Instituto de Pediatria | IPPMG/UFRJ
Instituto de Puericultura e Pediatria Martagão Gesteira

Case Report

Service of Allergy and Immunology

Fernanda Pinto Mariz

❖ KRSS, DB: 1/2/2007, male, natural from Rio de Janeiro.

❖ 2010 (3 yr. old) – referred to our Service to investigate PID.

PAST HISTORY

❖ Since 6 months – repetitive acute otitis and acute diarrhea.
Since 2009, he presented acute otitis every month.

❖Since 2 years old – pneumonia. Total: 4 - Hospitalization: 2 (no severity).

❖ Gestational history and childbirth: normal; normal development.

❖No vaccine reaction.

FAMILY HISTORY

❖ Oldest sister: hypogammaglobulinemia (1yr. 6m); died at the age of eleven.

❖ Father: died of external causes; repetitive pyodermitis during childhood;
Mother: healthy; no consanguinity.

PHYSICAL EXAMINATION FINDINGS

- BEG, eutrophic. Hepatoesplenomegaly.

LABORATORY TESTS

- Normal CBC.
- Liver biochemical tests - normal
- Immunoglobulins and lymphocytes profile

✓IgA: 4mg/dl; <P3
✓IgG: 140 mg/dl; <P3
✓IgM: 316 mg/dl; >P97
✓IgE: 1 kU/L

✓TCD4: 839/mm3 (24%); P10-50
✓TCD8: 2237/mm3 (64%); > P97
✓TCD4/TCD8: 0,37;
✓B cells (CD19): 70/mm3 (2%); < P10
✓NK (CD56): 210/mm3 (6%); P10-50

HYPER IgM SYNDROME

❖ 2010: mensal venous infusion of Human Ig and antibiotic prophylaxis was started.

OUTCOME – 2010-2011

❖ No infections;

❖ keeping hepatoesplenomegaly;

❖ Lymphoadenomegaly

❖ 2010 (3 yr old) – lymph node biopsy: no germinative center

❖ No switch memory B cells, increased CD8 efector T cells, decreased naive T cells

❖ 2010 (3 yr old) – "pneumonia – sepsis". No improve with antibiotics.

Pancitopenia. Increased levels of ferritin and triglyceride; decreased fibrinogen.

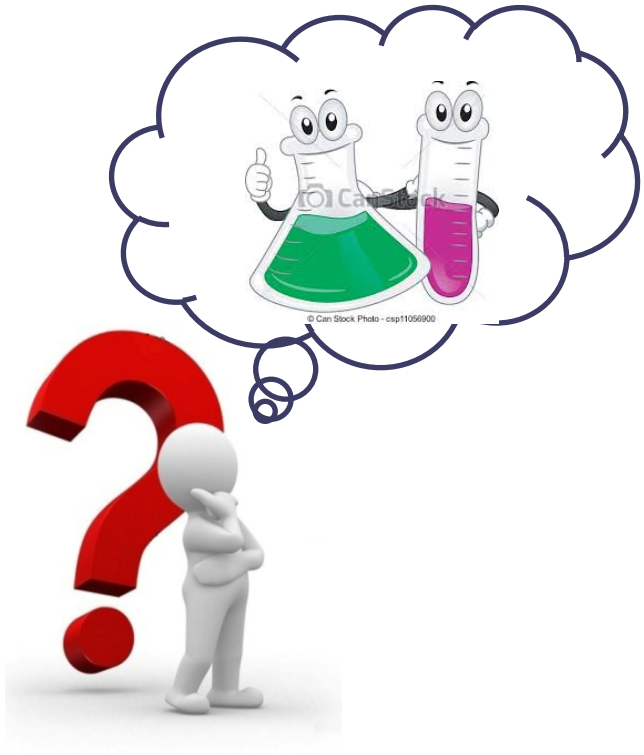
Positive EBV (PCR); Bone marrow biopsy ⟹ Hemophagocitic syndrome.

HLH 2004 protocol was started – good response.

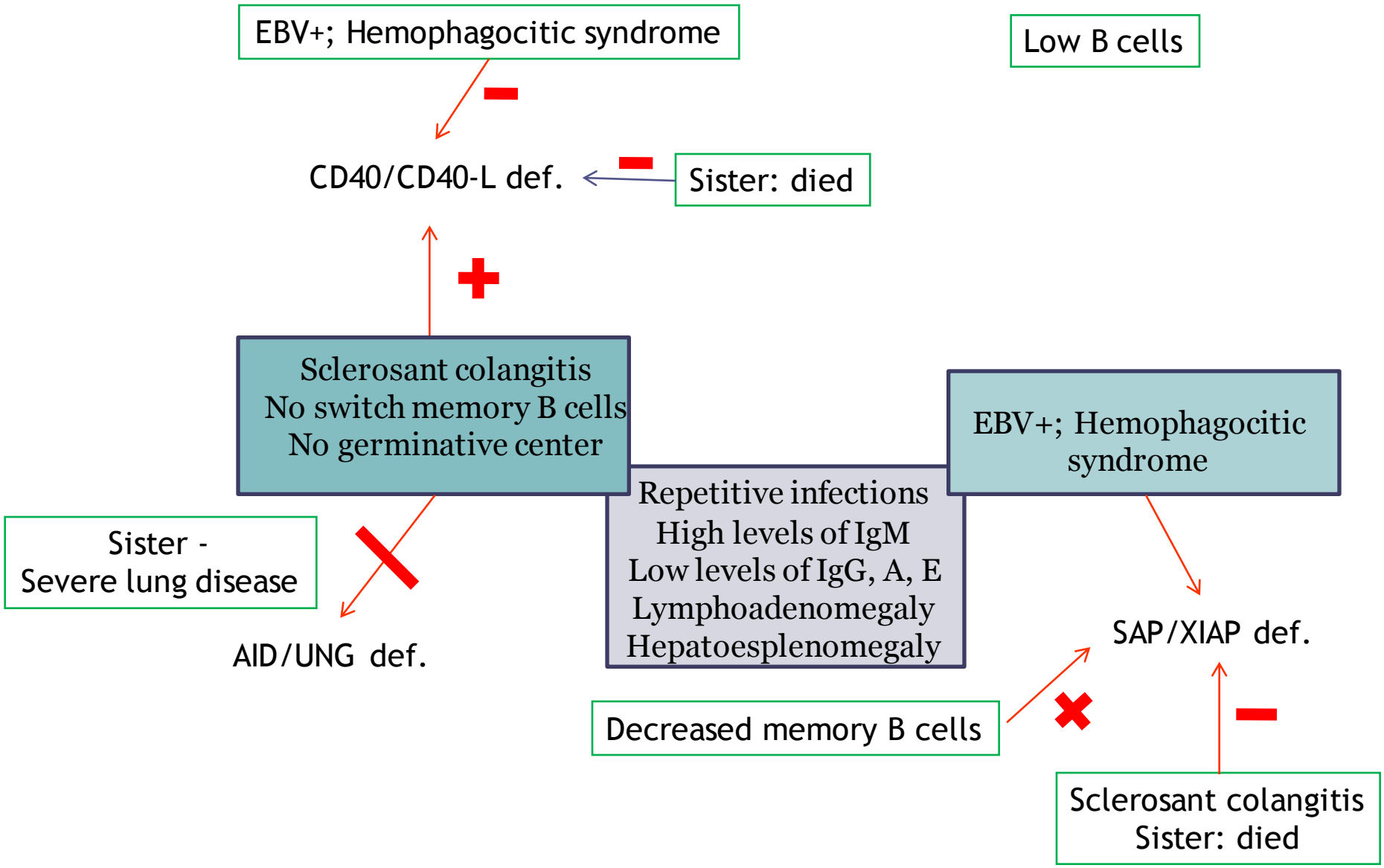
❖ 2011 (4 yr old) – sclerosant colangitis. Cryptosporidiun - negative.

High levels of alkaline phosphatase and γ-GT.

TO RESUME



- Male
- Repetitive infections; no severity
- Hepatoesplenomegaly
- Lymphoadenomegaly
- Hemophagocitic syndrome
- Sclerosant colangitis
- Hyper IgM
- High levels of CD8 T cells (CD8 efector T cells)
- No switch memory B cells
- No germinative center
- Sister that alread died – “hypogammaglobulinemia, repetitive infections and severe lung disease”


EBV+; Hemophagocitic syndrome
Low B cells
CD40/CD40-L def.
Sister: died
Sclerosant colangitis
No switch memory B cells
No germinative center
EBV+; Hemophagocitic syndrome
Repetitive infections
High levels of IgM
Low levels of IgG, A, E
Lymphoadenomegaly
Hepatoesplenomegaly
Sister -
Severe lung disease
AID/UNG def.
SAP/XIAP def.
Decreased memory B cells
Sclerosant colangitis
Sister: died

RESULTS

- CD40 e CD40-L expression: normal (IPPMG/UFRJ)
- Functional assay of CD40-L: normal (Otávio Marques; Antônio Condino-Neto)
- SAP/XIAP mutations: negative (J. Bosco)

OUTCOME – 2012- 2014

- Keeping Ig infusion (400 mg/kg/dose; 28/28) and SMT/TMP prophylaxis.
- Significant increase in lymph nodes – no criteria for hemophagocitic syndrome nor malignancy.
- Significant increase in hepatoesplenomegaly.
- Keeping high levels of alkaline phosphatase and γ-GT. High levels of AST and ALT.
- High levels trygliceride and LDL.
- Jaundice.
- Low IgG levels (< 200 mg/dl) ⟶ mensal higher doses were tryed (750 mg/kg/dose).
- 2013 (6 yr old): frequent infections; no severity; IgG < 200 mg/dl.

No increase in the seric IgG levels with shared doses in a weekly schedule (150 mg/kg/dose) nor 600 mg/kg/dose every two weeks.

- 2014 (7 yr old): digital clubbing; polyarthritis – corticotherapy.

LITERATURE REVISION – NEW DIAGNOSIS HYPOTHESIS?

Mutations in *PIK3CD* Can Cause Hyper IgM Syndrome (HIGM) Associated with Increased Cancer Susceptibility

M. C. Crank · J. K. Grossman · S. Moir · S. Pittaluga · C. M. Buckner · L. Kardava · A. Agharahimi · H. Meuwissen · J. Stoddard · J. Niemela · H. Kuehn · S. D. Rosenzweig

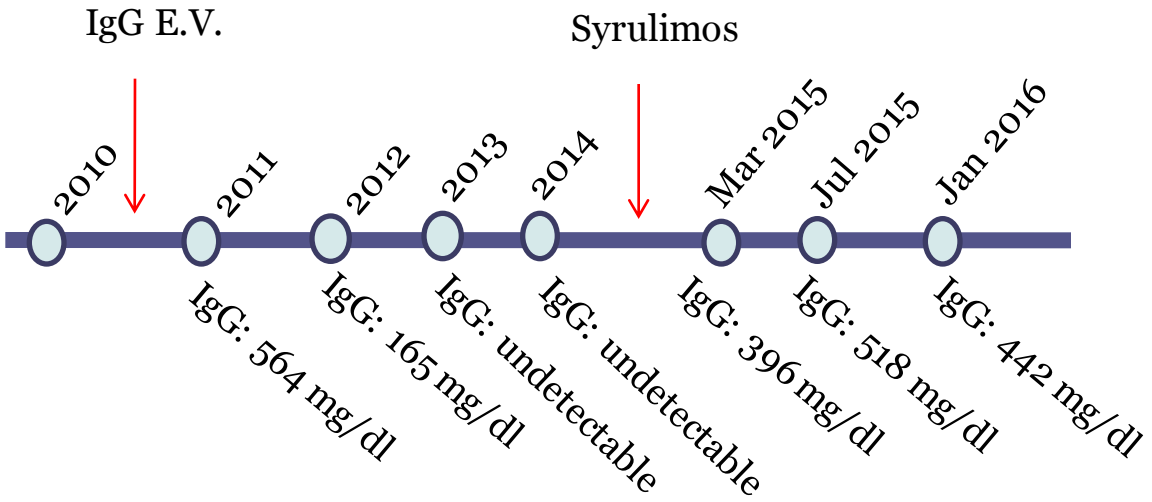
APDS ?

- dec/2014: heterozigotic mutation in the gene PIK3CD (exon 24 c.3062G>A, E1021K) Capucine Picard/Alain Fischer

- 2015: treatment with Syrulimos was initiated.
- Follow up CMV, EBV, liver function, trygliceride and cholesterol levels.

- Fev/2016: Syrolimo – 5.6 ng/ml ; Mar/2016 – 6.8 ng/ml

OUTCOME – 2015- 2016



Feb/Mar 2016

- ✓ TCD3: 89.7% (3079/mm³), >P97
- ✓TCD4: 19.5% (669/mm³), P10-50
- ✓TCD8: 66.4% (2281/mm³), >P97
- ✓TCD4/TCD8: 0.29
- ✓B cells (CD19): 1.4% (47/mm³) <P10
- ✓NK (CD56): 6% (202/mm³), <P10

- ✓IgA: undetectable
- ✓IgG: 556 mg/dl
- ✓IgM: 2821 mg/dl

PERPECTIVES

- ❖ Therapeutic seric levels of syrolimos (7-15 ng/ml)
- ❖Anti-TNF-α - arthritis
- ❖ Sub-cutaneous infusion of gammaglobulin
- ❖ Transplant → liver ?
  → BMO (donnor 10x10)

✓ Alergia/Imunologia

✓ Reumatologia

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Marta Felix

✓ Pneumologia

Clemax Sant´anna

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Fátima Pombo

✓ Nutrologia

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✓ Bárbara Andrade Rezende

✓ Alain Fischer/Capucine Picard

✓ Antônio Condino-Neto/ Otávio Marques

✓ João Bosco Oliveira Filho

✓ Martin Perez/ Alberto Orfao