CLINICAL CASE

Dr. Ana Carolina da Matta Ain, MD

IDENTIFICATION

- M.M.S., 3 years and 8 months old, male, white, born in the city Taubaté and living in São Bento do Sapucaí – State of São Paulo.

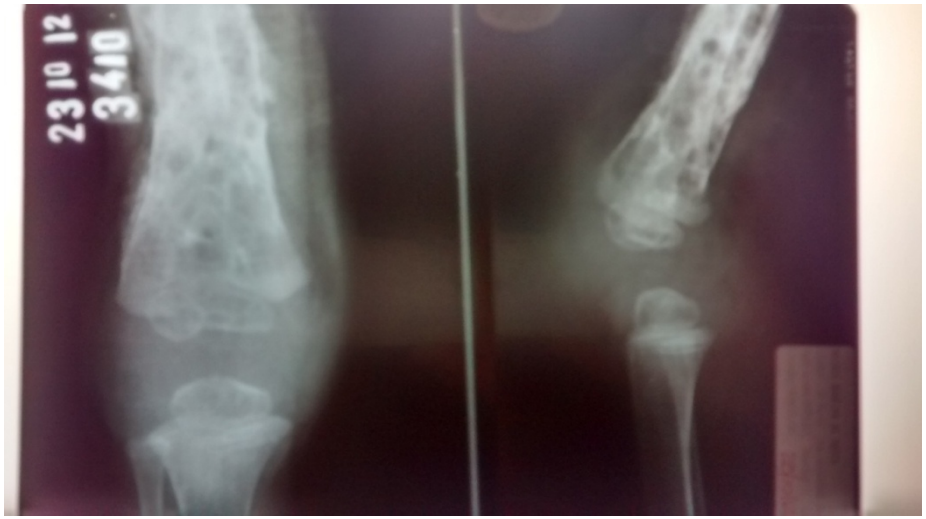
- Fall from standing position resulting in R knee trauma, progressing with pain and severe edema throughout right lower limb. One month later, he attended outpatient unit, and he was admitted for 10 days due to concurrent pneumonia. He progressed with severe anemia and worsening of RLL status, therefore no longer ambulating because of severe pain and edema. He was then referred to our service as to continue investigation.
- A chronic granulomatous inflammatory process was found in skin biopsy, which showed fungal structures suggestive of Aspergilus sp, thus raising the suspicion of systemic Aspergilosis.

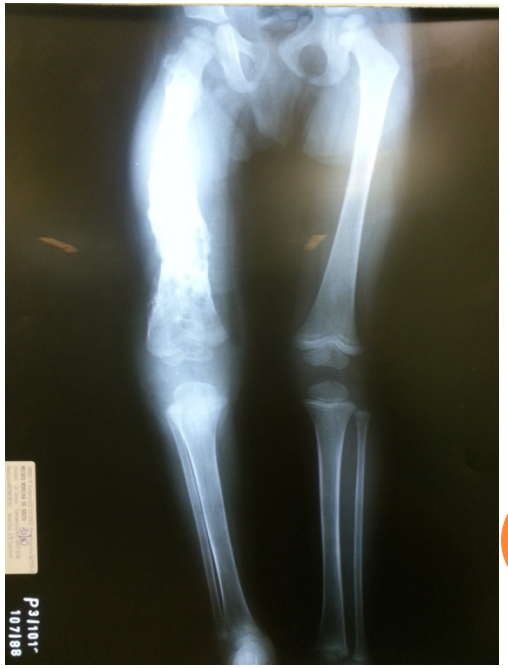
Past Medical History:

- Preterm, late-onset neonatal sepsis, and neonatal meningitis.
- 7 months old: admission due to UTI, fungal skin infection, and blood culture positive for Klebsiela Pneumoniae.
- Recurrent pneumonias resulting in hospital admissions up to the age of 3.
- Recurrent folliculitis.

Imaging tests

- Long bone x-Ray – areas of rarefaction and bone sclerosis in proximal metaphysis of left humerus. Morphostructural changes in right femur with areas of bone rarefaction and abundant new bone formation, compact laminar periosteal reaction and increased bone diameter.
- Bone Scintigraphy – hyper-uptake in R femur, head of L humerus, upper portion of R chest.





IMMUNOLOGICAL SCREENING:

- IGG 2443.3 mg/dL (> p97)
- IGM 211.7 mg/dL (> p97)
- IGA – 694.2 mg/dL (> p97)
- IGE – 43.4 IU/mL
- C3 245.1 u/CAE
- C4 44.5 mg/dL
- CH50 128 u/CAE
- CD3 – 1367 / mm3 (30/07/12) (p10: 1515/ mm3)
- CD4 - 709 / mm3 (30/07/12) and 556 / mm3 (p10: 780 / mm3)
- CD8 – 868 / mm3 / 671 / mm3 ok
- CD19 – 890 / mm3
- Anti-HIV - negative
- Anti HBsAg - positive

- Myelography with imunnophenotyping, bone marrow biopsy, skin and bone biopsy. The report of first skin biopsy was inconclusive, but the second one revealed osteosclerosis and remodeling with intense neutrophilic infiltrate, granulomas with multinucleated giant cells and fungal structures with non-septate and septate hyphae.

Treatment:

- Voriconazole + surgical drain.
- Vancomycin and Meropenem (osteomyelitis).
- Bactrim plus antifungal as prophylactic treatment, folinic acid.

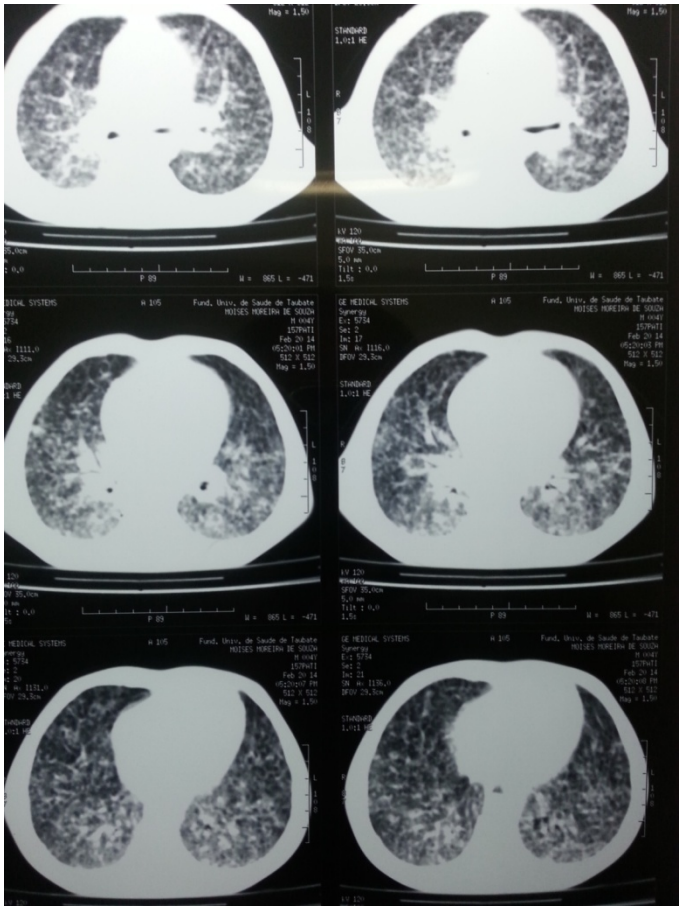
Progress

- 2013 (4 y.o.):
- 1 hospital admission for periorbital cellulitis
- Waiting for tests to be released
- DHR within normal range

- 2015 (5 y.o.):
- Hospital admission with severe pneumonia – radiological pattern of diffuse infiltrate
- IV human immunoglobulin

Bronchoscopy

- Lung biopsy identified Aspergillus.



DHR

	Controle		Paciente	
	Espontâneo	Estimulado (PMA)	Espontâneo	Estimulado (PMA)
Monócitos	1246	2411	987	789
Neutrófilos	2924	272640	1542	1398

Resultados expressos em MFI (mediana da intensidade de fluorescência).
Resultados alterados em comparação ao controle.

Quimiolumonescência:

	Controle		Paciente	
	Espontâneo	**Estimulado (PMA)**	**Espontâneo**	**Estimulado (PMA)**
Neutrófilos	$20,76 \times 10^7$	$75,64 \times 10^7$	$2,48 \times 10^7$	$2,23 \times 10^7$

Resultados expressos em AUC (área sobre a curva).
Resultado alterado em comparação ao controle.

DATA DA CHEGADA DA AMOSTRA: 20/05/15
NOME DO PACIENTE: Moises Moreira de Sousa
IDADE:
MÉDICO RESPONSÁVEL: Drª. Ana Carolina da Matta
TIPO DE AMOSTRA: Sangue periférico em Heparina
DOSAGENS SOLICITADAS: "Shedding"de CD62L – Avaliação de TLRs
REALIZADO POR: Marina Carvalho

PACIENTE:

	CD62L							
	NE	PMA	TLR1/2	TLR2/6	TLR2/Dectina-1	TLR4	TLR5	TLR7/8
centagem	72,85	34,5	4,8	7	4,2	5,9	57,3	7,4
MFI	1348	493	289,5	323	291,5	325	862	337

CONTROLE:

	CD62L							
	NE	PMA	TLR1/2	TLR2/6	TLR2/Dectina-1	TLR4	TLR5	TLR7/8
entagem	79,5	57,2	6,4	8,25	6,75	4,6	52,2	3,8
MFI	1607	866	203	374	353,5	341,5	786	331,5

Resultado dentro da normalidade de ativação de TLR.

- *CYBB* gene sequencing, which led to detection of a mutation responsible for **Chronic Granulomatous Disease**.
- The alteration was found in Exon 2 of *CYBB*, the gene that encodes gp91-phox protein of NADPH oxidase system.
- The mutation (p.Thr42lys; pT42K) presents with an A>C base substitution, thus causing replacement of the amino acid Threonine with Lysine, responsible for NADPH complex disorder in the production of reactive oxygen species.