminase tissue antibodies = 8.04 (NV< 10 U/mL), glycated hemoglobin(5,9 %) and blood glucose (74 mg/dL) was normal value.

The diagnosis was established severe hypothyroidism due to autoimmune thyroiditis, 2nd grade of obesity, Down syndrome and acute adenoiditis.

The **treatment** that we recommend included hypocaloric and hypoglucidic diet (1000 kcal distributed in 3 meals and 3 snacks); treatment of severe hypothyroidism with thyroid hormone- levothyroxine initial dose of 50 µg/day and raised until 100 µg/day. Also it was indicated to follow the growth curve parameters and in particular the intellectual development.

The clinical outcome after one month was favorable with normal bowel movements, improving general health and skin of normal appearance, weight=26 kg, height=109 cm, Wc= 78cm, biological investigation revealed the improvement of liver function (ALAT= 40 U/L, ASAT= 40 U/L, GGT= 20U/L), thyroid function (fT4= 2,13 ng/dL slightly increased and TSH= 0,009 μ Ul/ml). The dose of levothyroxine was decreased to 50 μ g/day.

The **particularity** of our case was the difficulty to recognize the clinical signs of hypothyroidism in a child with Down syndrome and the lack of thyroid tests since birth until now.

Discussions

Along the time it was observed that Down syndrome associates multiple autoimmune phenomena, as we mention hypothyroidism, severe pulmonary infections, celiac disease, diabetes mellitus and leukemia [1]. The effects of hypothyroidism in childhood can have unpleasant consequences on individuals with Down syndrome.

The screening for thyroid disease is suggested for children with Down syndrome by The American Academy of Pediatrics (AAP) which recommends "annual screening for thyroid disease for individuals one year and older and measure TSH annually or sooner if the child has symptoms that could be related to thyroid dysfunction" [3] and a study of P.A Gipson et al realized in 2005 recommend that "early positive results for auto-antibodies or isolated raised TSH (IR-TSH) can be used as a basis to select a subgroup for further testing at say, five yearly intervals unless new symptoms emerge in the interim". They also suggest early screening recommended by the AAC "is probably not justified in the first 20 years of life."

Moreover in Table 1 we described the recommendations of latest guidelines [3, 7] for further investigations at children and adolescents diagnosed with DS.

Table 1. The recommendations for further investigations at children and adolescents diagnosed with DS

Recommendations for patients with DS between 5 TO 13 years	Recommendations for patients with DS between 13 TO 21 years
 Ophthalmology: every 2 years Neurosurgery/orthopedic surgery → signs / symptoms of compression myelopathy ENT/pulmonologist consult if signs or symptoms are suggestive of OSA or an abnormal sleep study Endocrinology → thyroid function test are abnormal (hypothyroidism increases with age) Gastroenterology → screening results for celiac disease are abnormal Cardiology → history of cardiac defects Psychiatry/psychology/community treatment programs → examination/history is suggestive of autism, ADHD, or other psychiatric/behavioral problems Orthopedic surgery→ abnormal gait/mobility is suggestive of hip dislocation or patellofemoral instability 	 Ophthalmology: every 3 years Neurosurgery/orthopedic surgery → signs/ symptoms of compression myelopathy are present ENT/pulmonologist consult → signs/ symptoms suggestive of OSA or abnormal sleep study findings are present Endocrinology → thyroid function test results are abnormal (hypothyroidism increases with age) Gastroenterology → screening results for celiac disease are abnormal Cardiology → history of cardiac defects Orthopedic surgery → gait/mobility is abnormal, suggestive of hip dislocation or patellofemoral instability

Afterwards, the supervision of health status at individuals with DS involves numerous specialist physicians (pediatrician, cardiologist, neurologist psychologist, etc.) and should happen constantly. We have summarized the periodic physical examination and diagnosis studies for DS condition [3, 7] in Table 2.

Visits for Years 5 to 13	Visits for Years 13 to 21
History/ Clinical examination	History/ Clinical examination
 Monitor growth and developmental status. Review symptoms/signs suggestive of celiac disease Once a year, review symptoms and evaluate for signs of compression myelopathy related to AAI Review other signs of neurological dysfunction (including seizures). Sleep study/polysomnogram for all children with signs/symptoms of OSA No routine radiologic evaluation of the cervical spine, should be performed for symptomatic patients; 	 Monitor growth and developmental status. Review symptoms/signs suggestive of celiac disease, Review symptoms and evaluate for signs of compression myelopathy related to AAI, Review other signs of neurologic dysfunction (including seizures). Discuss with parents and assess for symptoms of OSA Discuss with parents and assess for any types of skin problems, such as dry skin (suggestive of hypothyroidism), atopic dermatitis, and seborrheic dermatitis. Examine annually for acquired mitral and aortic valvular disease Monitor for onset of cataracts, refractive errors, and keratoconus. Monitor gait and mobility (ligamentous laxity, joint hypermobility, and hypotonia).
Diagnostic Studies	Diagnostic Studies
 Annual audiologic evaluation TSH annually or if signs are suggestive of thyroid dysfunction (e.g., constipation, dry skin, and poor growth) Hemoglobin annually CRP and ferritin or CHr if the patient is at risk for iron deficiency or if hemoglobin is < 11 g/dl IgA transglutaminase Tissue antibodies and quantitative IgA if symptoms/signs are suggestive of celiac disease Sleep study/polysomnogram for all children with signs/symptoms of OSA Radiologic evaluation of the cervical spine should be performed for symptomatic patients; 	 Annual audiologic evaluation TSH annually or if signs are suggestive of thyroid dysfunction (e.g., constipation, dry skin, and poor growth) Hemoglobin annually IgA transglutaminase Tissue antibodies and quantitative IgA if symptoms/signs are suggestive of celiac disease Sleep study/polysomnogram for all children with signs/symptoms of OSA Radiologic evaluation of the cervical spine should be performed for symptomatic patients; Echocardiogram for patients with new cardiovascular symptoms (suggestive of mitral or aortic valvular disease)

Table 2. Physical examination and diagnosis studies for DS condition

Conclusions

The association of increased risk of obesity in DS [6] and hypothyroidism, whose primary manifestation are weight gain and chronic constipation, predisposing to develop early cardiovascular diseases, leading to increased morbidity and mortality.

The interpretation of the results of thyroid function tests required an endocrinologist who is aware that high levels of TSH are sometimes transitory in Down syndrome [5]. Therefore the thyroid function screening is very important in patients with Down syndrome. The endocrinological examination in patients with Down syndrome is important not only to evaluate the thyroid status (TSH,

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