CLINICAL CASE REPORT

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L.N.L., female, 6 years old, birth date: 18/04/2008

- Admitted in Hospital Infantil do Sabará in May 8th, 2014

- She was hospitalized because of a gingivostomatitis with secondary infection, for clinical support, parenteral hydratation and sistemic antibiotics
- During hospitalization, the immunology group was called to assess the patient due to a suspected immunodeficiency, with an altered previous screening test

- Medical history:

Recurrent otitis media
Recurrent tonsillitis
"Bacteremia" 10 months before the current hospitalization – She was hospitalized in an other Hospital and received Ceftriaxone, but blood culture was negative
Immunization: received the vaccination of the regular calendar

- Familial history:

Only child
No history of consanguinity or abortions
The father was descendant of Indians of the Amazon Forest
Mother Hashimoto´s tyroiditis

Exams:

02/10/2014 IgG 102 IgM 780 IgA <6

05/14/2014
CBC: HGB:12,1 WBC:12190 N:78,3 Eo:0,1 Ly10,1 – 1219 M:11,2 Pla.:406.000
IgG < 138
IgM 840
IgA <6
CD3:39-300 <p10
CD4:28,6- 222 <p10
CD8:6,5- 50 < p10
CD19:26,5- 619 p10-50
CD20:11,5- 89
CD56:11,8- 276 p50

Diagnosis:
Hypogammaglobulinemia with Hiper IgM

Treatment proposed:
IgG IV
Profilatic Sulfametoxazol + Trimetroprim

DATE	CBC	IgG	IgM	IgA	Liver enzymes	Imunofeno	Abdominal US	Torax CT	Dosis of IgG IV
05/14/2014	HGB:12,1 WBC:12190 N:78,3 Eo:0,1 Ly10,1 M:11,2 Pla.:406.000	< 138	840 (>p97)	<6		CD3:39-300 CD4:28,6- 222 CD8:6,5- 50 CD19:26,5- 619 CD20:11,5- 89 CD56:11,8- 276			600mg/kg
05/16/2014	HGB:11,7 WBC5510 B:2 N: 29 Eo:5 Ly:50 M:13 Pla.:495.000	1470 (post IgG IV)							600mg/kg
06/10/2014	HGB:10,4 WBC: 5840 N:43,5 Eo:2,7 Ly:43,7 M:9,2 Pla.:393.000	558 (previus IgG IV)				CD3:54-1386 (p10—50) CD4:32,8- 837 (p10-50) CD8:11,8- 300 (<p10) CD19:22- 561 (p10-50) CD20:19,8- 506 CD56:19- 484 (p50-90)			550mg/kg
07/01/2014		894	407	<6	TGO 33 TGP 24 GGT 19 FA 172				550mg/kg

DATE	CBC	IgG	IgM	IgA		Imunofeno	Abdominal US	Torax CT	Dosis of IgG IV
09/02/2014	HGB: 12,5 WBC :6760 N :37,6 Eo:4,9 Baso:0,6 Ly:44,2 M:12,7 Pla.:437.000	869							550mg/kg
10/14/2014		720							550mg/kg
11/25/2014		588							500mg/kg
12/30/2014		651							500mg/kg
02/03/2015		736							500mg/kg
03/17/2015		641							500mg/kg
04/22/2015		756			TGO 91 TGP 116 GGT 55 FA 202		NL	NL	500mg/kg
05/26/2015		766			TGO 46 TGP49 GGT 48 FA 227				500mg/kg

DATE	CBC	IgG		Abdominal US	Torax CT	Dosis of IgG IV
07/02/2015	HGB: 10,8 WBC: 4380 Bs: 3 N: 43 Ly: 50 4atip M: 9 Pla:320.000	718	TGO 76 TGP 95 GGT 68 FA 219 Alb.4			500mg/kg
						500mg/kg
08/04/2015		800				500mg/kg
09/08/2015		791				450mg/kg
10/13/2015		760		NL		450mg/kg
11/24/2015	HGB: 11,8 WBC: 7450 N:51,9 Ly: 33,3 M:14,4 Pla: 351000	666	TGO 99 TGP 123 GGT 90 FA 211 Bt 0,17 Bd 0,04 Alb. 4,4 U 21 Cr 0,35 Na 138 K 4,7			450mg/kg

DATE	CBC	IgG		Abdominal US	Torax CT	Dosis of IgG IV
12/29/2015		685	TGO 94 TGP 119 GGT 80 FA 216 Bt 0,17 Bd 0,04 Alb. 4,1 eletrof. Protein total 7,1 Albumin 4,3 ceruloplasmin33 anti DNA - FAN - ANTI MUSC. LISO - TP 100% INR 1 TTPA 22,9 R 0,65 Stool normal Cryptosporidium -	NL		400mg/kg
02/02/2016		743				400mg/kg
03/08/2016		754			NL	400mg/kg
04/19/2016	HGB: 1,28 WBC: 9730 N:57,9 Eo:0,8 Baso:0,3 Ly: 28,5 M:142,5 Pla: 391000	706	TGO 29 TGP 21 GGT 26 FA 215 Stool pendent			

Discussion:

Hyperimmunoglobulin M Syndromes (HIGM)

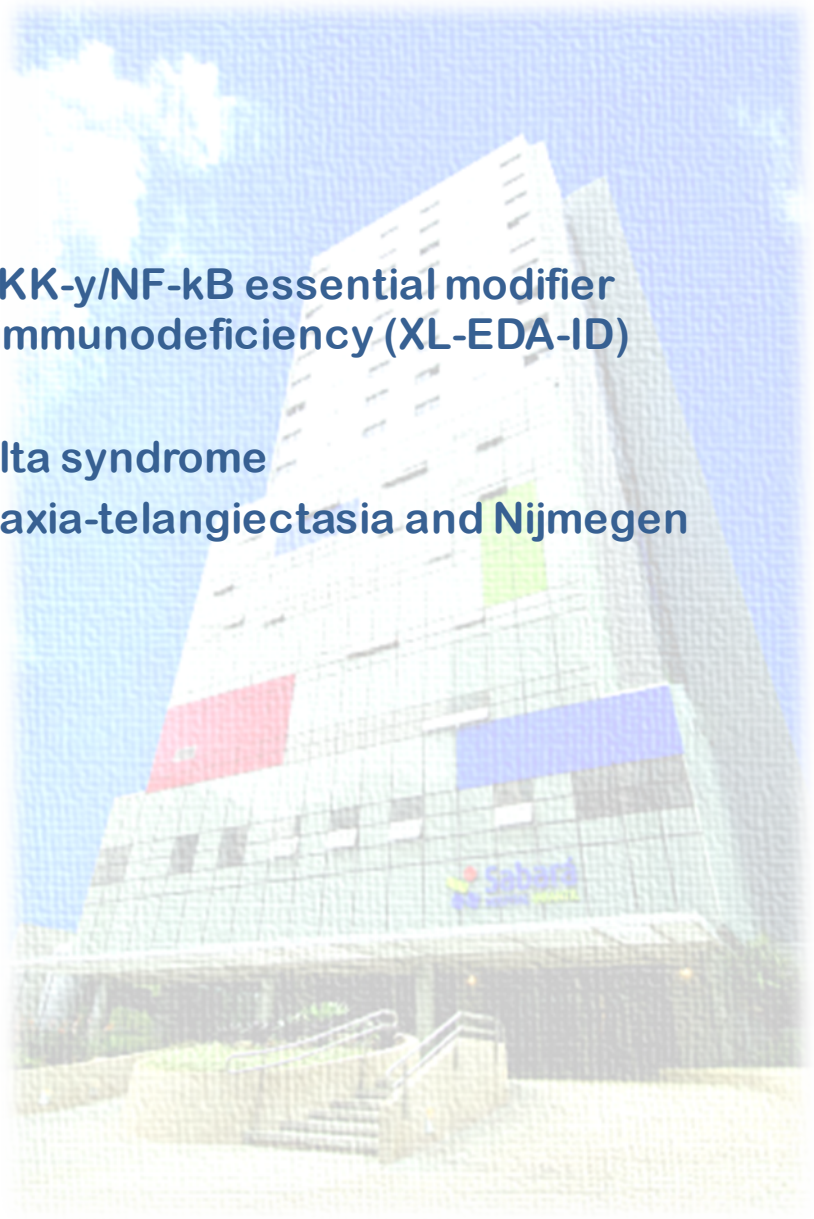
- Heterogeneous group of conditions characterized by defective class-switch recombination (CSR), resulting in normal or increased levels of IgM and deficiency of IgG, IgA and IgE and poor antibody function

- Several genetically determined diseases – CD40 ligand deficiency; CD40 deficiency; activation-induced cytidine deaminase (AID) deficiency; uracil N-glycosylase (UNG) deficiency

  - ✓ HIGM 1- CD40L deficiency – X-linked, mutation in *CD40LG* gene(*NFSF5)*
  - ✓ HIGM 2- AID deficiency – autossomal recessive / autossomal dominant nonsens mutation in the *ACIDA* gene
  - ✓ HIGM 3- CD40 deficiency – autossomal recessive
  - ✓ HIGM 4- no molecular defect identified, defective CSR downstream from S region DNA cleavage
  - ✓ HIGM 5- UNG deficiency – autossomal recessive

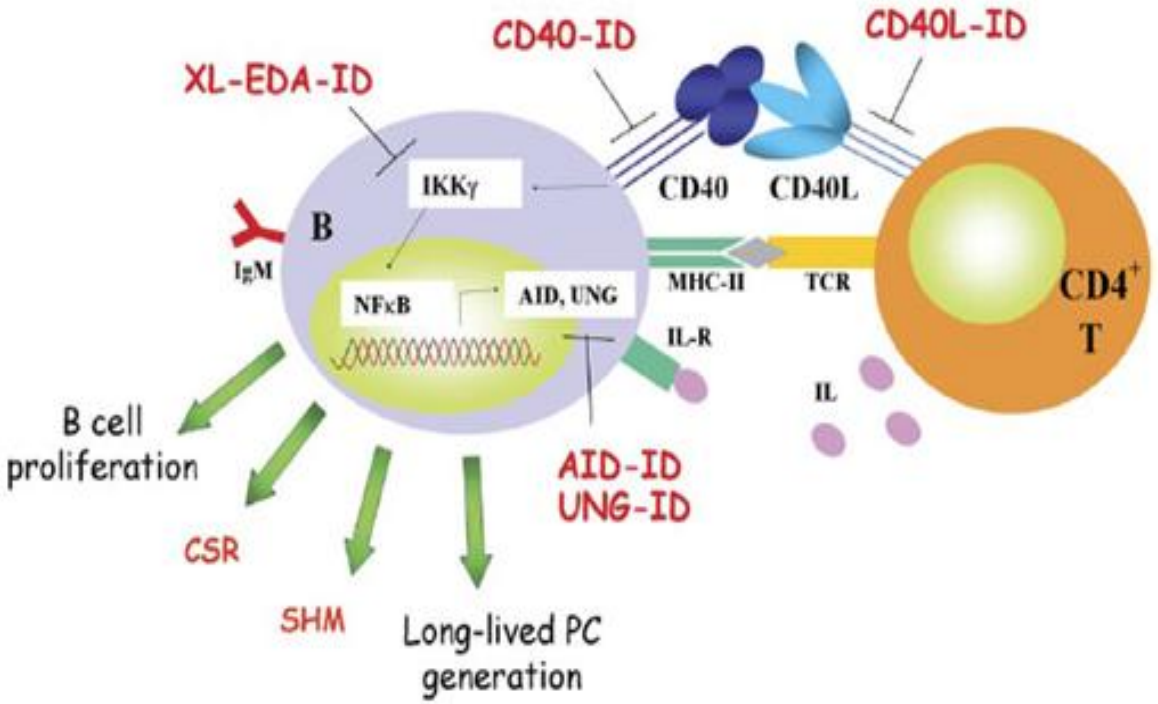
- Secundary to congenital rubeolla syndrome, use of phenytoin, T cell leuckemia or lymphomas

- Defective CSR also occurs in:
- ✓ Mutations of the IKBKG gene (encoding for IKK-y/NF-kB essential modifier [NEMO] – X-linked ctodermal dysplasia with immunodeficiency (XL-EDA-ID)
- ✓ Deficiency of PMS2
- ✓ APDS/PASLI and APDS2 - Activated PI3K-delta syndrome
- ✓ Diseases with impairment of DNA repair - Ataxia-telangiectasia and Nijmegen breakage syndrome (NBS)



Maturation of antibody response:

- Class-switch recombinations
- Somatic hypermutation – high-affinity antibodies
- Generation of memory B cells




DANKSCHEEN
BÏYAN
SHUKRIA
YAQHANYELAY
TASHAKKUR ATU
GRACIAS
SUKSAMA
EKHMET
THANK
ARIGATO
GRAZIE
MEHRBANI
YOU
SHUKURIA
GOZAIMASHITA
EFCHARISTO
JUSPAXAR
BOLZÏN
MERCI


No story lives unless someone wants to listen.
J.K. Rowling