A seven years quantitative MRI and MRS follow-up study on successful bone marrow transplantation for presymptomatic juvenile metachromatic leukodystrophy

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Introduction

Metachromatic leukodystrophy (MLD, OMIM 250100), a progressive and fatal autosomal recessive inherited disease due to functional deficiencies of the lysosomal enzyme arylsulfatase A, causes widespread damage to myelin membranes of the central and peripheral nervous system. Bone marrow transplantation (BMT) has been advocated as a treatment to halt the progression of MLD. However, detailed long follow-up reports have remained rare, and the effectiveness of BMT in the treatment of MLD is still questionable. We carried out a 7 years MRI follow-up on a boy with juvenile MLD who had received BMT treatment in the presymptomatic phase and remained free of MLD symptoms during the observation.

Materials and methods

Patient: The diagnosis of our patient was made at the age of 3.5 years after an advanced MLD was found in his older brother. An initial MR examination carried out at that time was reported to show discrete brain white matter abnormalities, although clinically he did not show any symptoms. He received bone marrow transplantation (BMT) one year later. In the following 7 years he had normal development without any symptoms of MLD clinically. He now attends a normal school, while he undergoes regular clinical follow-ups. *MR follow-up studies:* Nine MR follow-ups have been carried out during the seven years observation: at the time of 2 months, 10 months, 1.5 years, 2.8 years, 3.7 years, 4.2 years, 5 years, 6 years and 7 years, respectively, after the BMT. The same MRI protocol was used, which included an axial proton/T2 weighted triple turbo spin echo sequence, allowing to carry out brain T2 mapping with consecutive determination of the T2 relaxation times of the brain white and the grey matters. A STEAM sequence was used for single voxel spectroscopy at the parieto-occipital white matter. Informed consent was obtained from the parents of the child.

Results and Discussion

Conventional morphological MRI showed minor stable white matter lesions, as sign of a stagnancy of the demyelination process. Quantitative T2 measurements revealed that the T2 values were elevated in the first follow-up taken two months after BMT, proven the existing minor demyelination before the BMT. In the further following-ups the T2 values moved closer to the normal range. MR spectroscopy revealed a continually increased NAA at the white matter. Altogether the results of the quantitative T2-mapping and MR spectroscopy evidenced not only a stagnancy of the demyelination process but also an ongoing maturation of the brain.

After more than 20 years of performing BMT for MLD, the effectiveness of this treatment remains controversial. In a small number of reports on juvenile MLD cases it was concluded that BMT may halt disease progression but objective evidence of a significant biological effect is difficult to obtain. In the present study the combined results of T2 measurements and MR spectroscopy demonstrate for first time that a successful BMT therapy could not only halt the progress of MLD but also allow ongoing maturation of the brain, and the quantitative MRI methods such as T2-mapping and MR spectroscopy could add objective information on monitoring such experimental therapeutic effects.