Hematopoietic stem cell transplantation in mucopolysaccharidosis

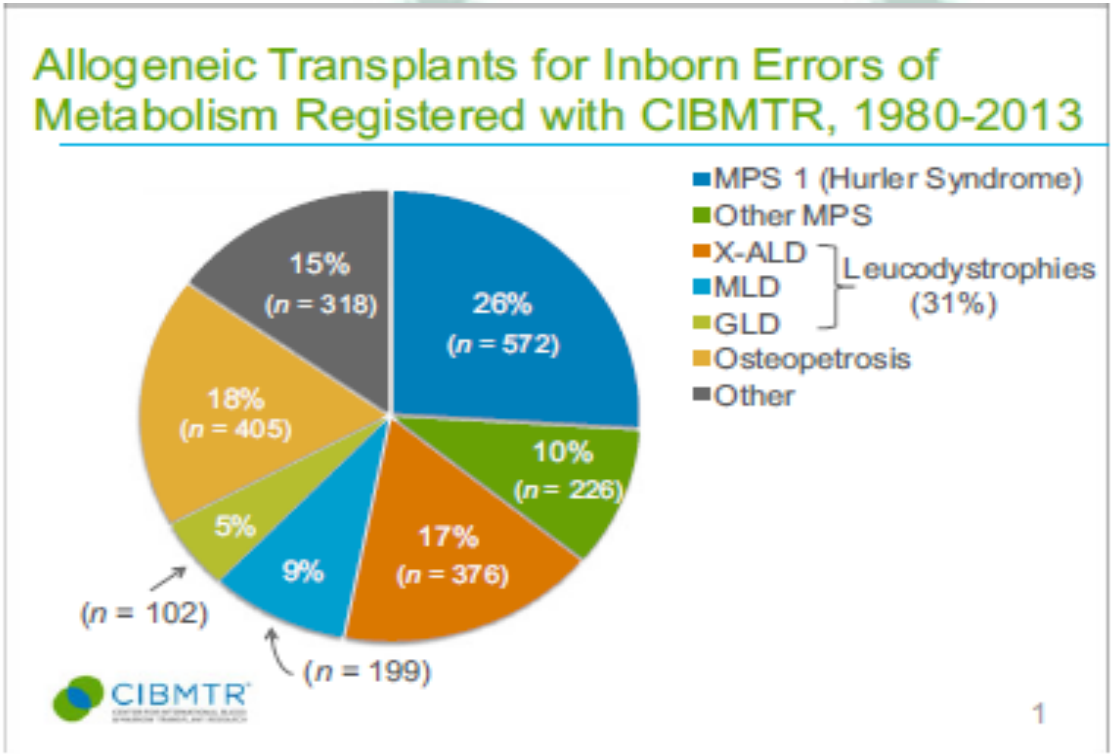
Vérképző őssejt-átültetés, mint terápiás lehetőség mukopoliszacharidózisban

Horváth Orsolya, Kállay Krisztián, Benyó Gábor, Kassa Csaba, Csordás Katalin, Stréhn Anita, Sinkó János, Kriván Gergely

Egyesített Szent István és Szent László Kórház, Gyermekhematológiai és Őssejt-transzplantációs Osztály

Transplantation in inborn errors of metabolism

- Allogeneic hematopoietic stem cell transplantation (HSCT) was researched in numerous lysosomal diseases, including MPS I, MPS II, inherited lysosomal leukodystrophies and Krabbe disease.
- The first HSCT in Hurler-syndrome was performed in 1981.
- Since the 1980s, 2000 patients with an inborn error of metabolism have been transplanted.



Boelens et al. Transplantation in inborn errors of metabolism: current considerations and future perspectives. BJH 2014

Stem cell transplantation

- Hematopoietic stem cell transplantation is a standard therapy for young patients with mucopolysaccharidosis I (Hurler-syndrome).
- HSCT is indicated when MPS I (Hurler-syndrome) patients are <2 years of age and show an intelligence quotient (IQ) of ≥ 70.

How can stem cell transplantation in MPSII help?

- Enzyme replacement therapy's efficacy has been demonstrated for visceral organ and soft tissue involvement, but poor or no efficacy was observed for brain involvement, because of poor penetration across the blood-brain barrier.
- HSCT allows donor-derived, enzyme-producing cells to migrate into the brain and other organs, providing a permanent form of enzyme replacement

How can stem cell transplanation in MPSII help?

- To evaluate the efficacy and benefit of stem cell transplantation in MPS II patients, a nationwide retrospective study in Japan was made (Tanaka A et al., Molecular Genetics and Metabolism 2012, 107: 513-20)
- HSCT showed effectiveness towards brain or heart involvement, when performed before signs of brain atrophy or valvular regurgitation appear.
- HSCT is worthwhile in early stages of the disease for patients with MPS II.

Stem cell transplantation is a worthwhile treatment for MPS II when it is performed before signs of brain atrophy and before heart valvular regurgitation appear

First MPS II HSCT in Budapest

- **15 months old boy at transplantation**

- His brother was diagnosed with MPS II with serious CNS complications
- The molecular genetic survey found a new mutation in the IDS gene
- The mother is heterozygote carrier
- From May 2013. 6 mg per week Elaprase was given

Firts MPS II HSCT in Budapest

- Conditioning therapy: Thiothepa, treosulfan, fludarabine + ATG
- 2013.08.06. Matched unrelated donor stem cell transplantation
- 10/10 HLA matching, bone marrow graft
- No serious complications after HSCT
- Patient engrafted in time
- Half year after transplantation he had mixed chimerism, only 15% donor derived cells
- The enzym level was low

- ERT is continued in every week
- The family moved abroad, a second unrelated donor transplantation can be a therapeutical option

Our Department

Second MPS II HSCT in Budapest

- 22 months old boy at transplantation
- 4 months: Hearing aid
- 6 months: Hepatomegaly in ultrasound
- 14 months: cranial MR in Kaposvár, possibility of MPSII
- Rostock, Germany: low iduronate-sulfatase activity enzym activity
- Molecular genetic survey: IDS gene de novo missense mutation
- 20 months: Elaprase enzyme substitution in every week

Second MPS II HSCT in Budapest

- Conditioning therapy: Thiothepa, treosulfan, fludarabine + ATG
- 2014.07.10. cord blood stem cell transplantation
- 10/10 HLA- matching
- Engrafted in time (ANC>500)

Second MPS II HSCT in Budapest

- Adenovirus infection: cidofovir
- Acute graft versus host disease with skin involvement, treated with steroid (hypertension, diet)

- 30 and 60 days after HSCT he had full donor chimerism
- Enzyme level and GAG in urine are measured on the 30th, 60th and 100th day after HSCT
- During the transplantation procedure he received ERT every week
- After donor derived hematogenesis, ERT shouldn’t be omitted

Risks and benefits

- The disadvantages of HSCT are the morbidity and mortality, associated with the transplantation procedure
- Graft versus host disease
- Infections: bacterial, viral, fungal, protozoon
- HSCT has became progressively safer due to the availability of enhanced techniques for human leucocyte antigen (HLA) matching, improved preparative regimens and supportive care.

All transplant decisions are based on a balance of risk and potential benefits.

Perspective

- Once engraftment has been established, the quality of life of patients will be better than of patients receiving weekly ERT treatment
- HSCT also improves morbidity, when it is performed early
- In the future, genetically engineered bone marrow cells, autologous cord blood cells, or other cells may become good sources for cell transplantation

Conclusion

- Hematopoietic stem cell transplantation is also an available therapeutical option in Hungary for Hunter- syndrome
- HSCT is worthwhile in early stages of the disease for children with MPS II
- Therefore, early screening for MPS II may result in improving of the prognosis

Démétér House

In Démétér House the whole family can live together during the transplantation procedure. After engraftment the children can also sleep and stay with their mother in the house.

www.demeterhaz.hu

Démétér Alapítvány

Thank you for your kind attention!

Köszönöm szépen megtisztelő figyelmüket!