Thyroid

PP116 - A Novel Mutation in the Thyroid Hormone Receptor Beta-Gene in a Patient Who Developed Thyroid Nodules

Hidalgo Coronado L [1], *Chamoux A* [2], *Brunetto O* [1], *Bre M* [1], *Laham M* [1], *Adrover E* [3], *Molina M* [3], *Rivolta CM* [3]

[1]Hospital de niños Pedro de Elizalde, HNPE; [2]Hospital de niños Pedro de Elizalde ; [3]Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Departamento de Microbiología, Inmunología, Biotecnología y Genética/ Cátedra de Genética. Buenos Aires, Argentina. CONICET-Universidad de Buenos Aires. Instituto de Inmunología, Genética

Background: Thyroid hormone Resistance (THR) is a genetic disorder characterized by decreased tissue sensitivity to thyroid hormones (THs). The key finding is the presence of high concentrations of THs in the presence of non-suppressed TSH. Clinical phenotype is highly variable since signs of hormone deficiency, sufficiency and excess could coexist. High TSH produces goiter, being the most common feature. It has been associated with increased risk of developing thyroid nodules, with malignancy risk. Management of nodules associated with THR is as other nodules, with fine-needle aspiration guided by ultrasound (US) as first approach and ATA recommendation of surgery in children when Bethesda category is III or higher.

Clinical case: A 11-year-old girl with diagnosis of triple X syndrome was referred because of goiter and abnormal thyroid function test with TSH 3.01 mIU/ml; fT4 2.5 ng/ml and T3 286 ng/dl. Antithyroid antibodies and TRAb were negative. She had no signs or symptoms of hyperthyroidism except for tachycardia. She received propranolol and methimazole for a short time which later was dropped because of suspicion of THR. In order to identify mutations causing THR, genomic DNA was isolated from blood cells. Exons 7-10 of THRβ gene, including the flanking intronic regions were direct sequenced. A novel missense mutation in exon 9: c.917A>C transvertion that results in a p.K306T substitution was revealed. The substitution is located in a position evolutionarily conserved and modifies the electrostatic surface of the THRβ. The mutation was not found in her parents. Two years later, a thyroid US revealed mixed nodules, mainly cystic in both lobes, the biggest of 20x10mm. FNA was performed and reported as Bethesda IV, so she underwent thyroidectomy. Histology was reported as nodular hyperplasia. Currently, she is euthyroid, on treatment with levothyroxine at high dosis.

Conclusion: Clinical expression of THR is variable and should be suspected in front of discordant biochemical patterns. Genetic analysis is important to confirm the diagnosis of THR. We identified a novel and de novo mutation in exon 9 of THRβ gene. Our patient showed as well as others reported cases, goiter but with multiple nodules. Goiter should be monitored by US in order to detect nodules that require evaluation, until further studies can demonstrate if there is any risk factor for developing nodules or malignancy in THR patients. As our knowledge, there are no such studies to date.

Keywords: *Thyroid hormone resistance; Thyroid nodule*

PP118 - Congenital Hypothyroidism Screening Program: Experience with a TSH Lower Cutoff in Buenos Aires City

Vieites A. [1], *Enacan R* [2], *Ropelato MG* [2], *Gotta G* [3], *Dratler G* [4], *Junco M* [5], *Maccalini G* [6], *Micenmacher V.* [6], *Aranda C* [7], *Chiesa A* [2]

[1]Hospital de Niños Ricardo Gutiérrez; [2]Hospital de Niños Ricardo Gutierrez; [3]Hospital de niños Ricardo Gutierrez; [4]Hospital de Pediatría Juan P Garrahan; [5]Hospital de Agudos José María Ramos Mejía; [6]Hospital de Agudos Carlos G. Durand; [7]Hospital de Agudos Carlos G Durand

Introduction: TSH cutoffs (CO) levels in congenital hypothyroidism (CH) neonatal screening programs (NSP) tend to lower worldwide. Nevertheless, reports on benefits and risks are not clear. The Buenos Aires City Government NSP for CH uses since 2001 a TSH CO of 10 mIU/L blood.

Methods: A prospective pilot NSP with TSH CO: 8 mIU/L blood (IFMA-DELFIA) was performed from 1/6/2013 to 1/6/2018. DBS were obtained from heel prick at maternity discharge. Newborns with TSH >10mIU/L blood were recalled, and usual confirmation procedures were triggered while babies with TSH levels 8-9.9 mIU/L blood assisted to a unique center to be clinically and biochemically evaluated. With serum TSH above the normal age-related limit, a TC99 thyroid scintigraphy was performed. Babies were followed up until confirmation or exclusion of CH.

Results: Out of 130.405 newborn screened 496 with TSH >10mIU/L were recalled, and 108 CH confirmed (Recall rate (RR): 0.38%).

208 extra babies were recalled with the new cutoff (Overall RR: 0.54%). 206 were localized and evaluated. In 176 (85%) TSH and thyroid hormones normalized within the first month of life. 30% of them reported iodide exposure and 4% were premature.12 (5.8%) were lately localized by social service having already normal thyroid function.

In18 (8.7%) TSH remained high: Nine (1 extreme preterm) confirmed CH (2 goiters with high thyroglobulin, 1 ectopic thyroid gland, 3 eutopic glands and 3 could not be characterized) and were treated (median age: 8 days). Nine (3 exposed to iodide, 1 preterm, 1 with maternal autoimmunity and 4 without relevant history) had persistent hyperthyrotropinemia. At a median age of 13 days their median serum TSH was 12.4 mIU/L with normal Free Thyroxine. All had an eutopic thyroid and when followed up without treatment, 5 normalized TSH levels within the first 3 months, 2 did it after 2 years of follow up and 2 are still in control, all with normal outcomes.

Conclusion: In view of the higher detection and still acceptable RR, our screening program decided to keep the lower cutoff. However, the follow up of the detected children will clarify the benefits on their early detection.

Keywords: *Congenital Hypothyroidism; Neonatal screening program*

Author Index

HORMONE
RESEARCH IN
PÆDIATRICS

KARGER

E-Mail karger@karger.com
www.karger.com/hrp