X- LINKED AGAMMAGLOBULINEMIA (XLA)

CASE PRESENTATION

Cristina Miuki Abe Jacob
Allergy & Immunology Division - Pediatric Department
Faculdade de Medicina da Universidade de São Paulo
São Paulo

MEDICINA USP
FUNDAÇÃO CALOUSTE GULBENKIAN
Instituto Gulbenkian de Ciência
FAPESP

XLA - CASE REPORT

FLD, male, born 1985, admitted 1989

Clinical History:

- Since **2 years**:recurrent upper respiratory infections

(2 suppurative otitis)

- **3y 2m-** cutaneous abscess - antibiotics 15 days
    - 2 episodes of edema and tenderness at both knees and one at left knee.
- **4 years-** hospitalization at our hospital with history of both knees arthritis without fever during 6 days. After exclusion of infectious arthritis he was admitted to Rheumatology Unit with probable diagnosis of JIA.

XLA - CASE REPORT

- **5 years-** abscess at gluteal region with fever- admitted at hospital for IV antibiotics (22 days). During this episode detected IgG=98mg/dL and the patient was referred to the Immunology Unit, where the XLA diagnosis was done. Prophylactic antibiotics and IM gammaglobulin were prescribed.

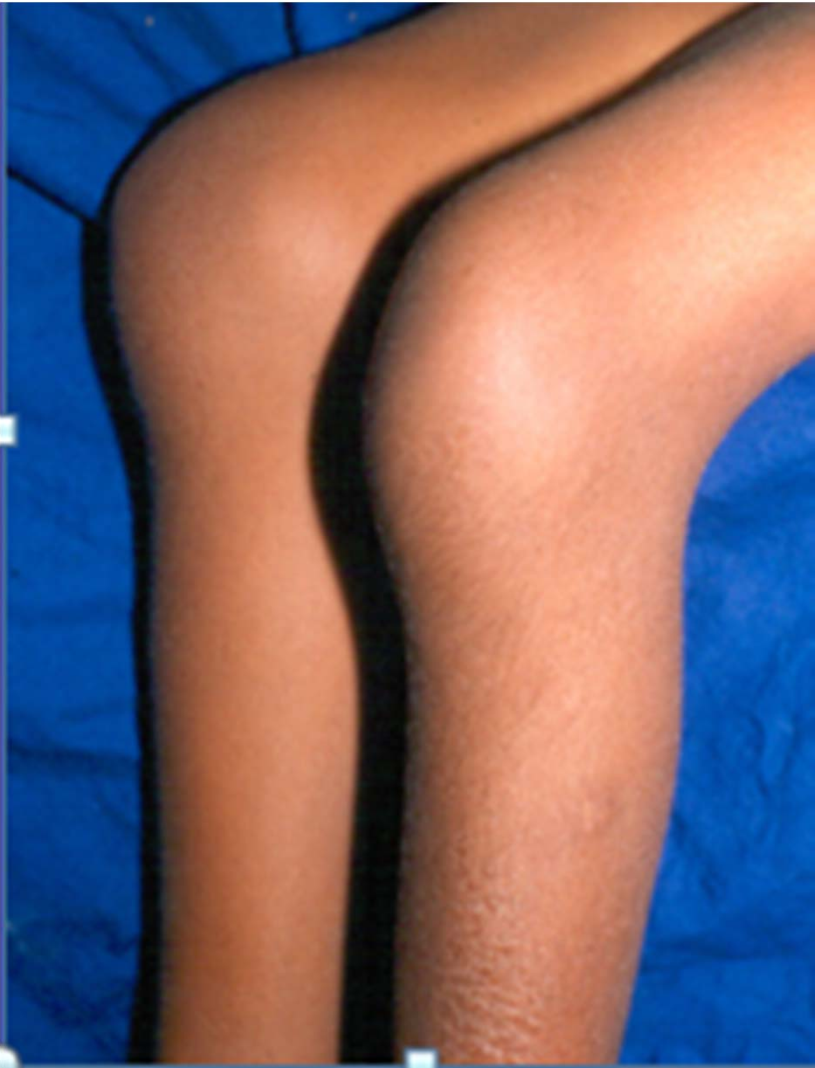
XLA - CASE REPORT

- **Family history-** no consanguinity. Brother died at 9 m by infectious process and chronic diarrhea

- **Vaccines-** all vaccines for age

- **Physical examination- important findings:**

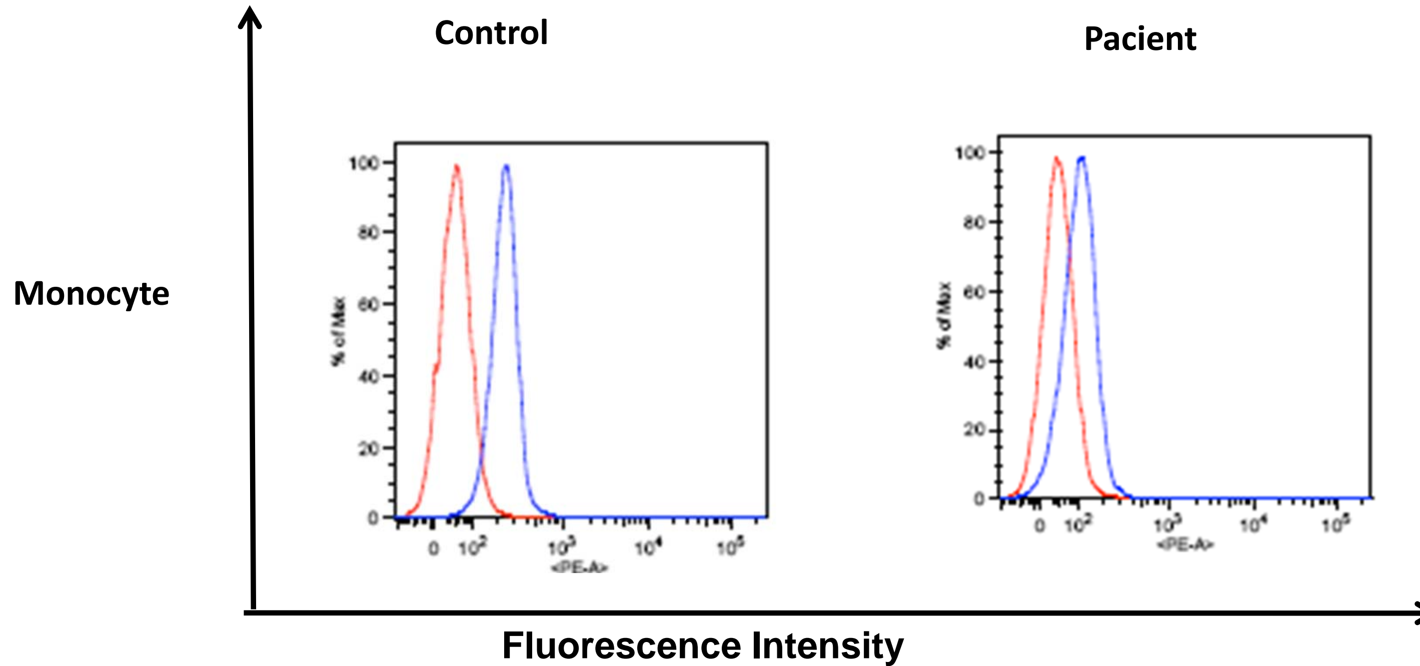
➢ weight and height - 15 percentile
➢ absence of lymphonodes and pharyngeal tonsils
➢ knees - tenderness, limitation on motion and edema



Laboratorial data at diagnosis

- Hb= 12,2 g/dL Ht=36 leuc= 12100/mm^3 (58%/1%/1%/38%/3%) plat = 540000/mm^3
- IgG= 98 mg/dL, IgA=3 mg/dL, IgM=10mg/dL, IgE=8UI/L
- CD4= 770, CD8=448, CD19=1%, CD56-6%
- Chest RX – normal
- **Exon 17- c1847C>T pR562w domínio kinase – missense mutation**
- **Treatment**- IM gammaglobulin monthly (tailored doses for serum level IgG=600-700mg/dL) and prophylactic antibiotics

Btk expression



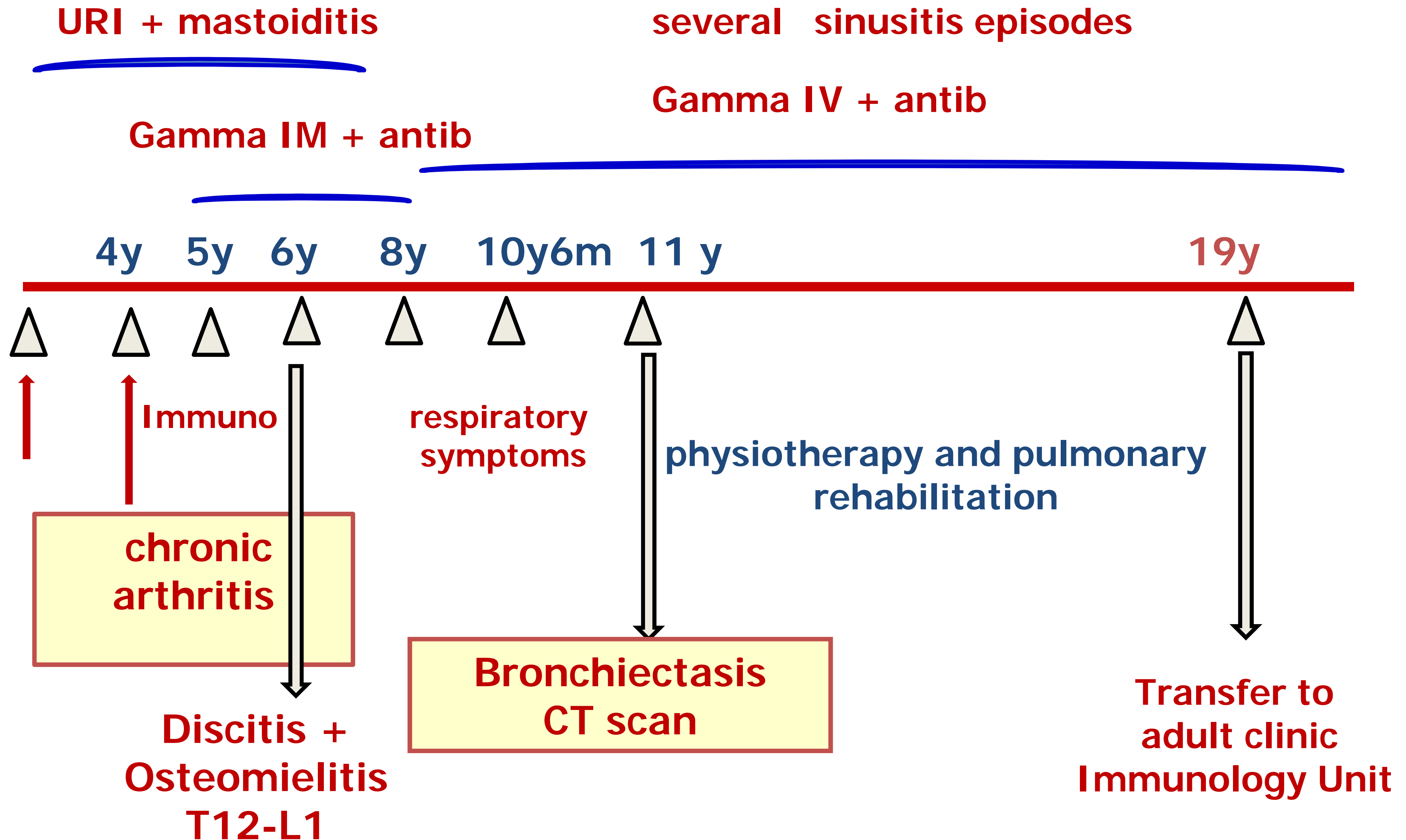
Healthy Control = 76,6 % Btk expression

Patient = 5,98 % Btk expression

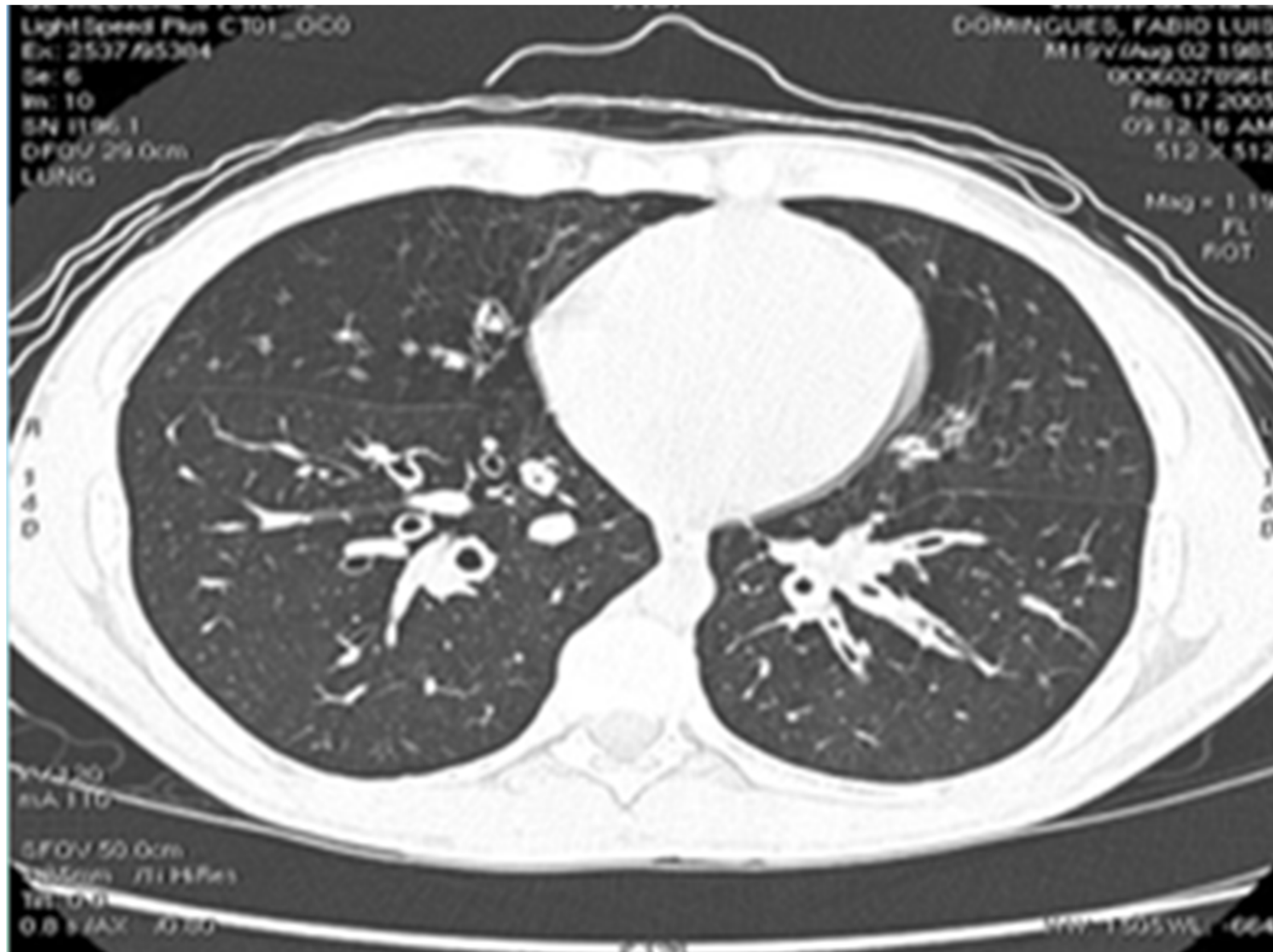
Red line: control antibody

Blue line: anti-Btk

XLA – Time line



Bronchiectasis XLA patient



XLA - CASE REPORT

Highlight points:

- **Arthritis as manifestation of PID**
- **Bronchiectasis under treatment with gammaglobulin and antibiotics**

Arthritis and PID

- Joint complications have been recognized in PID patients: infectious or not
- Arthritis may be the first clinical manifestation of PID
- Noninfectious joint anormalities similar to JIA have been showed due to infectious trigger
- The difficulties to identify agents may understimated the prevalence of infectious arthritis

Bloom KA, Chung D, Cunningham- Rundles, 2008

PID associated to arthritis

- Humoral PID : humoral more common: XLA, CVID, IgA def and Hyper IgM (5-40%)
- CGD
- Wiskott- Aldrich
- IRAK4

Arthritis and XLA

- Janeway, 1956- asseptic arthritis and XLA
- Arthritis associated to *Mycoplasma* infection

- Mechanisms:
- ➢ Infectious agent not identified
- ➢ Immune dysregulation related synovial tissue

- ➢ Good response to IV gammaglobulin- immunomodulation??

Machado P et al, 2008

XLA and Chronic Lung Disease

- XLA associated to lung chronic disease
- Recurrent or chronic respiratory symptoms
- Chest XR:
  - atelectasis
  - bronchial wall thickening
  - Bronchiectasis
  - CT scan – precocious detection

Despite regular gammaglobulin infusion

Buckley RH, 2004

XLA and Chronic Lung Disease

Monitoring the patients for subclinical, but progressive, pulmonary damage is important.............. Such monitoring may take the form of routine pulmonary function tests. High resolution chest CT may be of value in detecting early pulmonary damage , although the accumulated risk of radiation should be taken account....

Winkelstein JA, 2010