Agammaglobulinemia

Vilnius University Children's Hospital
Pediatric Center, R.Duobiene

Case report

- R.B., male, born on February 1997.
- The parents are consanguineous.
- Eyes' pathology in fathers' family (2 brothers, sister, mother).
- The boy has healthy brother.

Case report

- Second delivery after the 37 weeks of normal pregnancy.
- Birth weight 2,4 kg, height 52 cm.
- Respiratory dyspnea was mentioned during the first days (4) after the birth.

Case report

- Breast fed till 3 months old.
- Normal development till 3 months.
- BCG, polio, DTP, HB vaccines without apparent adverse reactions.

Medical history

- Recurrent respiratory infections - since 3 months.
- 7 m. – severe right pneumonia. (APV 5d., EM transfusion).
- Diarrhea.
- Failure to thrive.

Medical history

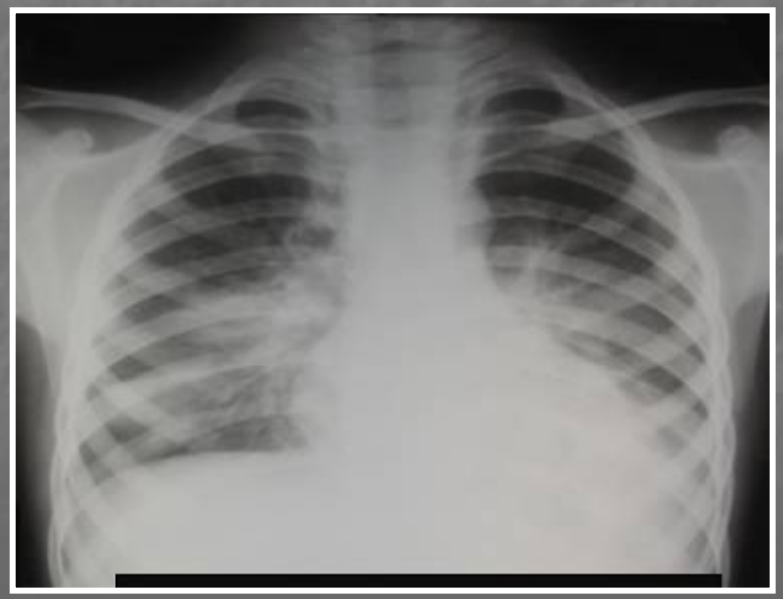
- 1year – cystic fibrosis due to :
  malabsorbtion,
  failure to thrive,
  recurrent bronchitis.

Further investigations excluded CF:
CFTR gene 508f mutation(-);
Serum chloride max until 53 mmol/l.

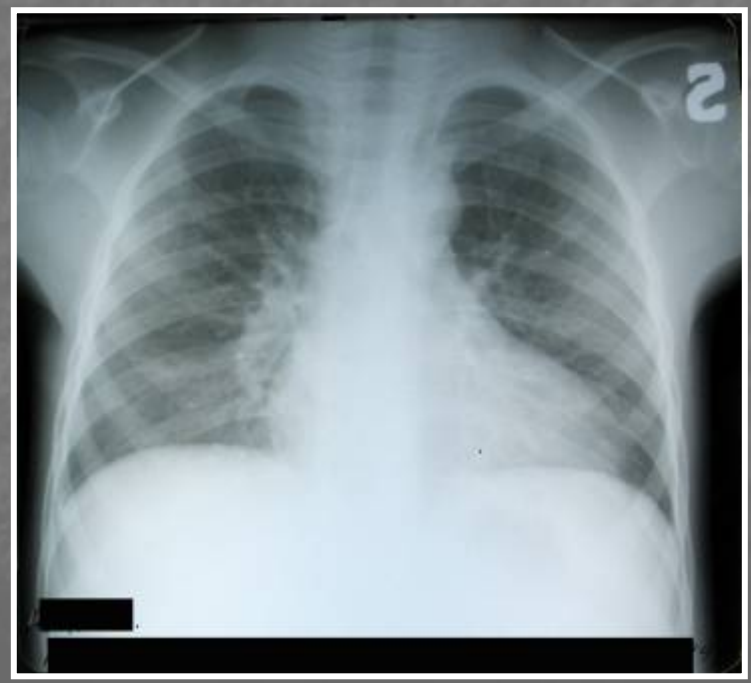
- 3 year – asthma bronchiale.
  Treatment without positive effect.

Medical history

- 3 - 6 year :
  - reccurent sinopulmonary infections every month,
  - pneumonia 4 times/year.



2003.01.07



2004.08.16

Medical history

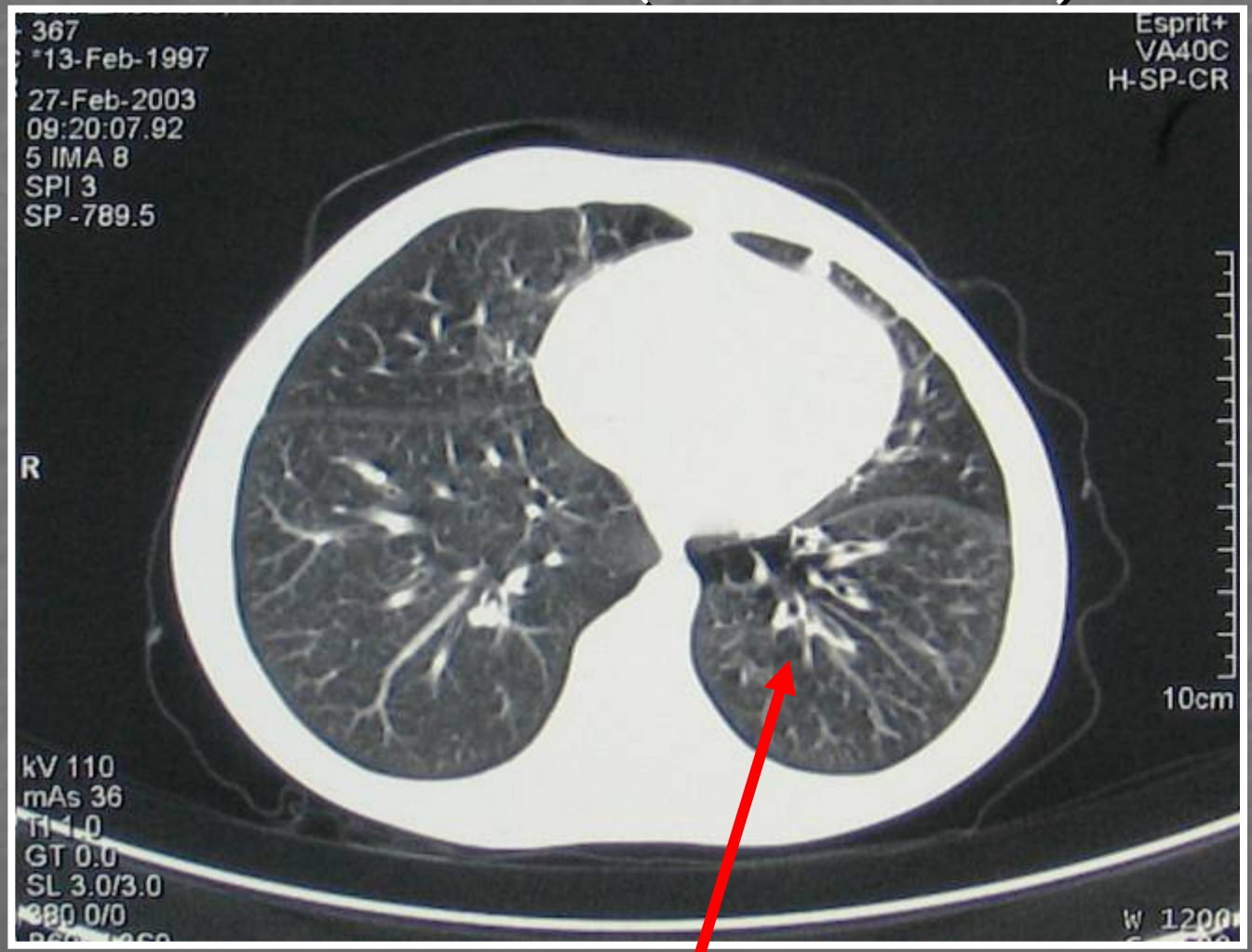
- 6 year – bronchiectatic disease.

  - bronchiectasias in left lung (S 8,9,10) by CT;

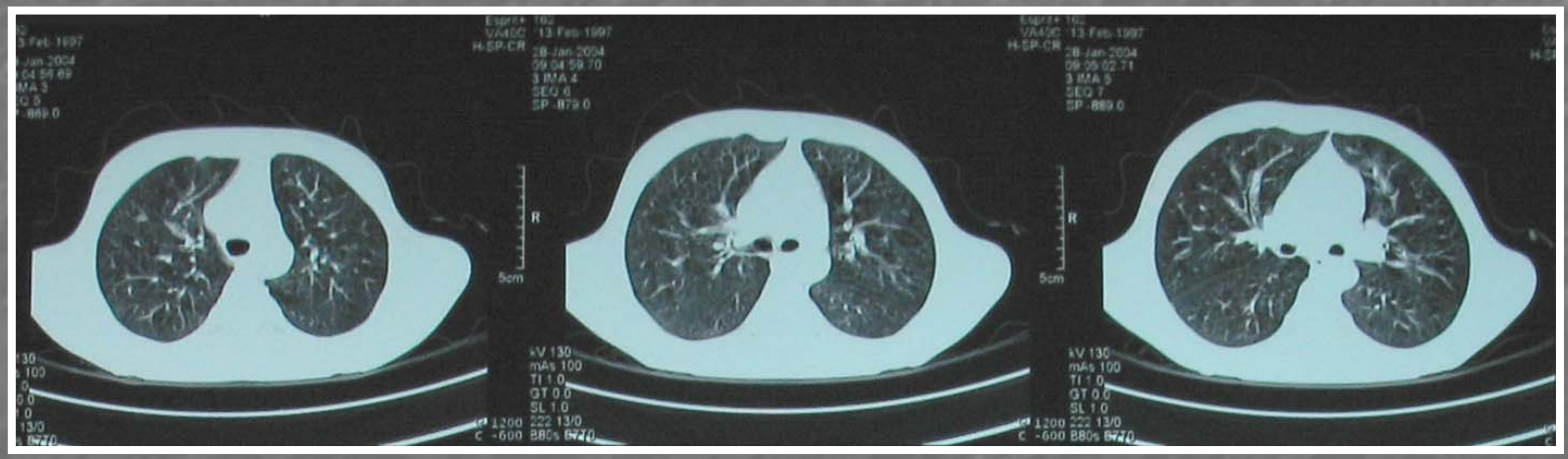
  - bilateral purulent endobronchitis by bronchofibroscopy;

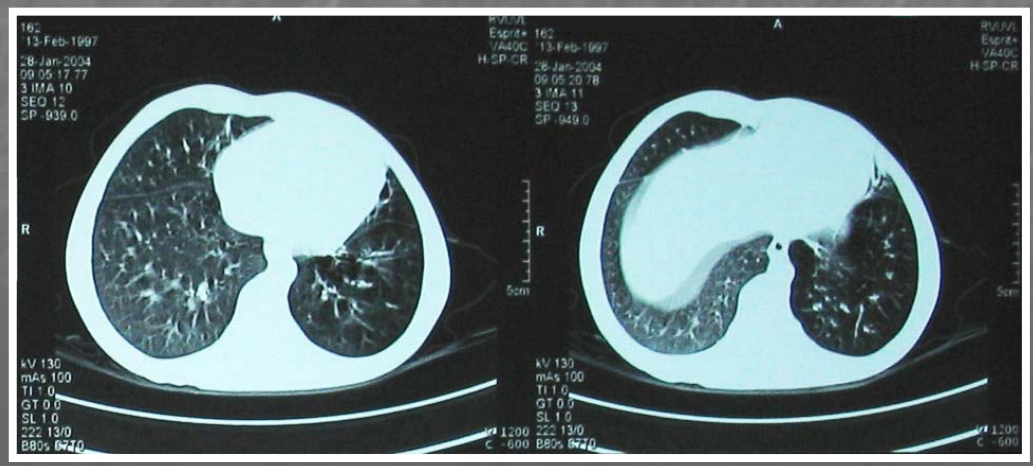
  - bronchial secretions bacteriological examination – Moraxella.

Chest CT (27.02.2003)



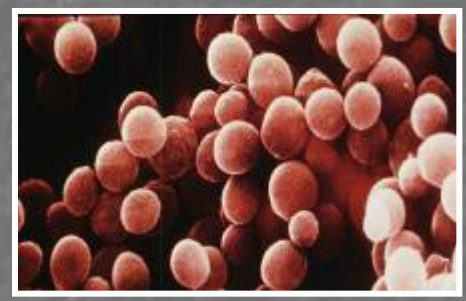
Chest CT (28.01.2004)

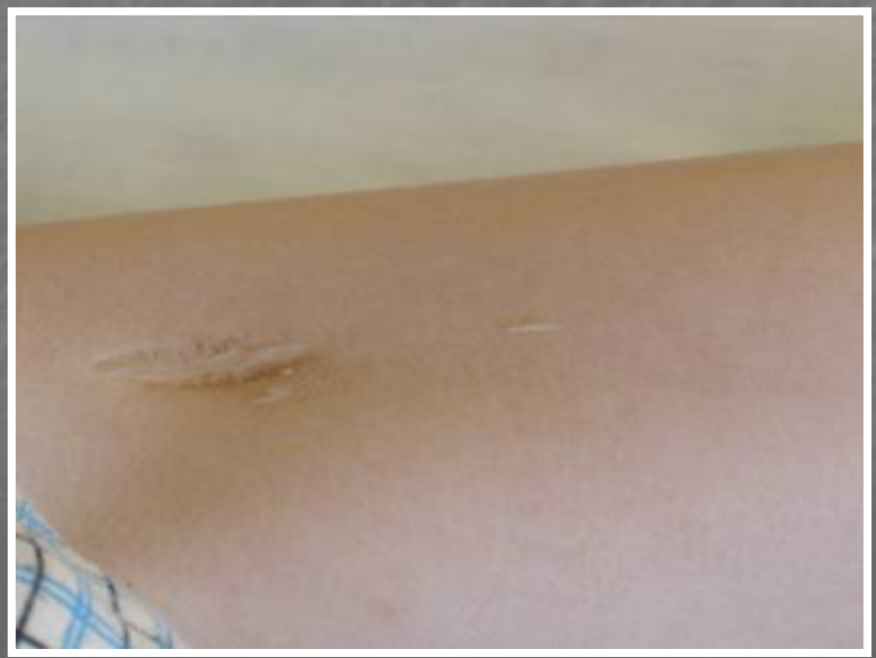


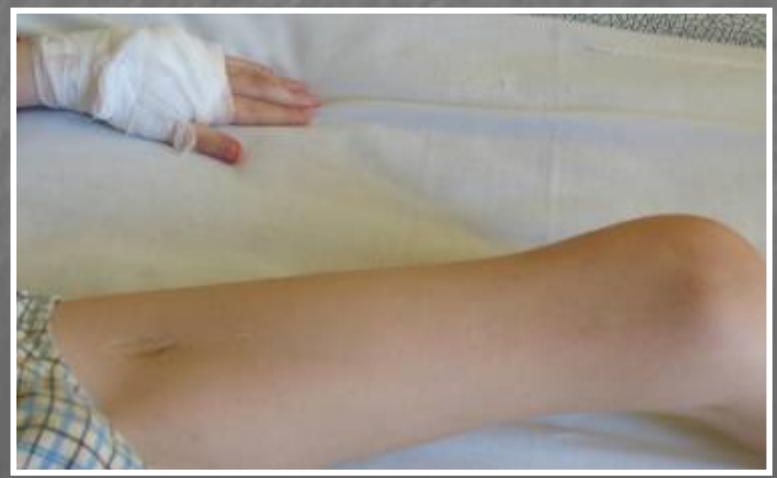


Medical history

5, 7, 8 year old - recurrent abscesses
of femur, finger, head, neck, ear, nose.
Bacteriologicaly - Staph.aureus.

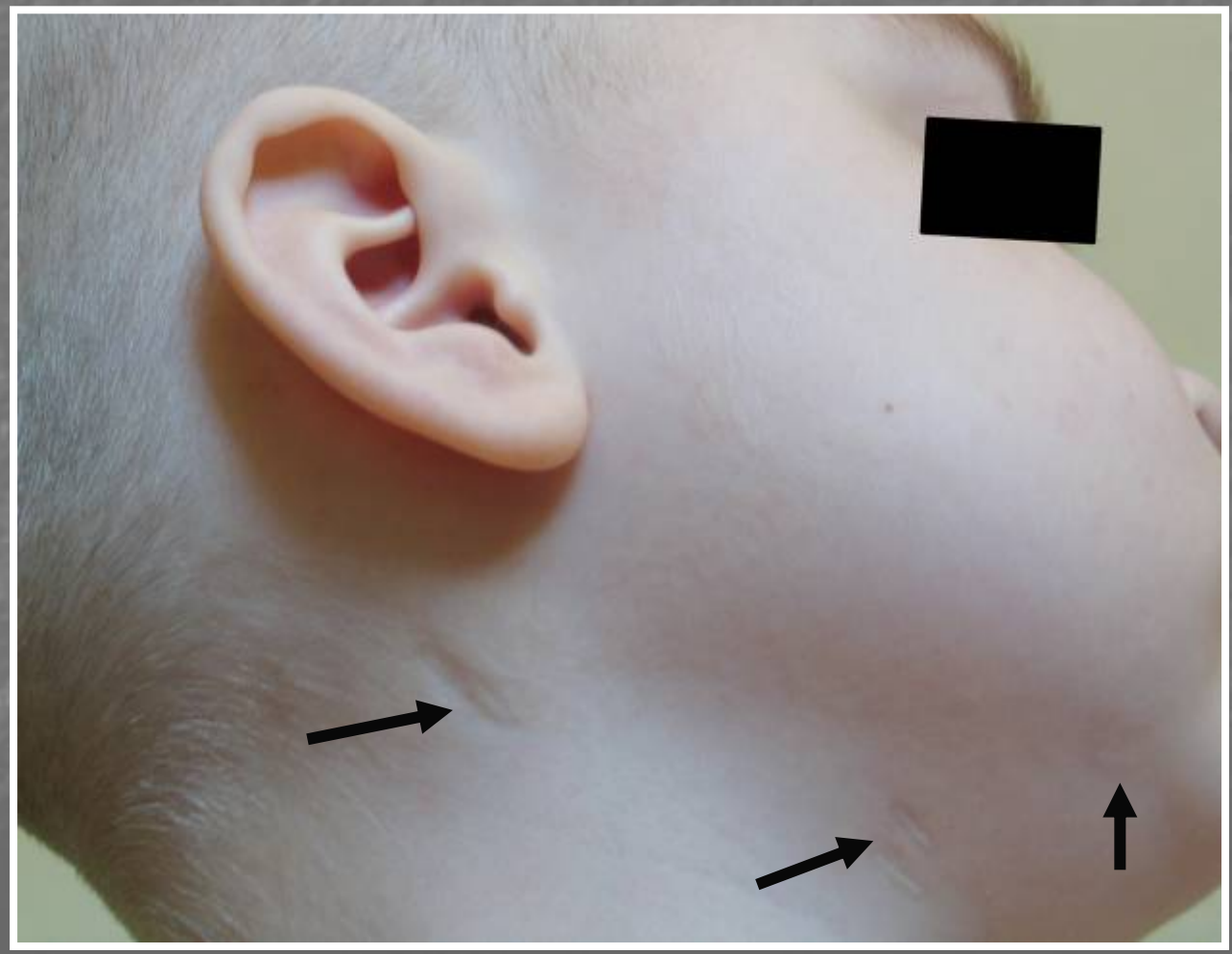






Medical history

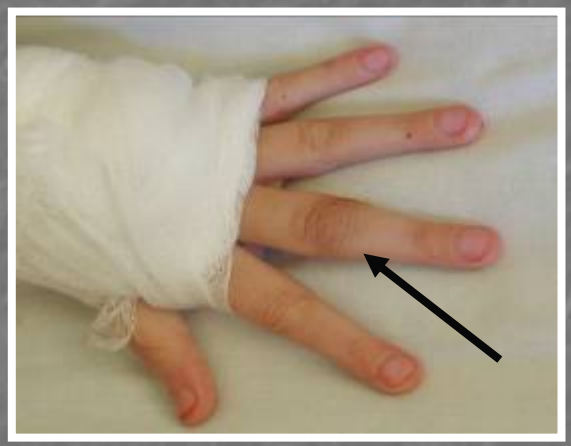
Scarring after abscesses

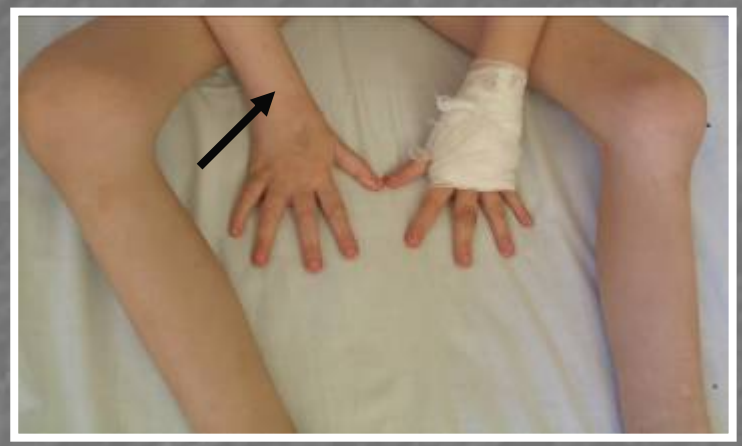


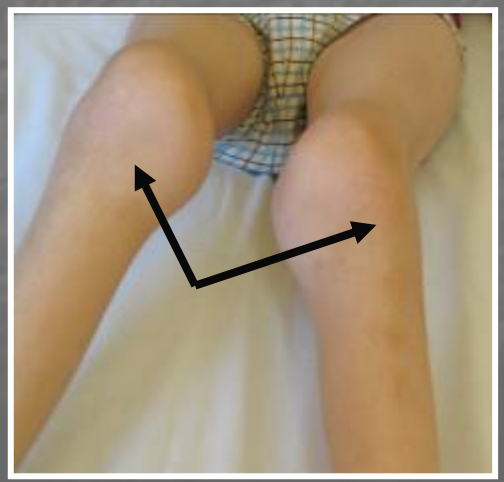
Medical history

- 6 year - onset of arthritis.
- 7 year – poliarthritis.

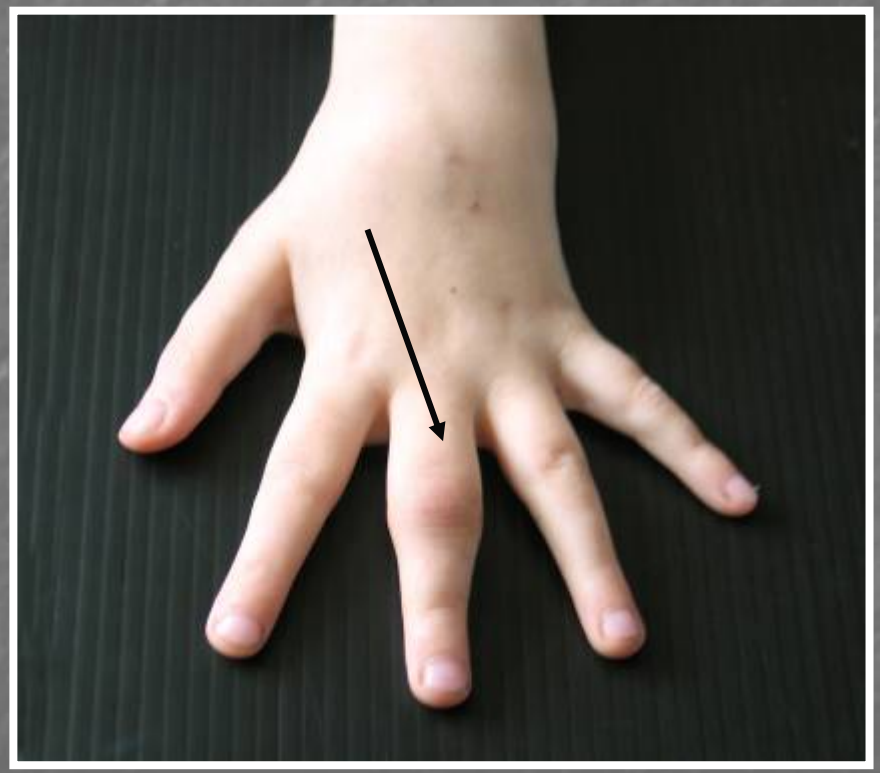
Medical history



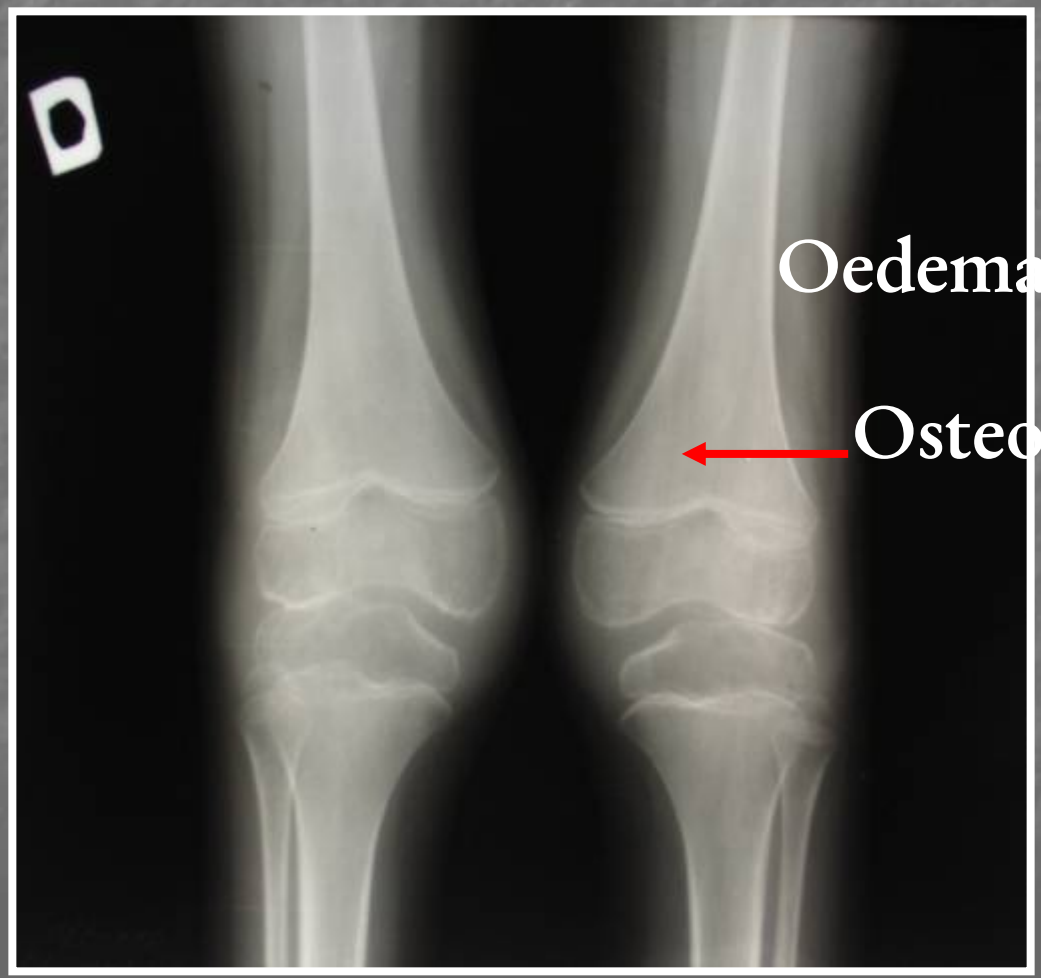


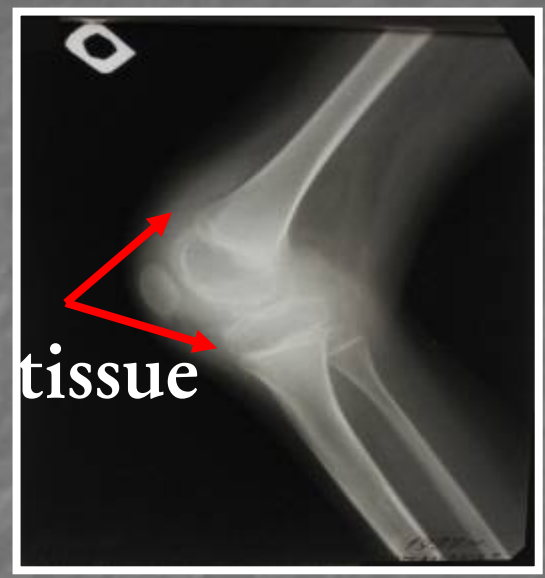


Medical history



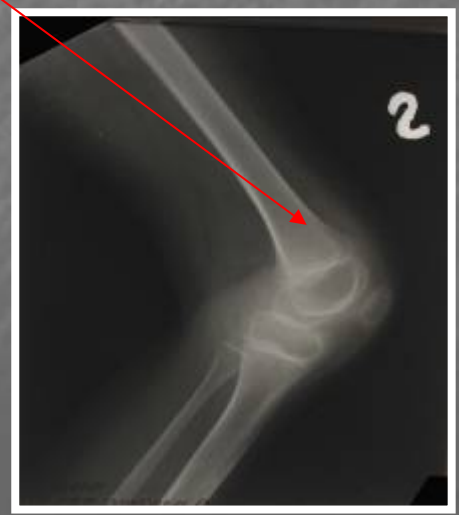
Knee joint x-ray





Oedema of soft tissue

Osteoporosis



Laboratory analysis

- Anemia – Hb 82-115g/l, MCV ~ 60fl,
  MCH ~ 20pg, Fe 3,2 mmol/l, feritin – 10 µg/l.

- Thrombocytosis from 1 year old:
  PLT 430 - 600 – 1474 x 10^9/l.

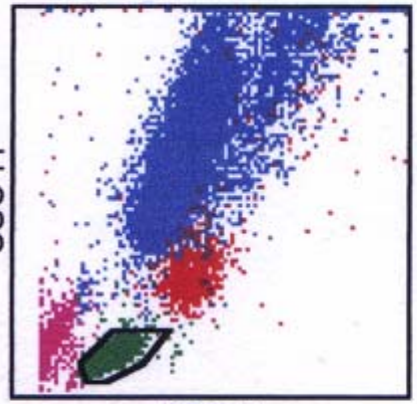
- Immunoglobulins:
  IgA - 0.22, IgG - 0.07, IgM - 0.17 mg/l.

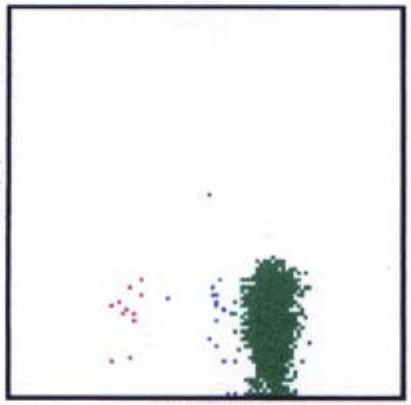
LYMPHOCYTES SUBPOPULATIONS 01.06.2004

Parameter	Value	Normal value (7-17 y)
Absolute lymphocytes count	21 % / 3402	36 – 43 % / 2000-2700 mm3
CD3+	96 % / 3266	66 - 76 % / 1400 – 2000 mm3
CD3+CD4+	38 % / 1293	33 – 41 % / 700 – 1100 mm3
CD3+CD8+	51 %/ 1735	27 – 35 % / 600 - 900 mm3
CD4+/CD8+	0,75	1,1-1,4
CD16+/CD56+	9 % / 136 mm3	89– 16 % / 200 – 3400 mm3
CD19+	0	12 - 22 % / 300 – 500 mm3
NBT	0	15-25%
NBT after stimulation	94	45-65%

LeucoGATE

000 Data Set:[1]



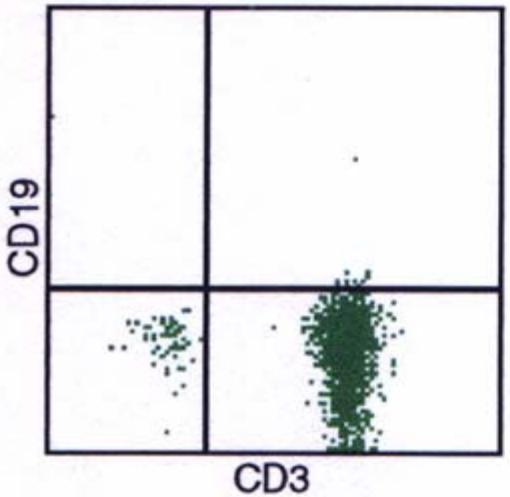


	FSC	SSC
Mean	63	26
Gate	42	23
	64	44
	100	45
	83	22
	58	10
	47	11

	Lymphs	Monos	Grans	Debris
n (%):	99	0	1	1

97% of all lymphocytes are in the gate

2000 Data set: [1]



CD3/CD19

Q	Cell Type	Conv %L
Q1	CD3- CD19+	0
Q2	CD3+ CD19+	1
Q3	CD3- CD19-	3
Q4	CD3+ CD19-	97

Subset Name	Conv %L
Total T (CD3+) Lymphocytes	97
Total B (CD19+) Lymphocytes	0

Treatment

- IVIG (Endobulinum) 500 mg/kg every 3 - 4 weeks. (2004.06 – ...
- Prednisolonum 1.5 mg/kg p/os (2004.04.05 – 2005.04)
- Triamcinolonum (Kenalog) 40mg intraarticular (x2)
- Methotrexatum 7,5 mg x 1 / week (x2) p/os (2005.03 -04)
- Sulfasalazinum (2004.05 -06)

Treatment

- NAP (nimesil, meloxicamum (moval), diclofenac, ibuprofenum) (2004 - ...
- Inhaler Flixotide (Fluticasonum), Seretide (Fluticasonum, salmeterolum)
  (2000 – 2005.04)
- Ferrosi sulfas, ac. folici.
- Antibiotics (cefuroximum/, clarythromycinum/, oxacillinum/, ampicilinum, ceftriaxonum, vancomycinum/, ceftazidimum, gentamycinum/, cephazolinum, biseptol).

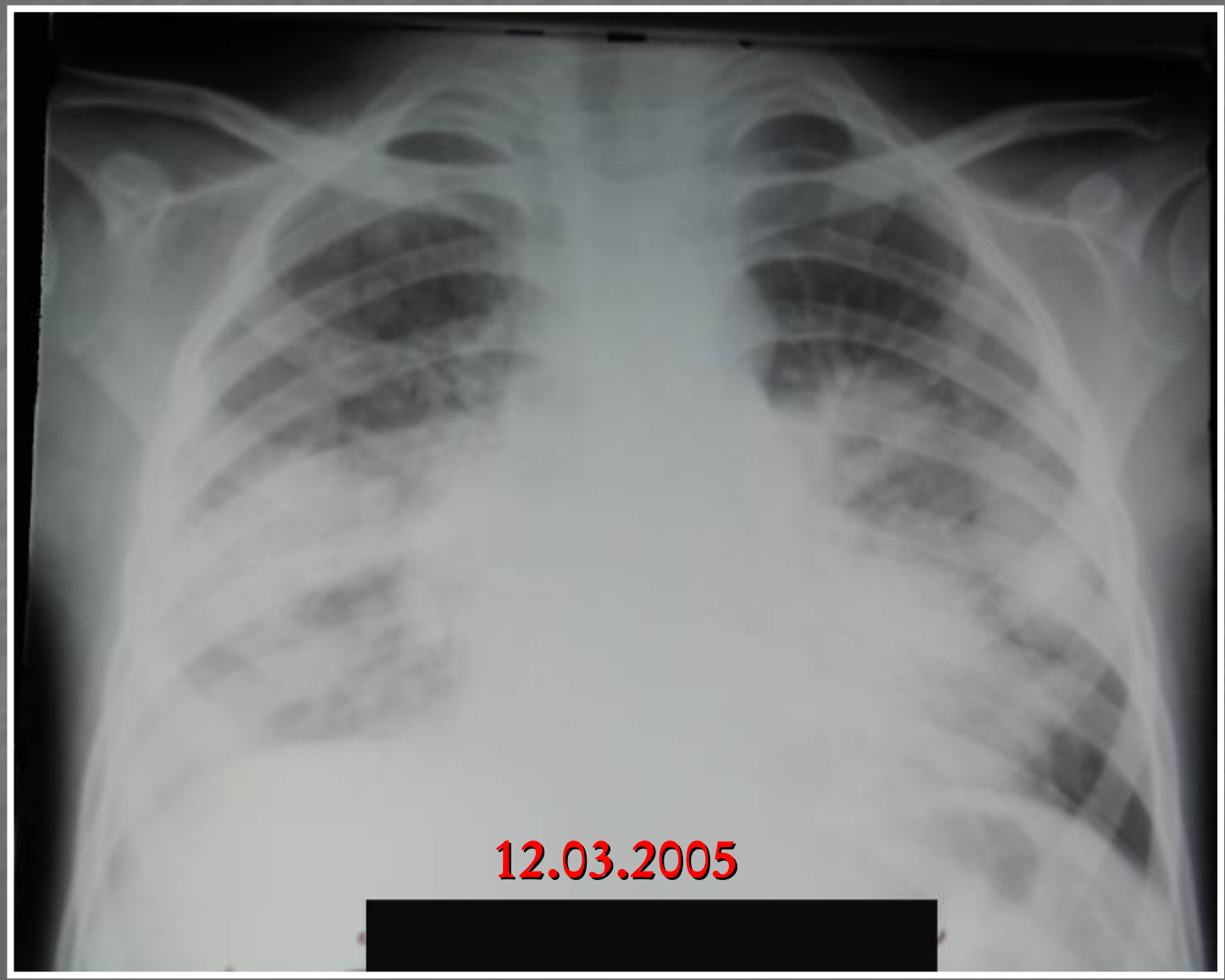
Immunoglobulins

	15.12. 2004	12.01. 2005	19.01.	10.02.	03.03.	18.03	30.03.
Ig A g/L		< 0,25	< 0,25		< 0,24		< 0,23
IgG g/L	5,63 →	1,93	5,36	6,45 →	2,54	7,14 →	2,44
IgM g/L		< 0,17	< 0,17		< 0,17		< 0,18
IgE IU/ml					< 4,5		

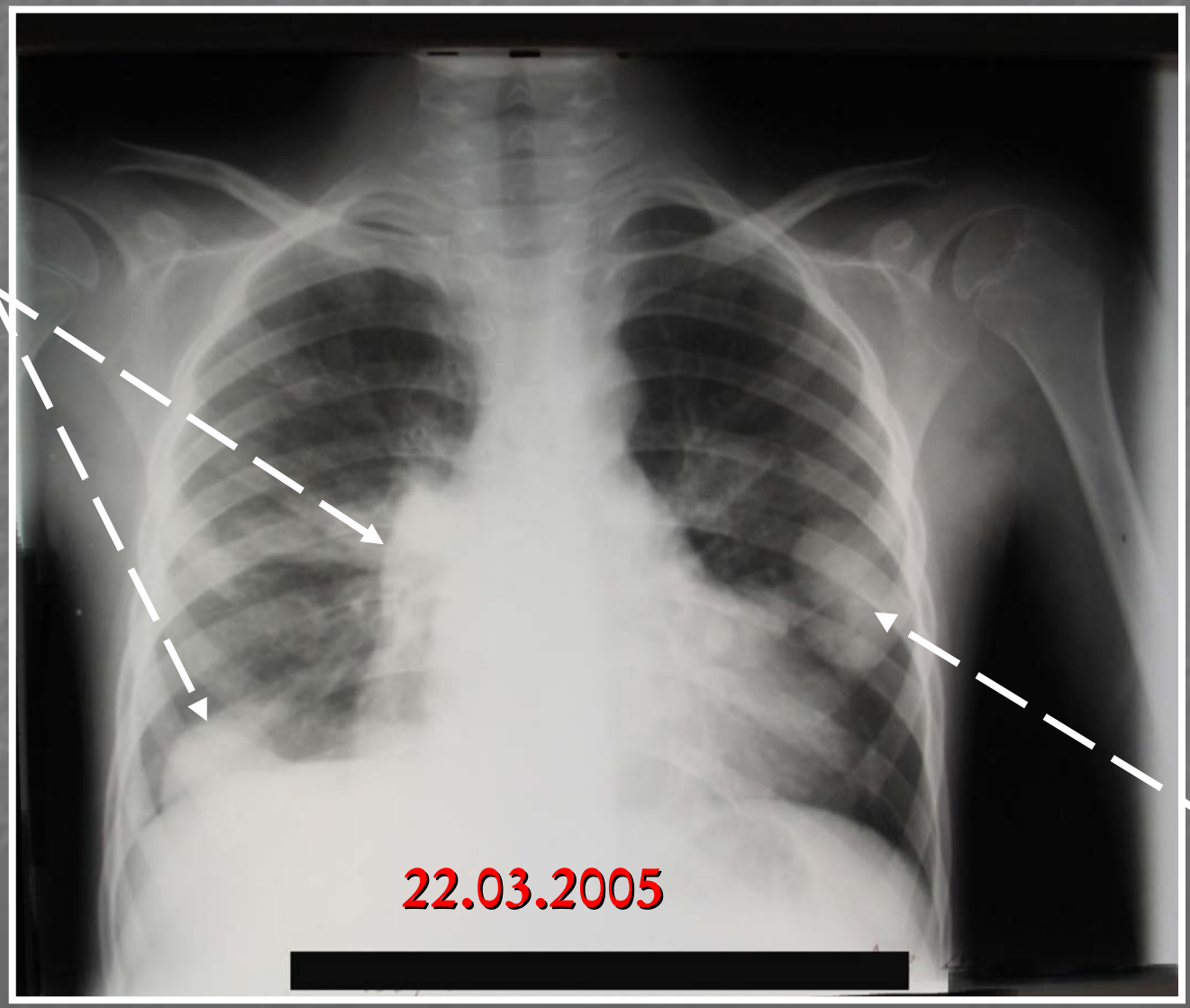
Blood count

	12.01 2005	21.02 2005	05.03 2005	16.03 2005	21.03 2005	27.04. 2005
WBC x10^9/L	17,9	25,6	30,1	52,3	41,2	17,3
LYM x10^9/L	8,1	4,4	7,6	5,7	6,6	6,62
%	45	17,2	25,4	11	16	38,3
HGB g/L	92		78	90	89	88
MCV fl	63,6	57	65,3	58,9	59,6	63
MCH pg	18,5	18,5	17,0	18,6	18,5	19,3
PLT x10^9/L	880	508	1389	849	708	722
ESR mm/h (W)	36	19	64	40	34	36
CRP mg/l				298		

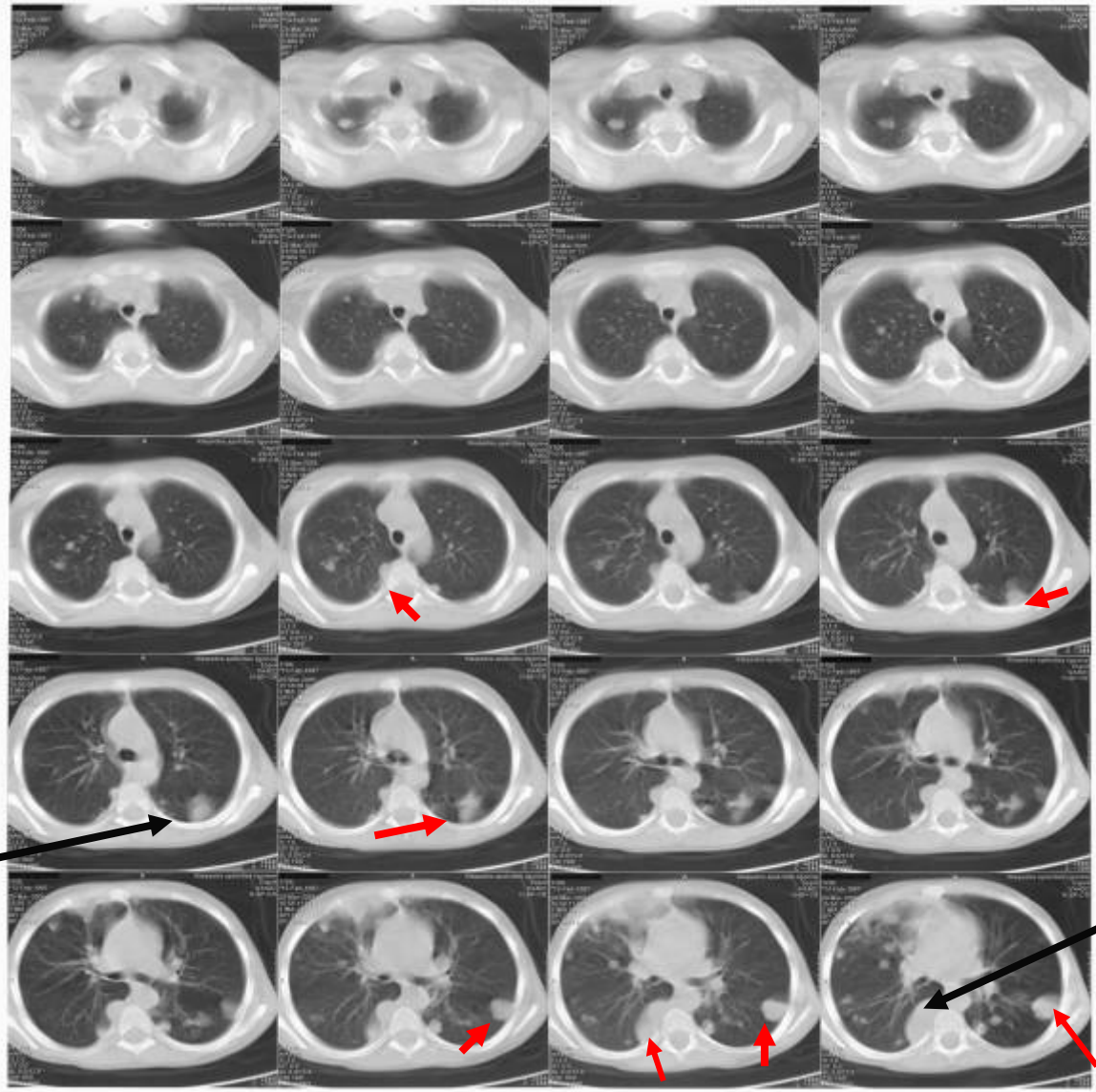
Disease Course (9 months later)



Disease Course (9 months later)



Disease Course (23.03.2005)

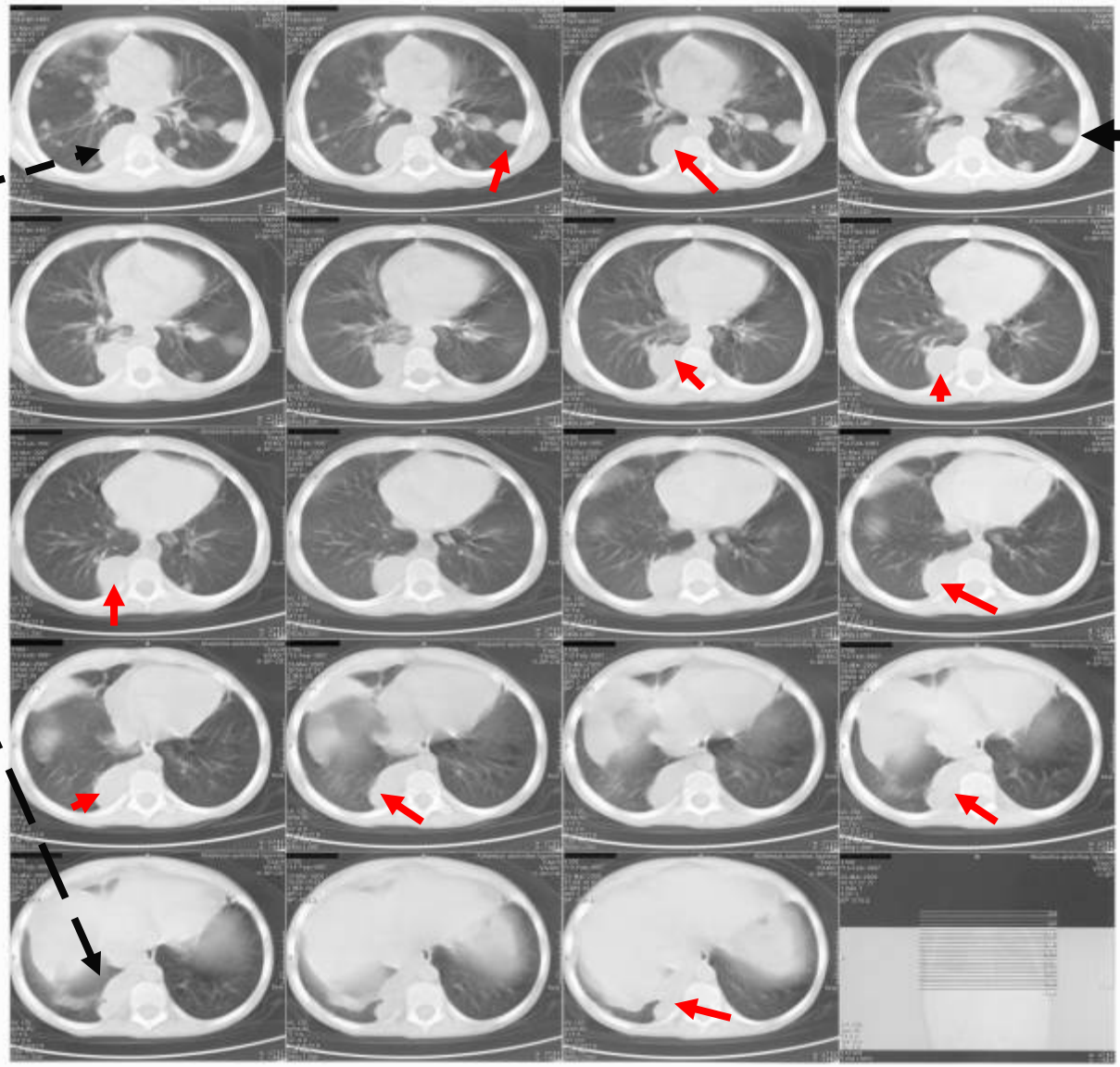


MTS ?

CT:
Neuroblastoma
in susp.

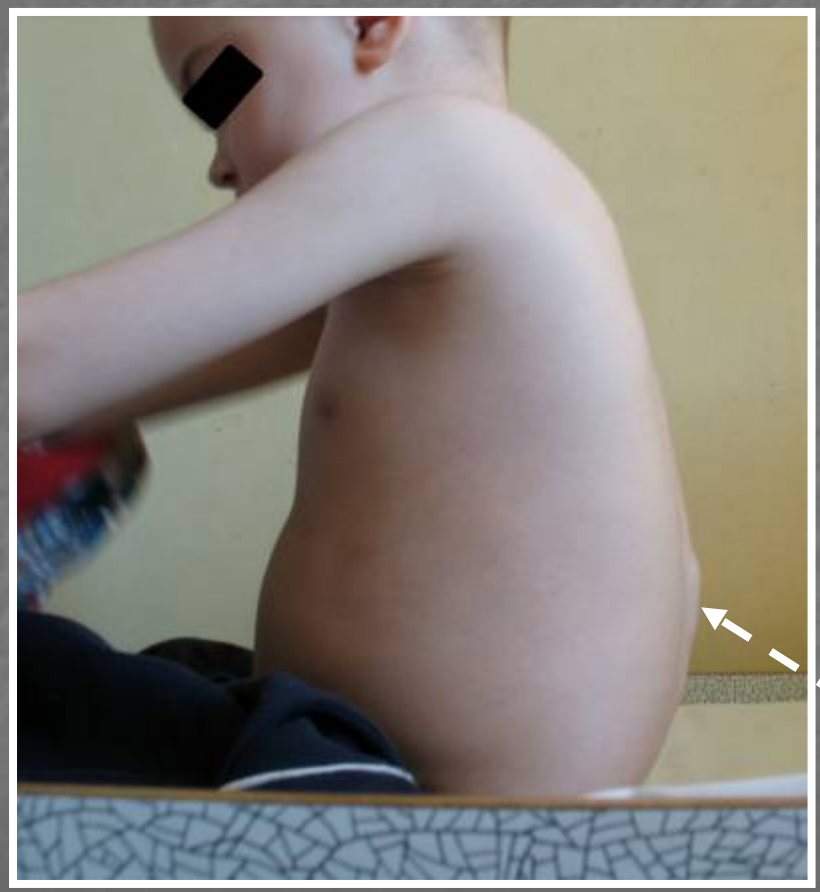
Disease Course (23.03.2005)

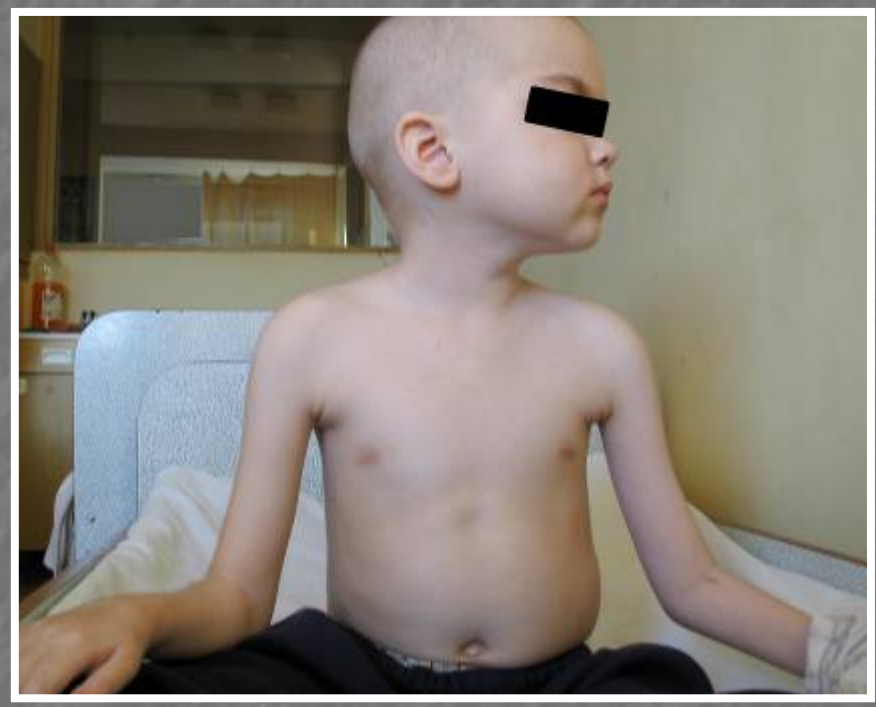
Chest CT:
Neuroblastoma
in susp.



MTS?

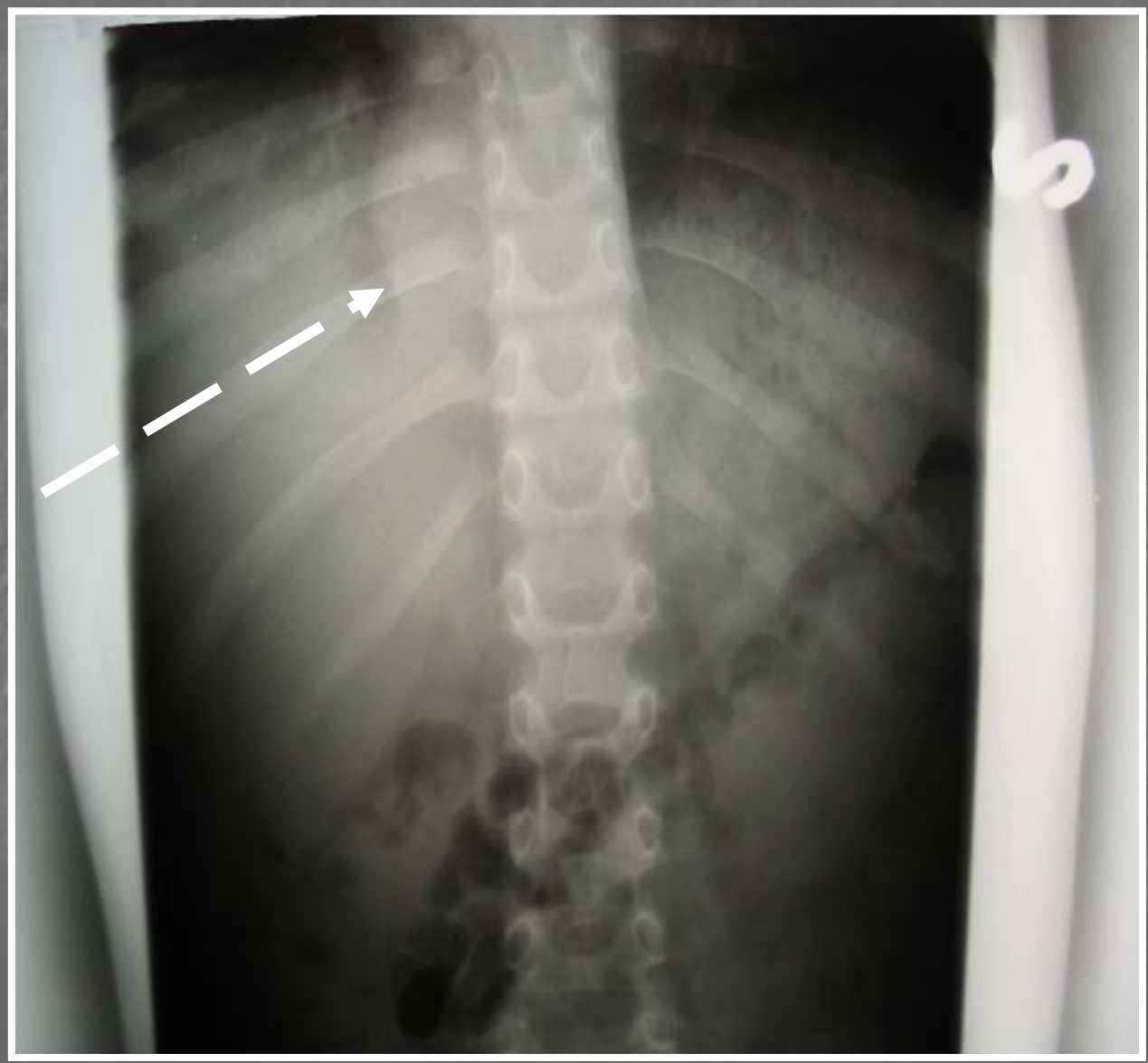
Disease Course





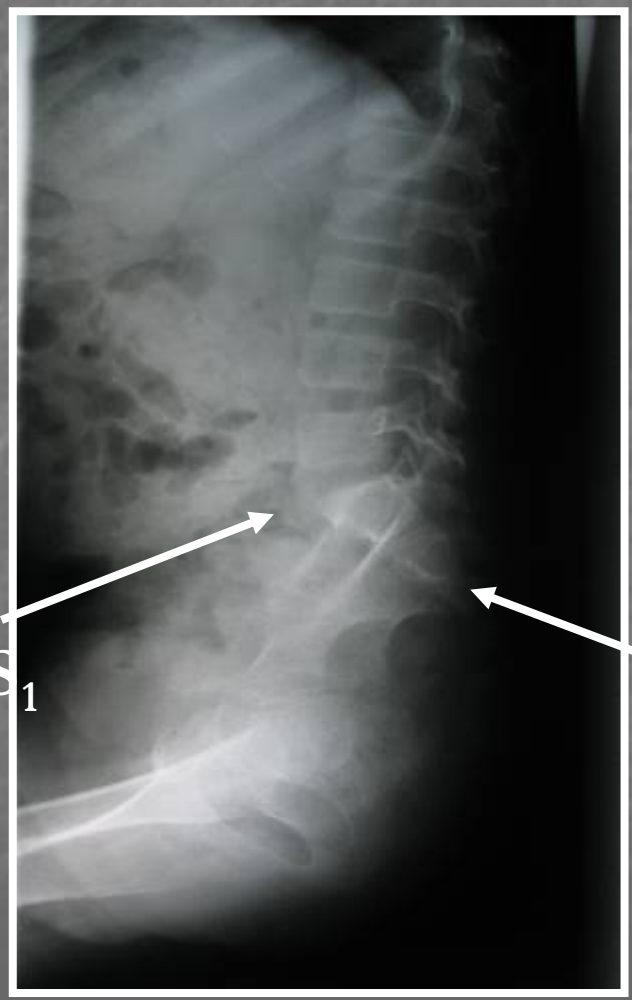
Spinal prominence

Thoracic spine x-ray (07.04.2005)



Paravertebral additional opacity Th VIII -XI

Thoracic spine x-ray (07.04.2005)



Prolabation of intervertebral disk L_5 - S_1

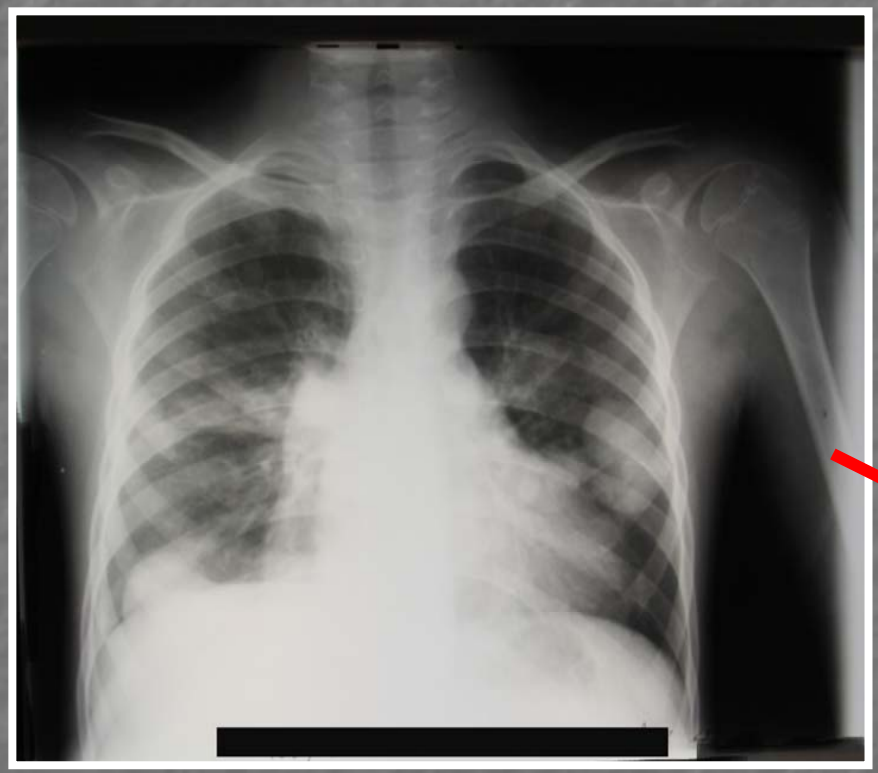
Painful lower back

Laboratory investigations

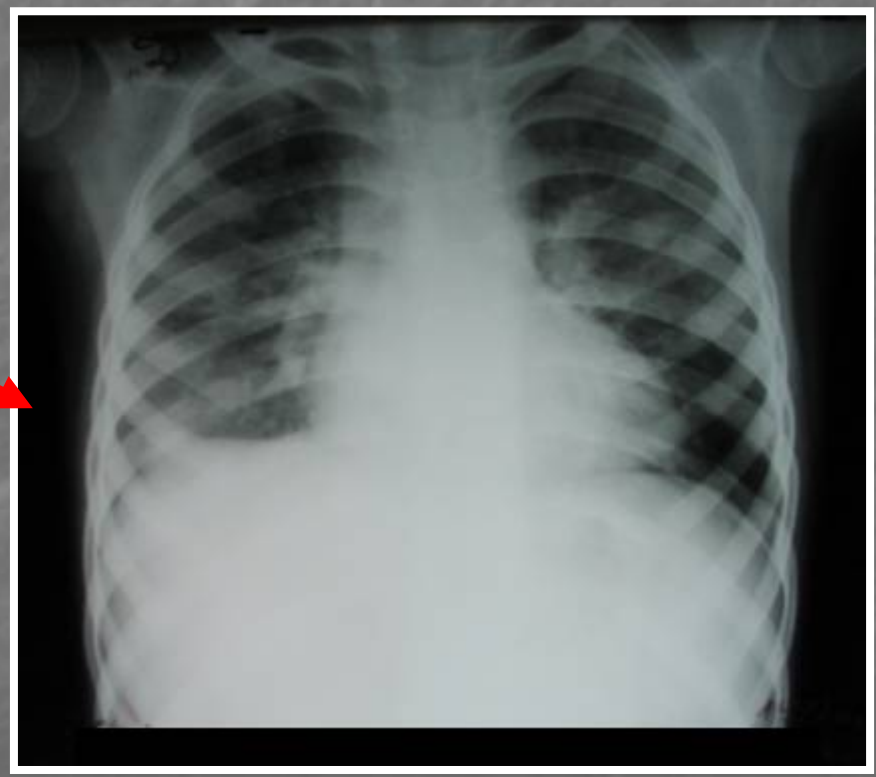
- Culture from synovial fluid (-).
- Hemoculture
  for aerobes, anaerobes, fungi (–).
- Stool for giardia cysts –
  giardia intestinalis (+).
- Bone marrow: haemophagocytosis.

Chest x-ray

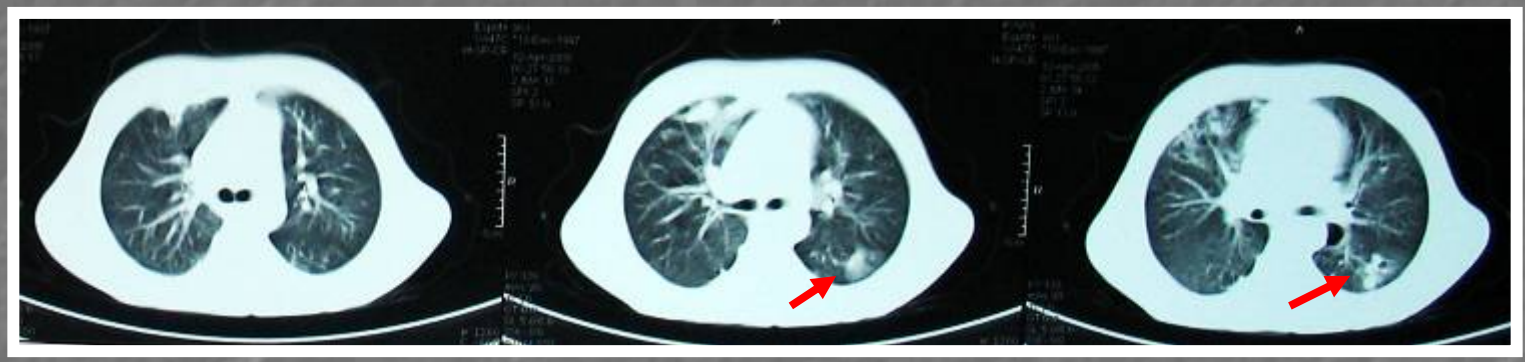
22.03.2005

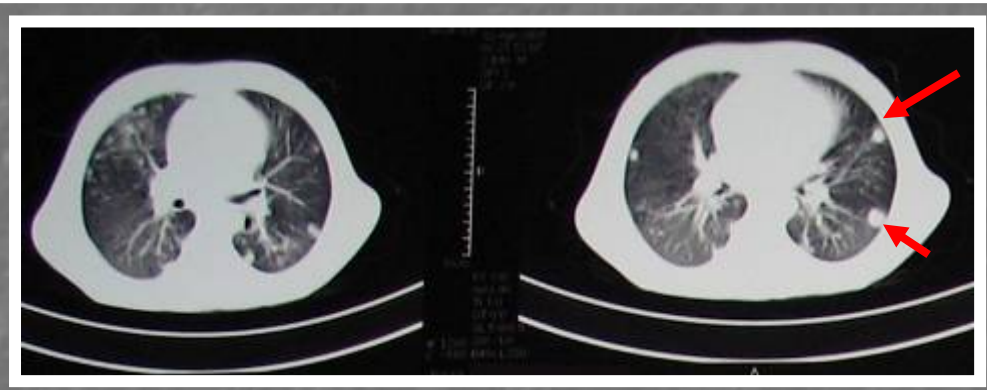


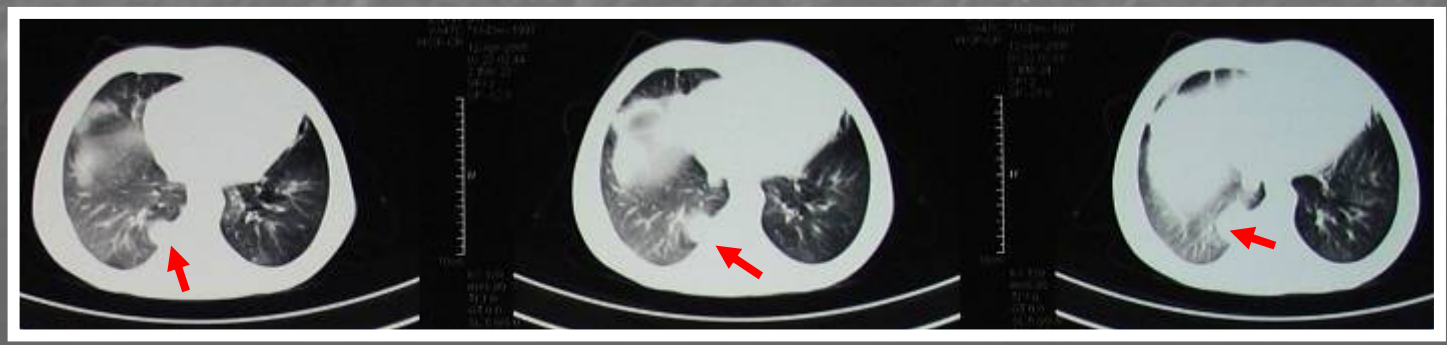
11.04.2005



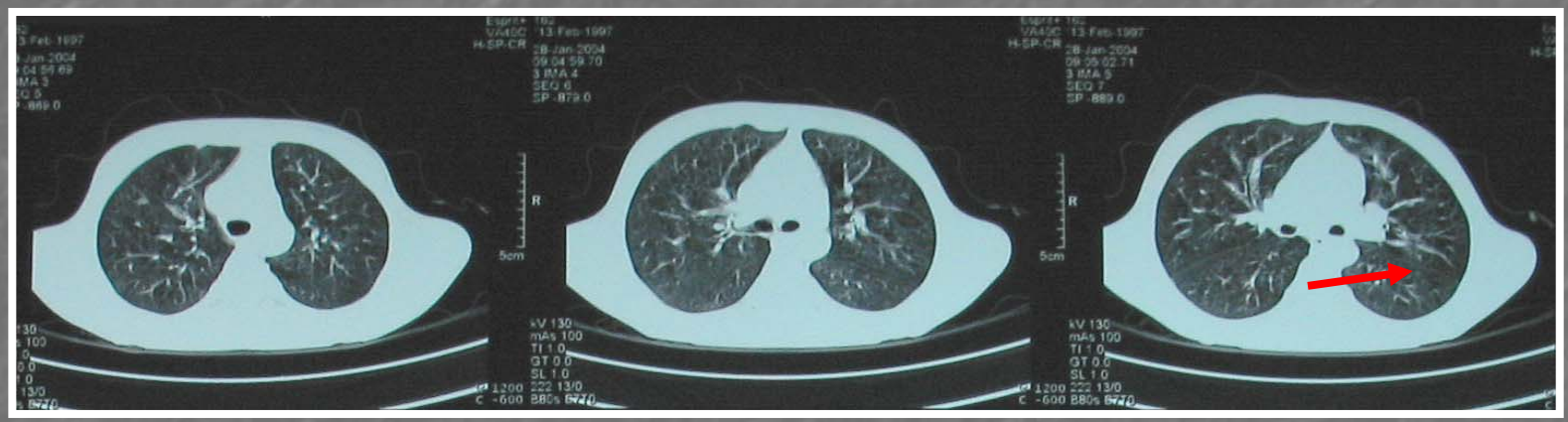
Chest CT (12.04.2005)

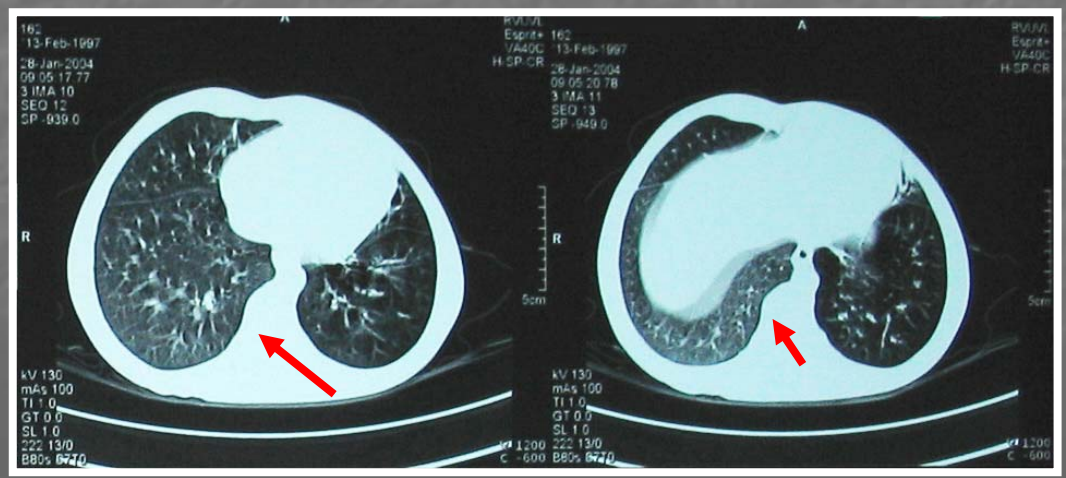


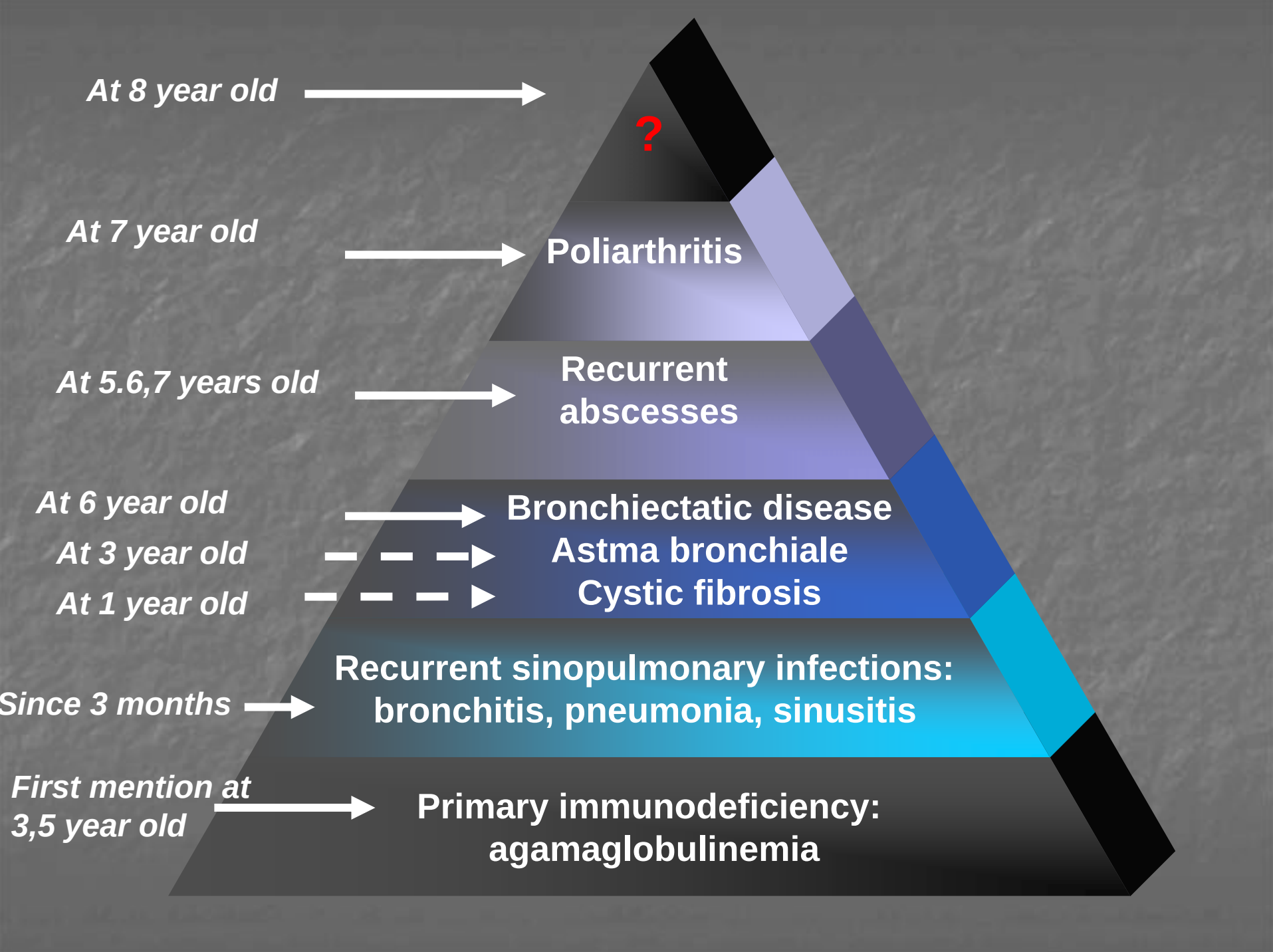




Chest CT (18.04.2005)






At 8 year old
?
At 7 year old
Poliarthritis
At 5.6,7 years old
Recurrent abscesses
At 6 year old
Bronchiectatic disease
At 3 year old
Astma bronchiale
At 1 year old
Cystic fibrosis
Since 3 months
Recurrent sinopulmonary infections: bronchitis, pneumonia, sinusitis
First mention at 3,5 year old
Primary immunodeficiency: agamaglobulinemia

Conclusions

- 85% of agammaglobulinemia patients are males suffering from XLA due to defect in the gene encoding BTK.
  So we consider that our case could be conjuncted with mutation in this gene.
- Persisting, recurrent pulmonary infections led to bronchiectasias.
- Agamaglobulinemia and recurrent infections –
  the reason of autoimmune poliarthritis.
- Patient's family members should be genetically tested.
- Delay diagnosis.

Questions

- Flow cytometric analysis of PB showed complete absence of B-lymphocytes. Could we have another type of mutation such as IGH-Cμ ?
- Could we escape poliarthritis with the earlier started substitution IVIG therapy?
- What etiology of lungs changes could it be?
- What further management do you suggest?
- Does a lobotomy of the lung would be helpful ?

Thank you for attention