
Thyroid

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

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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 THR β gene, including the flanking intronic regions were direct sequenced. A novel missense mutation in exon 9: c.917A>C transversion 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 THR β . 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 THR β 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

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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-DELFI) 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.

In 18 (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*

- Abiuso AMB 8
Acevedo G 37
Adrover E 49, 52
Aguilar L 19
Albuquerque EVA 30
Alconcher L 25
Alexandre AR 41, 43
Almeida MAAL 32
Almeida MQ 2
Almstrup K 5
Alonso G 36, 42
Altamirano N 19
Altamirano-Bustamante N 7
Altube M 15, 47
Amaral AB 14
Ambao V 47
Andrade NLM 14, 17
Antonini SR 1, 6, 11, 30
Antonini SRR 9
Antunes JMV 9
Antunes OAV 9
Aragon DC 9, 30
Aranda C 13, 49
Arcari AJ 44
Arguinzoniz L 19
Arguinzoniz-Valenzuela L 7
Armando R 13
Arnhold IJP 14, 22
Arozarena M 31
Artioli TO 13
Astudillo E 37
Aversa LA 31
Avila A 21
Avila S 27
Ayarzabal V 23
Azaretzky M 15
Aziz M 23
- Bailez M 28, 29
Balbi V 6, 34, 52
Ballerini MG 15, 16, 47
Bargman G 31
Barontini M 10
Barra A 21
Barra CB 35
Barrera G 3
Barreto TG 19
Barroso PS 5
Bastida MG 27
Batista RL 39
- Battelino T 20
Bazurto MM 31
Bedecarrás P 31, 44
Belgorosky A 6, 8, 28, 29, 33, 34, 48
Beltrão LA 33
Benedetti AF 2
Benedetti AFF 22
Benitez FJ 50
Berbara HMBL 47
Berenstein AJ 31
Berensztein E 8, 28, 29, 48
Bergadá I 10, 12, 13, 15, 25, 27, 31, 47, 51
Bergadá IB 44
Berger M 7
Bertola DR 30
Beserra ICR 47
Bettiol H 30
Biscotto IP 22
Blanco E 3, 4, 18, 26
Bodoni AF 1
Bonilla-Medina P 7
Boquete C 15
Boquete HR 15
Borrajo G 34
Boyantovsky L 46
Boywitt A 13
Braga BL 39
Braid ZM 11
Braslavsky D 15, 16
Bravo MPG 19
Bre M 49
Brenzoni L 25
Breyer F 40
Breyer FA 12
Breziniscki MP 8
Brufatto J P T 6
Brunetto O 49
Brunetto O H 28
Bueno AC 6, 11
Bunout D 3
Burrows R 3, 4, 18, 26
Busch AS 5
- Cabrera JO 37
Cabrera RJO 6
Caciatori J 50
Calzada R 19
Calzada-León R 7
Camassola B 50
Camper SA 16
- Campi V 46
Cardoso VC 30
Carlos GA 41, 43
Carneiro MS 42
Carreiro S 10, 31
Carvalho FM 48
Carvalho GQ 14
Carvalho JAR 8
Carvalho LC 36
Carvalho LRS 22
Casali B 13
Cassorla F 21, 39
Castro A 21
Castro ABS 42
Castro L 46
Castro LC 32, 41, 43
Castro M 1, 11
Castro SM 31, 33
Cavallini LF 45
Cechinel E 34, 38
Cerdeira T 18
Cespedes C 20
Cespedes WCJ 48
Cestino ML 12
Chagas NB 11
Chambo JL 2
Chamoux A 49
Chavarria NE 15
Chianca LS 41, 43
Chiesa A 49, 51
Ciaccio M 23, 28, 29, 33, 52
Cidber E 18
Clément F 12
Codner E 21
Coeli-Lacchini F 1, 11
Coll J 18
Coll M 20
Cominato L 25, 26, 27, 48
Coniglio S 52
Contreras CV 50
Contreras-García GA 29
Cordero MD 6
Correa FA 22
Correa-Burrows P 3, 4, 26, 18
Corredor V 37
Cortez RV 26
Corvalan C 5
Costa EMF 39
Costa-Júnior DA 14
Costanzo M 28, 29

Cruz NRC 14
 Cuglia N 40
 Cunha DFS 48
 Cunha SB 9, 42
 Curado MP 2

 D'Alessandro P 28
 D'Amato S 25
 da Cruz AD 2
 Damiani D 25, 26, 27, 42, 48
 Danne T 20
 Dauber A 16
 de Almeida LEA 30
 De Bellis R 13
 De Carli C 27
 De Dona V 24
 De Miguel V 10
 De Tezanos-Pinto A 21, 35, 51
 Deboni M 27
 del Rey G 13
 Delgado IA 19
 Della Manna T 26
 Demartini AC 8
 Demissie M 20
 Di Palma MI 23
 Díaz-García L 7
 Diaz S 27
 Dies-Suárez P 17
 Domené H 16
 Domenice S 39
 Domínguez AE 6
 Domínguez E 37
 dos Santos TJ 18
 Dratler G 49, 52
 Dujovne N 23, 24, 33
 Duran P 20
 Durval D 27
 Dzembrowski L 15

 Enacan R 49
 Erbes JM 34, 28
 Escobar ME 44
 Espinosa-Espindola M 17
 Espinosa RT 6
 Espinosa TM 37
 Espósito M 52

 Fagundes GFC 2
 Fasano MV 34
 Fernandes RGAL 36
 Fernandez MC 12, 13
 Fernández Mentaberry MV 40
 Ferreira FO 14
 Ferreira NP 22
 Ferreira TL 35
 Fideleff G 15
 Fideleff HL 15

 Figueroa GV 28, 44
 Filgueiras MFTF 9, 42
 Filho HCM 26
 Filho MHC 25, 27, 48
 Finkielstain G 6
 Fittipaldi Y 36
 Flanagan S 19
 Florio S 33
 Forclaz V 25
 Forero C 20
 Forlin RB 8
 Fortes JS 2
 Fragoso MB 2
 França SN 8
 Franco D 20
 Franco RR 25, 26, 27, 48,
 Frascino A 26, 27
 Freire AV 15, 44
 Freire BL 14, 39
 Freitas PHR 46
 Frez DCL 10
 Frossard TNSV 14
 Fujimoto M 16
 Funari MFA 14, 17, 22, 39

 Gaete X 18, 21
 Gahagan S 3, 4, 18, 26
 Gallardo JM 50
 Gallardo R 28
 Galluzo L 29
 Galluzzo ML 28
 Garcia RMR 10, 31
 Garcia TS 34, 38
 Garrido PN 6, 28, 29
 Gómez GS 33
 Gariza AC 38
 Gazez N 23, 33
 Gebenlian JL 1
 Geremia C 50
 Gil S 23, 24
 Giraudo F 21
 Godoy PC 40
 Gomes DC 36, 37
 Gomes LN 39
 Gonçalves I 50
 Gonzalez RJ 23
 Gonzalez V 34, 52
 Gotta G 15, 49
 Gottlieb S 31
 Goyeau H 20
 Graciela EO 31
 Grinspon R 27
 Grinspon RP 31, 44
 Gryngarten MG 44
 Guercio G 28, 29
 Guimaraes AG 2
 Guntsche Z 40

 Gurjão M 3
 Gutierrez A 15
 Gutiérrez G 23
 Gutiérrez M 12, 31

 Hamilton 25
 Hernandez MI 35, 51
 Hernández TKE 19
 Herrera I 39
 Herzovich V 23, 33
 Hidalgo CL 49
 Homma TK 14, 30
 Hwa V 16

 Imel EA 4
 Iñiguez G 21

 Jeronimo T 27
 Jorge AAL 5, 14, 17, 22, 30, 39
 Junco M 49
 Junior JADF 39
 Juul A 5

 Kannemann A 31
 Kawamura T 20
 Keselman A 13, 15, 16
 Kitzman J 16
 Kochi C 3, 13
 Kopacek C 10, 31, 33
 Kraemer GC 8
 Kraus J 16
 Krebs I 33
 Kuba VM 42
 Kuspel MF 36, 42

 La Serna JE 38
 Lacerda FL 8
 Laham M 49
 Lam Chávez AE 19
 Lardone MC 21
 Latronico AC 2, 5
 Lazzati JM 23, 28, 29, 33
 Lee JS 34, 38
 Leone C 42
 Leopoldino AM 1
 Lerario AM 5, 22, 39
 Lima MLLC 9
 Lima PLM 8
 Lima RLS 14
 Lima-Amato LG 5
 Lobo de la Vega V 28
 Lombardi GM 12
 Longui C 3
 Longui CA 13
 Lopes FSC 32, 41, 43
 López AC 40
 Lopez Dacal J 28

López-González D 17
 López LA 50
 López M 18
 López P 21
 Lopez Perez D 50
 Lubieniecki F 23
 Luciano TM 30
 Lyra A 3

 Maccalini G 49
 Maccarini J 50
 Madeira M 14
 Mafra JR 35
 Malaquias AC 14, 30
 Malievsky O 20
 Manna TD 25, 27, 48
 Mantovani RM 35
 Maqueda-Tenorio S 7
 Marino R 6, 28, 29, 34
 Marino S 52
 Marquez P 40
 Marti M 16
 Martin A 12
 Martin R 52
 Martin S 46
 Martins CS 6
 Masnata ME 51
 Mastella L 31
 Matsuura CO 43
 Mattone C 29
 Mattone MC 24, 28
 Mazzucchetti L 41
 Medina FA 19
 Meira AS 3
 Meixueiro CC 50
 Mejia L 37
 Melardi JW 48
 Menconca BB 17
 Mendes LL 42
 Mendonca BB 2, 5, 14, 22, 39
 Mericq V 5, 21
 Merino P 21
 Mermejo LM 6, 11
 Micenmacher V 49
 Millan PMI 16
 Minaberry L 44
 Minasi LB 2
 Minuzzi GM 44
 Miranda-Lora AL 17
 Miras M 46
 Moenne K 51
 Molina M 49, 52
 Mondillo C 8
 Monteiro GMC 45
 Monteiro RV 2
 Montenegro LR 5
 Morais TK 13

 Morales CA 1, 6, 11, 24
 Moreira LN 26
 Moreno BM 8
 Moresco A 6
 Morín A 34, 52
 Muñoz L 46
 Munoz T 32, 51

 Nakaguma M 22
 Nascimento Jr OL 45, 46
 Nascimento ML 34, 38
 Neto LH 14
 Niemoeller E 20
 Nigro N 28
 Nishi MY 14, 39
 Nishimura E 19
 Noronha RM 30
 Notaristéfano G 6
 Nunes ACB 3

 Obregón G 6
 Obregon MG 23
 Ochetti M 46
 Oleastro M 23, 24
 Oliveira ALV 46
 Oliveira KC 9
 Oliveira LCV 45
 Oliveira LE 35
 Oliveira MA 45
 Oliveira RS 32, 41, 43
 Oneto A 40
 Orellana-Cárdenas P 7
 Ortega X 51
 Ostrow V 7

 Pacheco NS 41
 Pacheco NSS 43
 Palacio J 18
 Palma A 24
 Papendieck P 51
 Pasqualini T 36, 42
 Pavia MA 20
 Pedrassoli GH 8
 Peixoto VG 3
 Pelliza C 46
 Pennisi PA 12
 Pereira A 5
 Pereira MA 2
 Pereira RM 8
 Pesantez KA 6
 Petenuci J 2
 Pezzuti IL 35
 Pichott M 21
 Pieper D 39
 Pietropoli A 7
 Pignataro OP 8
 Pinto RM 2, 45, 46

 Pires JVG 37
 Plomer P 23
 Plomer PG 24
 Polak M 7
 Porta G 27
 Potter M 27
 Prada P 31
 Pratesi R 32
 Pujana M 6
 Pumputis FRC 18
 Puñales M 50

 Quiroga S 52

 Rachid L 26, 27
 Radominski RB 8
 Ramirez P 6, 23, 28, 29
 Recabarren A 40
 Reinoso A 52
 Remor KVT 41
 Requejo F 23
 Resende RC 46
 Rey MR 27
 Rey R 13, 16
 Rey RA 31, 44, 47
 Ricci J 52
 Riu C 40
 Rivarola MA 6, 48
 Rivolta C 52
 Rivolta CM 49
 Rizzotto MIB 10, 31
 Roa SLR 6
 Robles-Valdés C 7
 Rocha AJ 3
 Rodrigues R 37
 Rodrigues TB 43
 Rodrigues TMB 14
 Rodriguez F 39
 Rodriguez ME 15, 47
 Rogan J 3, 18, 26
 Rohrer T 7
 Rojas MVC 29
 Roman R 18, 21, 32
 Ropelato G 13
 Ropelato MG 15, 16, 31, 44, 47, 49
 Rosenfeld P 25
 Ross J 7
 Rossi ICB 36
 Rugilo C 23
 Ruibal G 15
 Ruiz M 19
 Ruiz-Reyes M 7

 Salazar KAA 42
 Salazar-González JJ 18
 Salinas A 21
 San Martin J 4

Sánchez Curriel-Loyo M 17
Sangri RE 50
Sanguineti N 16
Sanguineti Nora 13
Sanso G 10
Santos CH 11
Santos APP 14
Santos HV 46
Santos IN 25
Santucci Z 34
Sanz C 28
Sanzone M 31
Scaglia P 16
Scaglia PA 15
Segundo GR 37
Selistre L 31
Semer B 48
Sequera AM 15
Signorino M 46
Silva CM 14
Silva EFF 9
Silva IN 9, 35
Silva IT 14
Silva JM 22, 41, 43
Silva JVP 45
Silva LCB 35
Silva PCA 34, 38
Silva RDCH 45
Silva TS 3
Silva-Camarena M 7
Silvano L 46
Silveira LFG 5
Simoni G 34, 38
Skrinar A 4
Soares NF 35
Sobral LM 1
Sobrero G 46
Soto B J 5
Soto MF 23, 24
Souza CSB 45, 46
Srougi V 2
Stecchini MF 30
Steinmetz L 25, 26, 27, 48
Stivel M 40
Suárez M 15
Suco S 16
Taddei CR 26
Tamborlane WT 20
Tanno FY 2
Targovnik H 52
Tarifa C 46
Toma RK 26, 27
Tommasi F 52
Tournier A 34, 52
Touzon MS 6, 28, 29
Troiano M 36, 42
Tyzinski L 16
Urdinez L 24
Vaiani E 6, 23, 24
Valdés GW 6
Valdés W 37
Varela ML 8
Vargas PR 31, 33
Vasques GA 5, 14, 17, 30
Velázquez LL 19
Velhote MC 27
Velhote MCP 26
Velloso-Rodrigues C 14
Venara M 27
Venara MC 12
Vescovi ES 41
Vescovi JS 41
Viale ML 44
Vieites A 10, 49
Vilche JA 52
Villegas F 13
Vishnopolska S 16
Vitale L 52
Vitale LE 34
Viterbo G 23, 24
Viterbo GL 24
Ward LM 4
Wardecki M 20
Werneck G 18
Wiest P 33
Yamauchi F 2
Ybarra M 27
Zaidman V 28, 29, 33
Zerbini MN 2