Is allogeneic hematopoietic stem cell transplantation a good indication for patients with SIFD syndrome?

V. Bordon[1], C. Dhooge[1] and P. Verloo[2]

[1] Department of Pediatric Hematology, Oncology and stem cell transplantation, Ghent University Hospital, Ghent, Belgium

[2] Department of neurology and metabolic diseases, Ghent University Hospital, Ghent, Belgium

Background

SIFD syndrome is characterized by sideroblastic anemia, B-cell immunodeficiency, periodic fevers, and developmental delay.

This syndrome is caused by TRNT1 (CCA-adding transfer RNA nucleotidyltransferase) enzyme deficiency.

TRNT1 catalyses the addition of a terminal CCA trinucleotide residue to nuclear and mitochondrial tRNA and this residue binds the amino acid to the tRNA and delivers it to the ribosome during protein biosynthesis. TRNT1 is therefore essential for maturation and function of all cellular tRNAs.

Methods and case description

We report the case of a girl with a history of intrauterine growth retardation and oligoamnios. At neonatal age, she developed anemia; further investigations established a sideroblastic anemia whit hypogammaglobulinemia in association with B-cell deficiency. A compound heterozygous TNTR1 mutation was found, and an SIFD syndrome was diagnosed.

At the age of 7 months, she underwent an allogeneic HSCT with bone marrow of a 10/10 MUD donor. The conditioning was Treosulfan 3x 12 gram/m² + Fludarabine 5x 30 mg/m² + Thiotepa 2x 3.5 mg/kg and ATG. At that moment, she had a mild neurodevelopmental delay with axial hypotonia.

Brain MRI revealed mild bifrontal cerebral atrophy and periventricular brain white matter lesions compatible with demyelination.

The conditioning was well tolerated, and there were no major transplant-related complications.

After HSCT, there was a resolution of the hematological and immunological problems; the sideroblastic anemia was solved, leading to transfusion independence. However, the developmental delay worsened and five months after transplant the girl suffered from epileptic seizures .

The child died at the age of 24 months due to metabolic decompensation. Brain CT scan showed diffuse cerebral edema with loss of gray and white matter differentiation.

Conclusion

SIFD syndrome is newly described congenital metabolic disease, with the range of clinical severity correlating with the degree of TRNT1 loss of function.

Allogeneic HSCT can improve /resolve hematological and immunological aspects in severely affected patients.

However, successful HSCT could not improve the metabolic/neurological aspects of this enzyme deficiency.

The effectiveness of allogeneic HSCT in patients with TRT1 mutations needs to be further investigated; more data is needed for the adequate counseling of patients and their families.

References

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Contact

victoria.bordon@uzgent.be