

# CIS 2016 School in Primary Immunodeficiency Diseases

**CIS** Clinical Immunology Society

**October 6-9, 2016**  
The Confidante  
Miami Beach, Florida

## Mystery Diagnosis Case

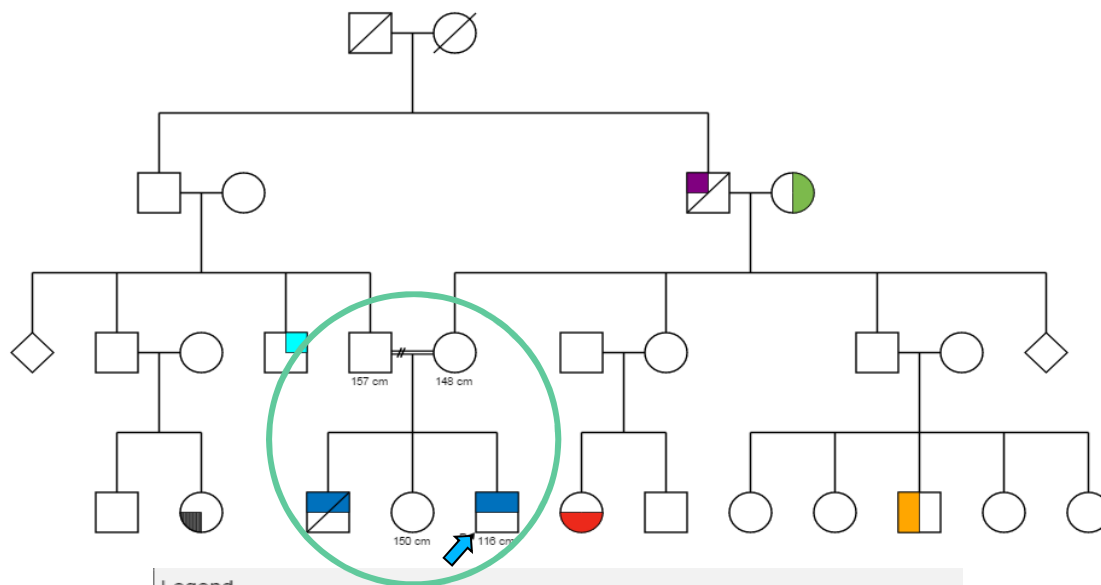
### *Hypogammaglobulinemia and autoimmune hemolytic anemia*

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# CASE REPORT

- Francisco GFB, a 16 year-old boy from northeast of Brazil was referred from Hematology to Immunology in order to assess splenectomy risks for treatment of refractory AIHA, and has a diagnosis of CVID; receiving IVIg since 11y of age.
- Parents are first cousins and had another male child who died at 14y due to lung infection, with previous history of chronic diarrhea, growth failure and anemia, splenectomized at 4y.



Legend	
	Polio
	Lung cancer
	Mental retardation
	Hematologic disorder
	Recurrent infections + AHAI + Hypogammaglobulinemia + Lymphocytopenia
	Bone overgrowth?
	Mental retardation + Deafness

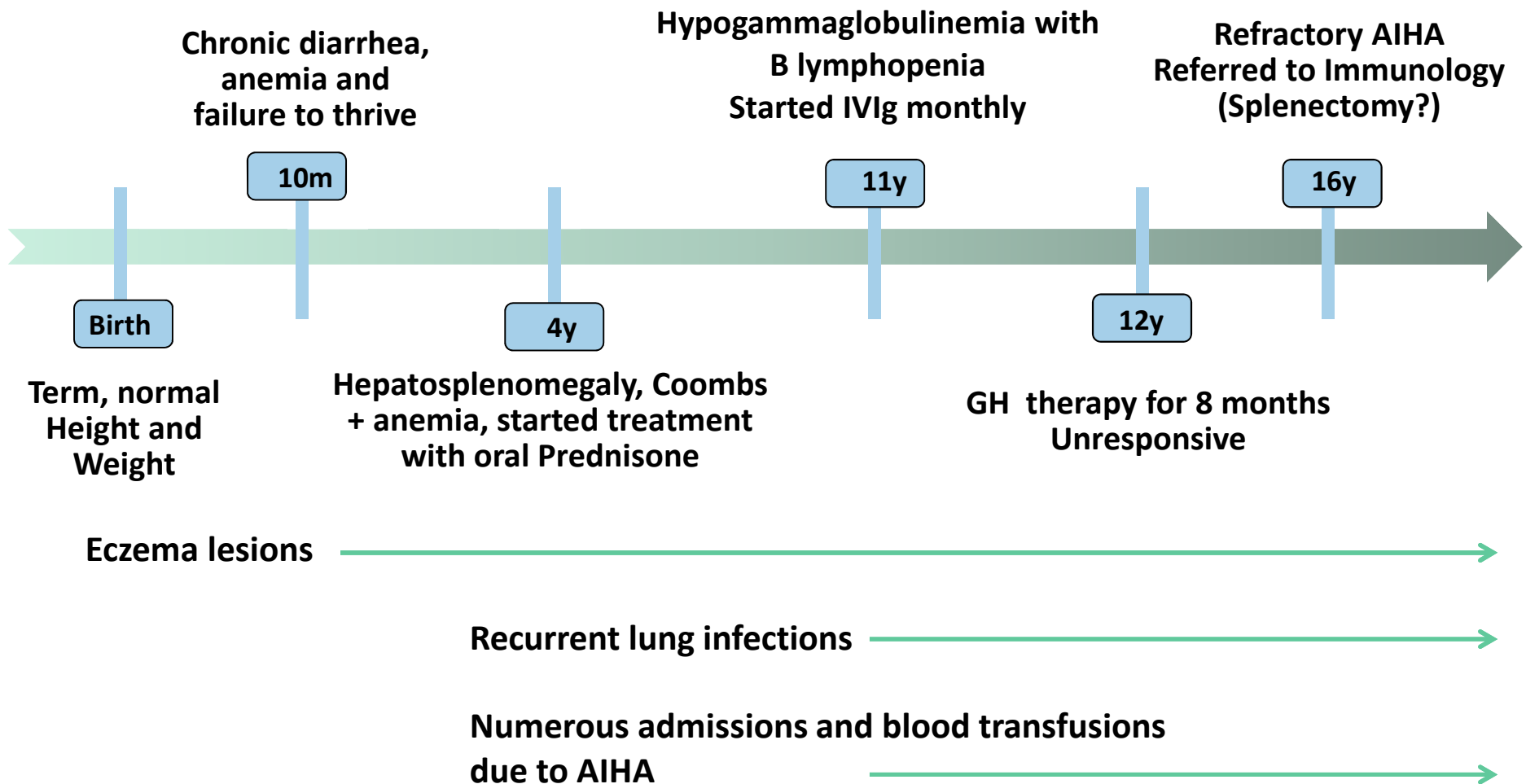
Mother, 37y  
148 cm



Patient, 14y  
117 cm (- 6.5 Z Score)



# CASE REPORT



# IMAGING and LABORATORY STUDIES

## HEMATOLOGIC ASSAYS

Blood Count Cells	<b>Hb 9.7, Ht 32.3%</b> Leuc 5080 (Neut. 3400, Eos. zero, <b>Lymphocytes 1570</b> , Mono. 100), Plat. 228000
Reticulocytes	<b>12%</b>
Coombs Test	<b>Positive</b>
Isohemagglutinins (O+)	IgM anti-A [16] and anti-B [2]
Myelogram	Erythroid hypercellularity

## HORMONAL ASSAYS

GH	0.34 ng/ml	≤ 0.97
IGF -1	279 ng/ml	159 - 373
IGFBP-3	3.9 mg/L	3.5 – 7.0
Prolactin	9.8 ng/ml	3.4 – 18.6
TSH	5.39 μIU/mL	0.27 - 4.20

## IMAGES

Abdominal Ultrasound	Hepatosplenomegaly - homogeneous echo texture <b>Spleen with 577 cm<sup>3</sup></b>
Skeletal X-ray	<b>Hand bone age of 9 years</b> Osteopenia Mild scoliosis Mild reduction of the vertebrae height in the dorsal segment
Chest CT	Bronchiectasis in lung bases

## IMMUNOLOGIC ANALYSES

IgG mg/dL	<b>451* (&lt; p3)</b>
IgM mg/dL	<b>10.6 (&lt; p3)</b>
IgA mg/dL	<b>undetectable</b>
IgE UI/ml	<b>undetectable</b>

\* under IVIg

## IMMUNOPHENOTYPING

CD45 <sup>+</sup> /CD3 <sup>+</sup>	1979 cells/mm <sup>3</sup>	1000–2200
CD45 <sup>+</sup> /CD3 <sup>+</sup> /CD4 <sup>+</sup>	799 cells/mm <sup>3</sup>	530–1300
CD45 <sup>+</sup> /CD3 <sup>+</sup> /CD8 <sup>+</sup>	993 cells/mm <sup>3</sup>	330-920
<b>CD4<sup>+</sup>/CD8<sup>+</sup></b>	<b>0.8</b>	
CD4 <sup>+</sup> CD25 <sup>high</sup> CD 127 <sup>low</sup> Foxp3 <sup>+</sup>	1.1%	day control: 0.92%
CD45 <sup>+</sup> /CD3 <sup>+</sup> /CD4 <sup>-</sup> CD8 <sup>-</sup>	8%	
<b>CD4<sup>+</sup>CD45RA<sup>+</sup></b>	<b>101 cells/mm<sup>3</sup></b>	<b>230-770</b>
CD4 <sup>+</sup> /CD45RO <sup>+</sup>	710 cells/mm <sup>3</sup>	240-700
CD45RA <sup>+</sup>	1226 cells/mm <sup>3</sup>	(53.1%)
CD45RO <sup>+</sup>	958 cells/mm <sup>3</sup>	(30.7%)
<b>CD45<sup>+</sup>/CD19<sup>+</sup></b>	<b>127 cells/mm<sup>3</sup></b>	<b>460-1143</b>
CD45 <sup>+</sup> /CD3 <sup>-</sup> /CD16 <sup>+</sup> /CD56 <sup>+</sup>	158 cells/mm <sup>3</sup>	70-480



# DIAGNOSTIC HYPOTHESIS

*Hypogammaglobulinemia + Refractory AIHA + Short Stature*

Whole-Exome Sequencing

Gene/ Transcript	Variant	Allele frequency	Zygoty	Inheritance	Classification
IL2RA/ NM_000417	Exon 4: c.398A>C, p.N133T	0.0%	Homozygous	Autosomal recessive	Variant of uncertain significance



- *Lymphoproliferation assays (with and without IL-2)*
- *STAT5 phosphorylation upon IL-2 stimulation*