

Follow-up of a patient with CERNUNNOS deficiency

Edyta Heropolitańska-Pliszka

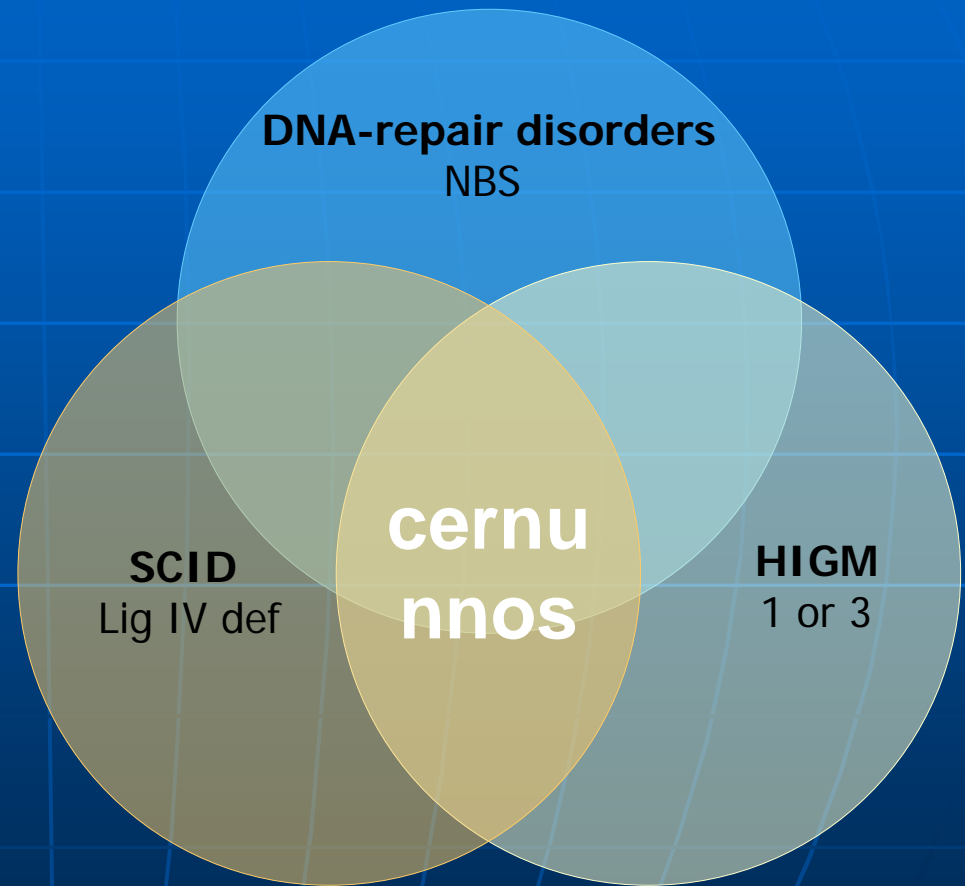
Immunology Department

Children's Memorial Health Institute

Warsaw, Poland

CERNUNNOS / XLF

a new type of
radiosensitive
T-B-NK⁺ SCID



Cernunnos deficiency

core components

- consanguinity
- recurrent bacterial and opportunistic infections
- microcephaly
- severe growth retardation
- dysmorphic features
- hypogammaglobulinemia IgG and IgA
- fluctuating level of IgM
- mild to severe B and T lymphopenia, NK cells not affected
- all T cells of memory phenotype (CD45 RO+)
- impaired response of T cells to PHA
- chromosomal translocations in lymphocytes
- increased radiosensitivity

8-year-old boy

- irrelevant family history
- recurrent bacterial and viral infections of upper and lower respiratory tract since infancy period (otitis, bronchitis and pneumonitis every 2 months)
- significant microcephaly (-5 SD)
- birdlike face
- growth retardation (< 3 pc)

Immunologic investigation

- IgG 120-530 mg/dl,
IgA 6-18 mg/dl,
IgM 921-1390 mg/dl
- CD19+ 4,3% - 81 cells/ul
CD3+ 32% - 380 cells/ul
CD16+56+ 43% - 665 cells/ul
CD4+ CD45RO+ 91,8% - 600 cells/ul
CD8+ CD45RO+ 64.7% - 466 cells/ul
- PHA 2635+/-7
anty-CD3 838+/-65
- spontaneous chromosomal fragility
increased radiosensitivity of patient's fibroblasts

CERNUNNOS deficiency

homozygous
stop codon mutation
Y167X

HSCT

- March 2006 - MUD PBPC
(CD34+ $12,7 \times 10^6$ /kg b.m)
- Conditioning regimen reduced because of
breakage of chromosomes (FluCyATG)
- Early outcome:
 - +12 day - GVHD II stage in skin (steroids)
 - +17 day - good haematological
reconstitution
 - +27 day - complete chimerism

+ 62 day

- good clinical condition, no symptoms of infection
- complete chimerism, no signs of GVHD
- immunosuppression: CsA and steroids (Encorton 0,5 mg/kg b.m.)
- prophylaxis: Co-trimoxazole, Azithromycin, Acyclovir, Fluconazole

+155 day

- hemorrhagic cystitis of unknown origin (polioma-, adeno-, CMV, EBV excluded)
- treatment: forced diuresis, IVIG substitution, intravenous Acyclovir
- +210 day – good clinical condition, normal blood and urine tests, complete chimerism

+385 day

- Protracted fever with lymphadenopathy, skin changes (chronic GVHD)
- CMV PCR (-)
- Aspergillus ELISA 0,452 PCR (-)
- Cryptosporidium sp. PCR (-)
- EBV DNA 140-560 copies
- Diagnosis: EBV infection
- Treatment: Azithromycin, Co-trimoxazol, Acyclovir, Worikonazol, IVIG every 10 days, UDCA
- WBC – 7,8 K/uI
 - N-29% L-35%
 - E-27% AL-2%
 - M-7%
- Hgb – 10,2 g/dl
- Plt - 135 K/uI
- GOT – 110 U/I
- GGTP – 335 U/I
- CRP - 1,2 mg/dl
- LDH – 245 U/I

+425 day - last follow-up

- IgG 590 mg/dl,
IgA 41 mg/dl,
IgM 60 mg/dl
- CD19+ 12,3% - 405 cells/ul
CD3+ 69% - 2310 cells/ul
CD16+56+ 13% - 469 cells/ul
- Alone 337+/-80
PHA 16871+/-645
CD3 16199+/-125
- Complete chimerism

Thank you for attention

