A strange case of unspecified hypogammaglobulinemia

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- 8-year old male child
- First child born to non-consanguineous parents.
- No family history of PID.
- Full-term, natural childbirth.
- Normal weight and length.
- Up-to-date with National immunization program (BCG, OPV, DPT, Hib, Hep-B, PCV-13, Men-ACWY, MMR).
- Severe Atopic Dermatitis.
- Since he was born, he had intermittent episodes of fever at least once a month, without any other clinical manifestations.

- At the age of 2 years 8 months:
  - Bacterial Pneumonia
  - Admitted to hospital and treated with i.v. antibiotics.
- At the age of 3 years 1 month:
  - Pansinusitis + periorbital cellulitis
  - Admitted to hospital and treated with i.v. antibiotics.

HCT	Hg	WBC	Lymphocytes	Platelets	CRP
35%	11.8 g/dl	**19,500 uL**	25% (4,875)	445,000 uL	108 mg/L

He responded well both times to first line therapy.

- At the age of 4 years old:
  - Admitted to hospital after 2 days of:

High fever	Headache	Arthralgia	Myalgia
Cough	Odynophagia	Purpuric lesions	

HCT	Hg	WBC	Lymphocytes	Neutrophils	Platelets	CRP
34%	11.3 g/dl	**2,600 uL**	**65% (1,690)**	**0%**	**15,000 uL**	57 mg/L

  - Liver function, biochemical and coagulation tests were all within the normal range.
  - Blood culture (-) and no infectious cause was detected.
  - Chest x ray: Retrocardiac opacity.
  - Managed as neutropenic fever: cefotaxime, cloxacillin and several platelet transfusions.

- Third day of hospitalization: Epistaxis

HCT	Hg	WBC	Lymphocytes	Neutrophils	Platelets	CRP
21.8%	**7.1 g/dl**	4,480 uL	72% (3,225)	**2% (89.6)**	**4,000 uL**	57 mg/L

- Myelogram: Bone marrow infiltrated by 76% pathological promyelocytic cells.
- Acute myeloid leukemia M3 (FAB classification) was diagnosed and chemotherapy was immediately started:
  - All-trans retinoic acid for three days, until we got the negative translocation 15 ; 17 test report.
  - Induction schedule with cytarabine, idarubicin and etoposide.
  - 8th day: a second reading of the same myelogram ruled out acute myeloid leukemia, indicating medullary megaloblastosis and granulocytic hyperplasia with just 5% of abnormal promyelocytic cells, so chemotherapy was interrupted.

- The child recovered, and this episode was interpreted as a secondary pancytopenia probably triggered by an infection.
- He was discharged and referred to the Immunology outpatient clinic.

HCT	Hg	WBC	Lymphocytes	Neutrophils	Platelets
31.3%	**10.4 gr/dl**	10,240 uL	38% (3.891)	48% (4,915)	395,000 uL

$CD3^+$	$CD4^+$	$CD8^+$	$CD19^+$	$CD16/56^+$	IgG	IgM	IgA
3,750	2,468	1,307	**0**	230	1,148	**34**	**43**

- 3 months later:

$CD3^+$	$CD4^+$	$CD8^+$	$CD19^+$	$CD16/56^+$	IgG	IgM	IgA
3,645	2,250	1,350	**0**	630	**352**	**22**	**4.9**

  - All serotypes of pneumococcal specific antibodies were low.
  - Memory B lymphocyte with isotype switching was impossible to perform because of the absence of B lymphocytes.

- Since then, he has been receiving IGIV infusion monthly (400 mg/kg), without presenting new infections in the past 3 years.
- We recently again checked his lymphocyte subpopulation, and he still shows complete absence of B lymphocytes.
- Interestingly, after having missed two and three months of his IGIV infusion, he maintains moderate IgG (250-350 mg/dl) levels.

- **How can we classify this humoral immunodeficiency?**
- **Why did he have normal IgG counts in absence of B lymphocytes at the beginning?**
- **Could this be XLA? Or CVID?**