Corpus Callosum Agenesia and Lymfopenia

Case Report

- 2e child of non-related parents
- Healthy sister
- No familial history

Born at 38 weeks

GG 3485 gr

First week of life event free

After first week

- failure to thrive
- recurrent episodes of fever

Physical examination

Hypotonia, opistotonus
G 3960 gram
Kinky hair
Cataract right eye
High palatum
Enlarged liver and spleen

Westeinde op 13/6 (lft. 7 weken) voor failure to thrive

Urineweginfectie 15/6

LP: bloederig: vermoeden intra-cerebrale bloeding: verwijzing JKZ

Neurologisch

MRI brain: corpus callosum agenesia
Opistotonos
Hypotonie
Microcefalia
High palatum
Elevated CK

Eyes	Cataract
	VEP: blindness of cerebral origin

Hematological findings

Several episodes of Normocytaire anemia with reticulocytosis

Coombs negatif

Bilirubine normal

No signs of occult blood loss

Gastro enterological findings

Elevated Liver enzymes

- AST 255 U/L
- ALT 139 U/L
- LDH 1240 U/L
- Ferritin max. 45442 mg/l

Immunological findings

Recurrent fever (3 days/week)

Persistent and chronic Candida Albicans infection

Very few positive cultures

1x pos. E. Vulneri

Urine Proteus

Urine Klebsiella

Cardial complication

- Severe Myocarditis with admission for several weeks.
- Recovered
- No infectious agent shown

	31-07-2006	3-08-2006	2-11-2006	05-03-07
leucocyts	10900	3500	11500	4600
lymphocyts	3400	2200	1610	1909
CD3	2480	1502	996	1418
CD3+CD4+	2070	1307	837	1132
CD3+CD8+	440	98	160	278
CD3- CD56+CD16+/-		131	135	126
CD3-CD56+CD16+		113		77
CD19+	580	509	494	303
CD20+		512	490	307
CD4 RA CD4 RO		1118 170	592 224	832 258
CD8 RA CD8 RO		169 30	133 28	233 44
CD19 CD27		2%	5%	4%

T cell stimulation tests

PHA: 400 (> 17000)

CD2-CD28: 36300 (>17000)

CD3: 70 (> 1500)

CD3-CD28: 7000 (> 17000)

Background 105 (< 500)

Immuunglobulines

1 month	8 months
IgA 0.4 g/l	0.44 g/l
IgM 0.3 g/l	0.67 g/l
IgG 4.5 g/l	4.59 g/l

IgD Normal

Normal respons to vaccination

Diagnosis?

- Mitochondrial depletion Syndrome?

Fatal neonatal-onset mitochondrial respiratory chain disease with T cell immunodeficiency.

Reichenbach et al

Pediatr Res. 2006 Sep;60(3):321-6.

Severe recurrent infectious diseases

Anemia, and thrombocytopenia.

Severe psychomotor retardation,

Axial hypotonia,

Disturbed pain perception

Hypoplasia of corpus callosum

Impaired myelinization of the temporo-occipital region

Lack of CD8(+) T lymphocytes and NK cells

Decrease CD45RO- CD8(+) lymphocytes

Diminished Activation of T lymphocytes via IL-2

Conclusion

- Infant with recurrent fever, chronic Candida Albicans infection and multiple neurological problems
  - T-cel penia (CD8, CD4 to a lesser extent)
  - Bad proliferation respons to CD3, PHA
  - Probably normal B cell compartment
  - Normal NK cells
- Mitochondrial DNA depletion syndrome?