HSCT in a patient with hyper IgM syndrome - our recent experience -

Aleš Janda, Renata Formánková

Department of Immunology
Clinic of Paediatric Haematology and Oncology
2nd Medical School of Charles University
University Hospital Motol, Prague

ONDŘEJ, 8 month old boy

ONDŘEJ Personal history

- vaccinated with BCG
- in **3 months** **lymphnode enlargement in armpit** ➡ suppuration ➡ puncture ➡ healing
- in **4 months** **cough**
- **runny yellow-green stool** longterm
- since **2 month** of age **failure to thrive**

ONDŘEJ

Growth chart

ONDŘEJ Symptoms at diagnosis

- in **8 months** thrush in oral cavity
- afebrile, **weight loss** (⬇ 200 g from check-up in 6 months), **tachypnoea**
- **sat. O_2 80%, leukocytosis 37 x10^9/l,** Hgb 10,4 g/dl, trombocytosis 837x10^9/l
- ⬇ ESR, ⬇ CRP

ONDŘEJ Microbial investigation

- **PCR CMV** **blood + BAL +**
- **PCR *Pneumocystis carinii*** **blood + BAL +**
- PCR mycobacteria blood - BAL -
- test of stool on *Cryptosporidia* negative

ONDŘEJ Immunological investigation

↓ **IgG**	**0,6**	g/l	[NR 3.6-7.7]
↓ **IgA**	**< 0.06**	g/l	[NR 0.1-0.6]
↓ **IgE**	**< 1**	IU/ml	[NR 0-30.0]
↑ **IgM**	**1,98**	g/l	[NR 0.3-1.4]

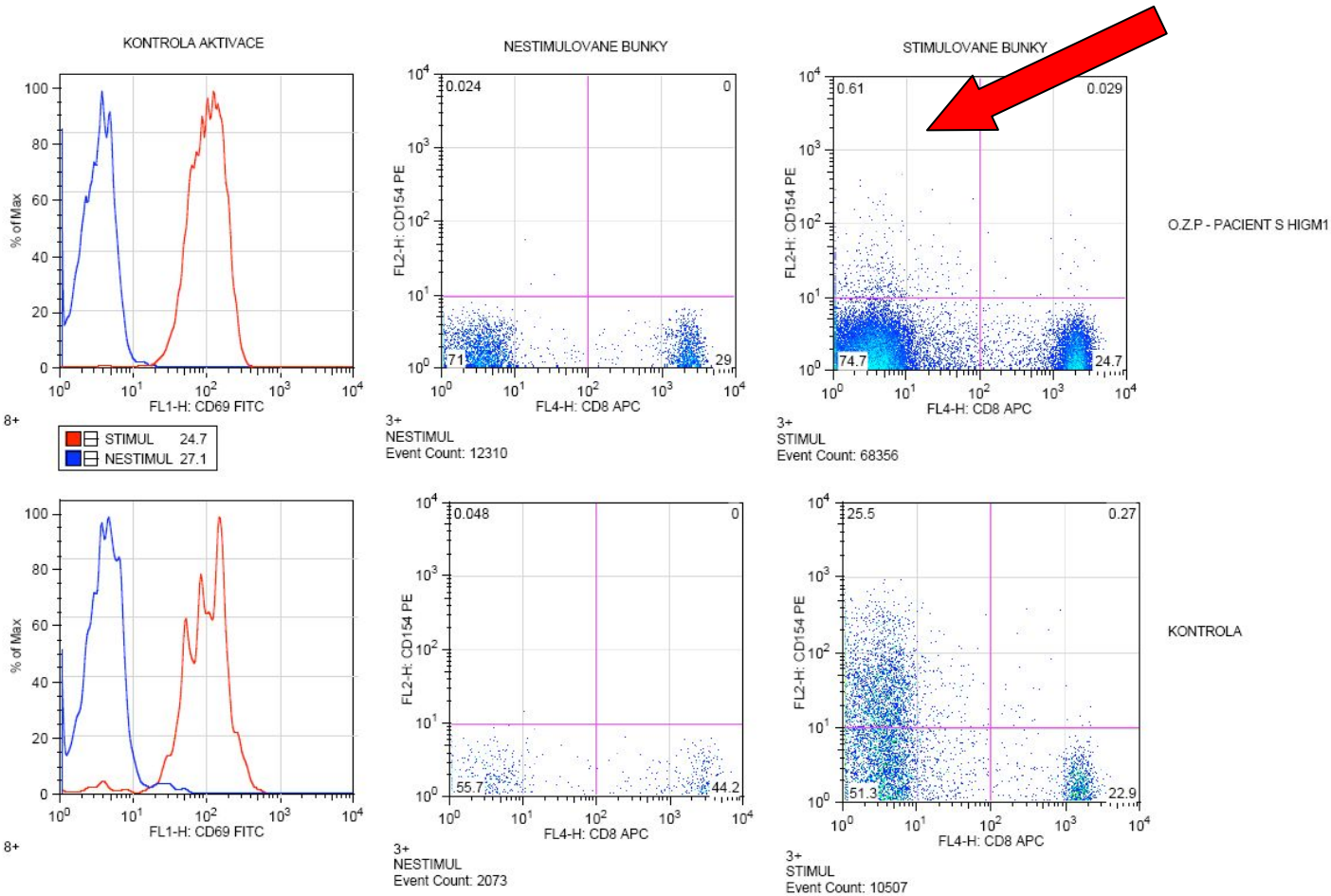
number of lymphocytes

functional tests

- (blastic transformation)
- (NBT)

} normal

ONDŘEJ Flow Cytometry

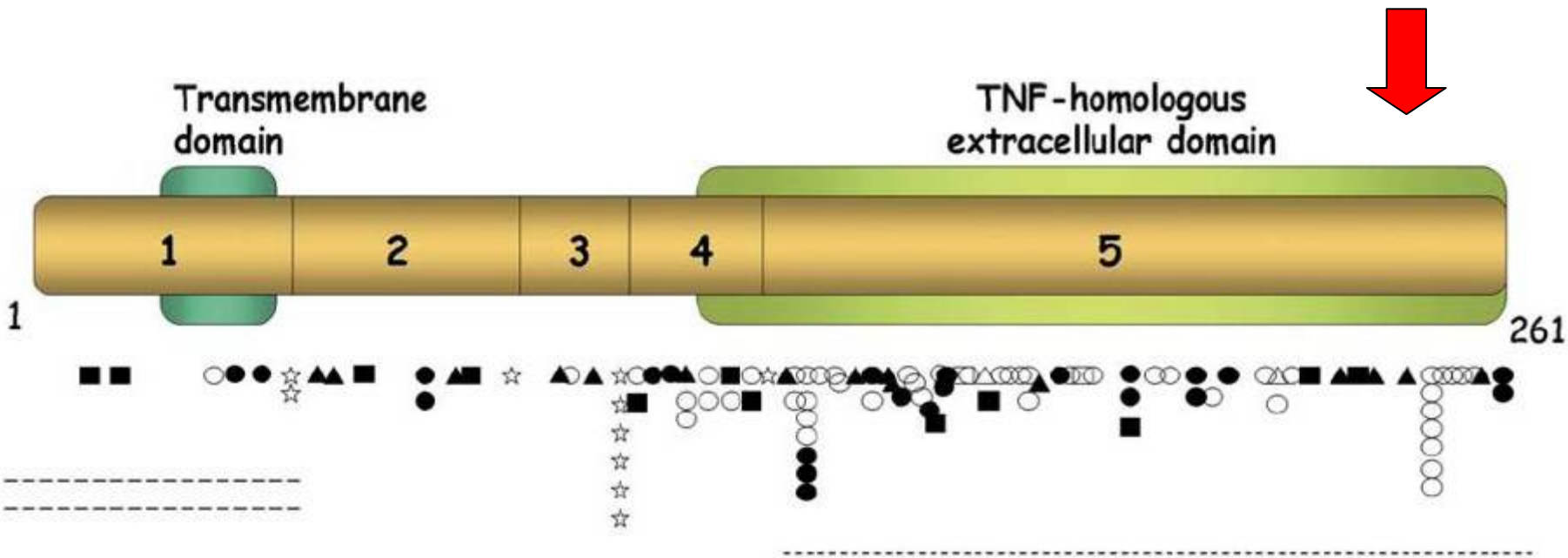


Molecular genetics

ONDŘEJ

Xq26

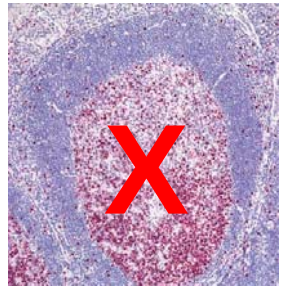
Mutation in 5th exonu of CD40L gene
Aminoacid substitution Tre254Met
(dr. Genevieve de Saint Basil, Neckar, Pařiž)

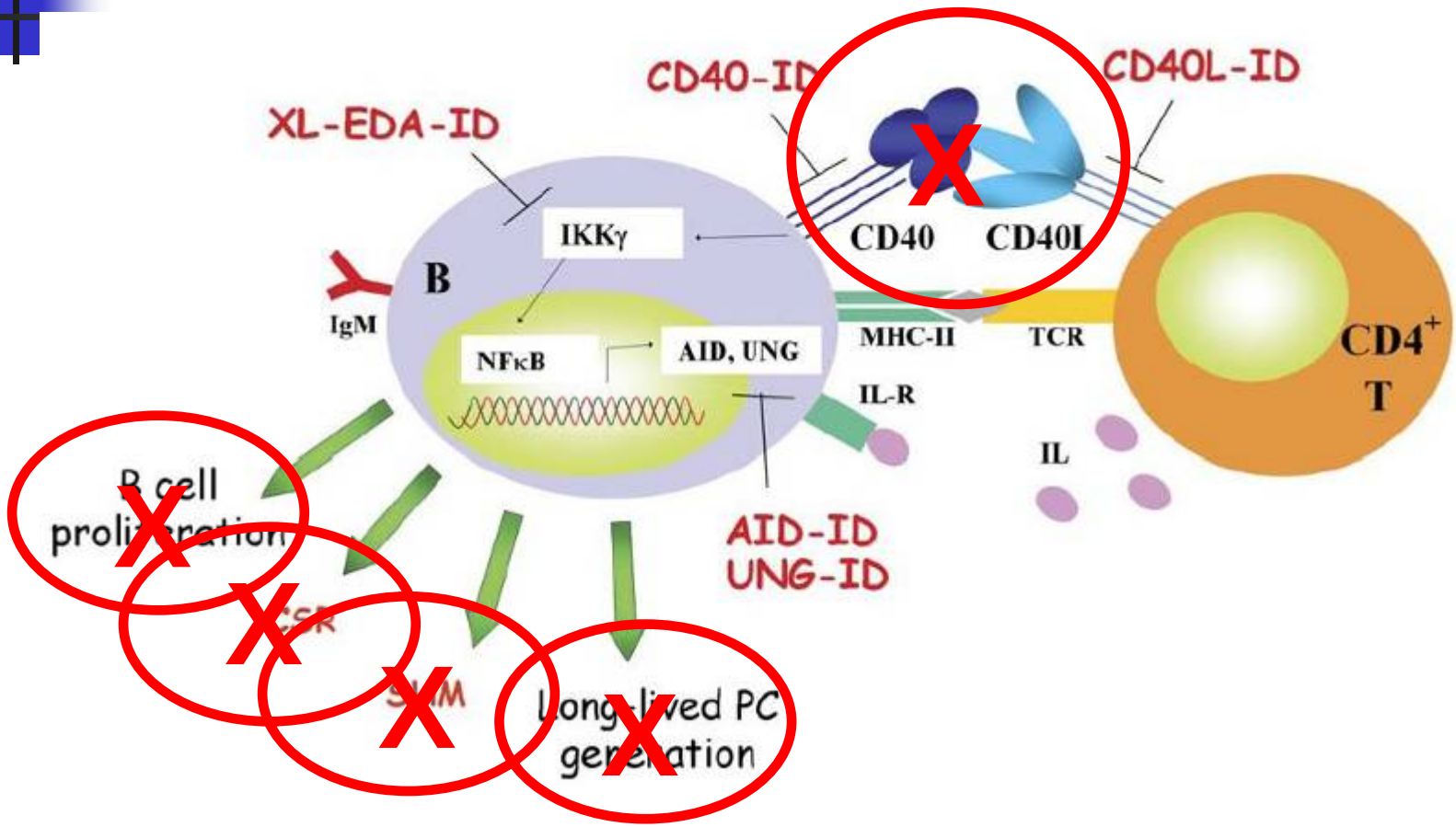


Mother is carrier

Notarangelo, J Allergy Clin Immunol 2006, 117, 855-64

Defects in HIGM





Notarangelo, J Allergy Clin Immunol 2006, 117, 855-64

Clinical symptoms

- insufficient antibody production ➡ **bacterial inf.**
- defect of cooperation T-DC ➡ **opportunist, viral inf.**
- Defect in negative selection of autoreactive clones in thymus ➡ **autoimmunity**
- antigenic stimulation (inf.)
- inaccurate regulation

} ➡ **tumours**

HIGM1 Treatment and prognosis

- regular IVIG substitution
- prevention of **pneumocystic** pneumonia: cotrimoxazol
- in case of neutropenia: G-CSF
- prevention of **cryptosporidial** infection: hygienic regime, use of boiled water
- in case of malabsorbtion: total parenteral nutrition
- sometimes liver transplantation needed
- **only 40 % of patients reach 25 years of age**

- **HSCT is curative**

Gennery, Blood 2004,103, 1152-1157

ONDŘEJ Supportive therapy

- **trimetoprim** 20 mg/kg/day
- **ganciclovir** for 3 weeks
- **antimycotics** (fluconazol)
- **azitromycin** to prevent cryptosporidial infection
- **antiTBC drugs** (INH, RIF) to prevent BCG infection
- **IVIG** 0.5g/kg every 3-4 weeks
- **G-CFS** if ANC < 1000

- **indicated for allogeneic SCT from identical sibling**

ONDŘEJ January 2007 – before SCT

- no signs of respiratory infection
- good oral intake, no diarrhea, but persistent failure to thrive (7,5 kg)
- no signs of cryptosporidial infection, normal hepatic function and ultrasound imaging
- Chest X-RAY - slight residual interstitial changes

ONDŘEJ Stem cell transplantation I

- **February 9, 2007** (aged 12,5 months)

- **Donor:** HLA identical sister (16 years)
- **Graft:** BM (NC 8,6x10^8/kg, CD34+ 11,5x10^6/kg)

- **Conditioning:** Busulfan (20mg/kg)
  Cyclophosphamide (200mg/kg)

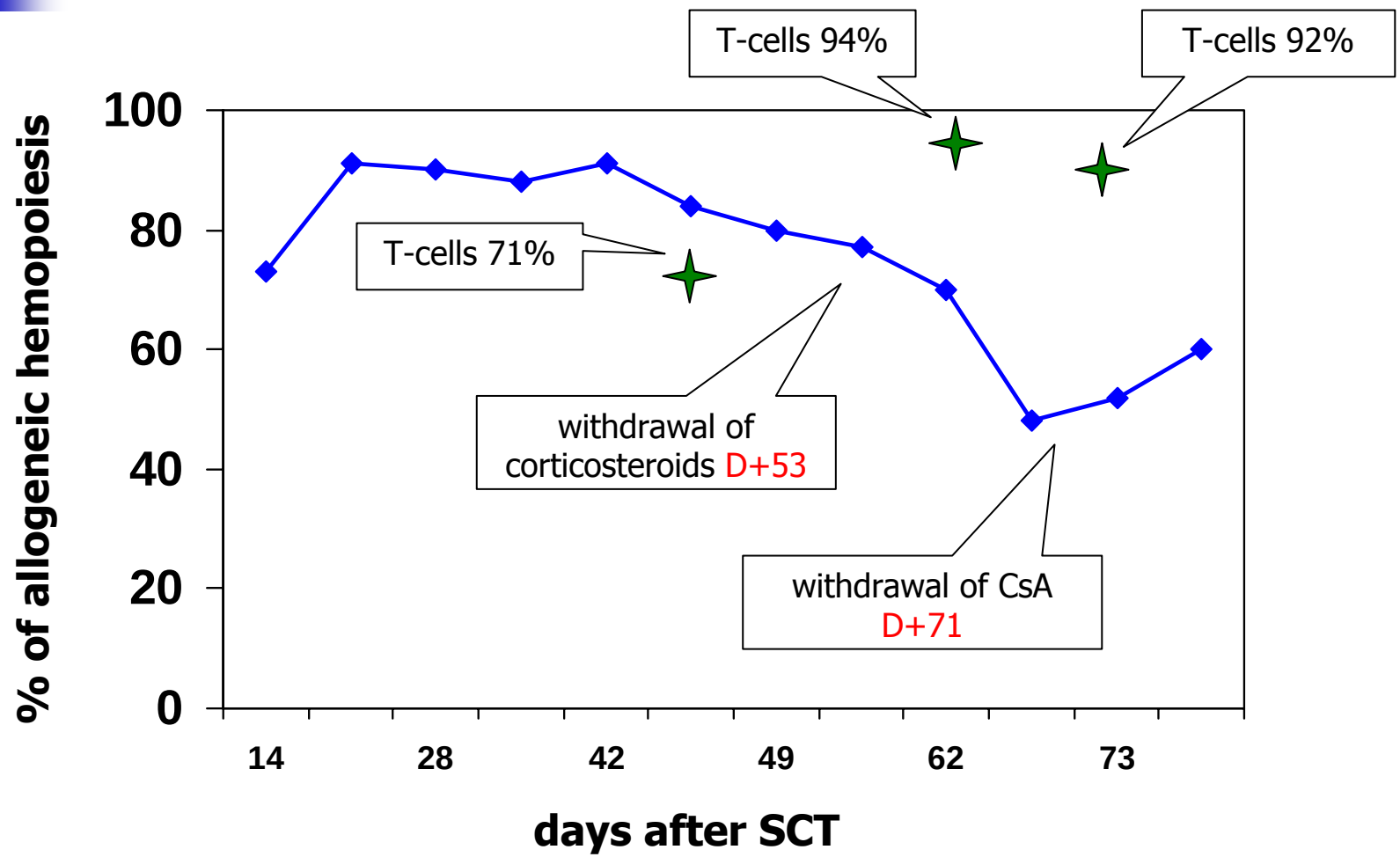
- **GVHD prophylaxis:** Cyclosporine A, Methotrexate

ONDŘEJ Stem cell transplantation II

- **Engraftment:** ANC D+21, Plt D+20
- **GVHD:** gr. II (skin 3, GIT 1) on D+28
  therapy: corticosteroids 2mg/kg
- **Complications:** febrile neutropenia (D+11)
  CMV infection (D+32) – GCV
- **Discharge from SCT unit:** D+ 80 (aged 15 months)

ONDŘEJ

Hemopoietic chimerism



ONDŘEJ 3 months after SCT

- without immunosupressive treatment
- no GVHD
- no signs of infection

- **stable mixed chimerism**
  (50-55% of allogeneic hematopoiesis in PB;
  90-95% in T-lymphocytes)

ONDŘEJ Team work

- Vlastimil Král
- Dalibor Jílek

Centre of Immunology and Microbiology
Ústí n. L

- Veronika Skalická
- Jakub Zieg
- Květa Bláhová
- Jan Lebl
- Renata Formánková
- Petr Sedláček
- Jan Starý

Pediatric Clinic

Clinic of Pediatric Haematology and Oncology

- Aleš Janda
- Jiřina Bartůňková
- Anna Šedivá

Department of Immunology
University Hospital Motol, Prague

- Genevieve de Saint Basile

INSERM, Necker, Paříž