HKU leads the Asia's first genetically modified hematopoietic stem cell transplantation for late juvenile metachromatic leukodystrophy patient (MLD)

Supplementary information

Background of MLD and its prevalence

MLD is a devastating lysosomal storage disease caused by a deficiency of arylsulfatase A (ARSA). Without ARSA to breakdown accumulated sufaltides, neural system is toxic and presents progressive damaged. Patients die within a few years and no cure in current clinical management. According to the age of onset of the first symptoms, MLD is divided into early infantile (< Age 1), late infantile (Age 1–2), early juvenile (Age 2–6), late juvenile (Age 6–16) and the adult form (>Age 16). The late-onset forms of MLD, late juvenile and adult, usually present with a more insidious manifestation of a wide range of neurological symptoms, offering ample opportunity for possible therapeutic interventions. Symptoms include, incoordination, lower intelligence, paralysis, Epilepsy and nerve injury. The patient's moving ability will be deteriorated and finally die. MLD is a genetic disease with a fast onset and poor prognosis, which seriously affect patient's quality of life. Apart from supportive therapy, there is no effective treatment for MLD patients.

The prevalence of MLD is about 1.4–1.8 per 100,000 live births, every year, there is around 1,900 new cases worldwide. It is a rare disease: there are estimated to be around 41,000 alive patients worldwide, over 10,000 cases of MLD in Mainland China and around 40-50 patients in Hong Kong. Nonetheless patients with MLD often die before a correct diagnosis is made and those with later onset MLD are often misdiagnosed with attention deficit disorder, such as Attention Deficit Hyperactivity Disorder, or a psychiatric condition. Thus the true frequency of the condition may be higher than reported.

The proportion of male and female patients is nearly the same, with the most common outbreak among infantile, which counts around 50 – 60% of all cases. For juvenile onset, there is around 30-40% while adult form only counts around 5-10%. Results from MRI of MLD patient shows demyelination in brain, and from the blood ARSA checking, the activity of ARSA is lower than normal people by at least 20 %.

About the collaboration

1. The Li Ka Shing Faculty of Medicine, HKU team

The clinical outcome of genetically-modified hematopoietic stem cells was the collaborative work of the team led by Dr Lian Qizhou, Assistant Professor at the

Department of Ophthalmology and Department of Medicine, Li Ka Shing Faculty of Medicine, HKU. Team members include Dr Kent Tsang Kam-sze, Research Scientist of Department of Bone Marrow Transplantation and Cellular Therapy, St Jude Children's Research Hospital，USA, who helped assisting in the positive selection of hematopoietic stem cells for gene transduction, and Dr John Wang Junwen, Associate Professor of Centre of Genome Sciences, Li Ka Shing Faculty of Medicine, HKU assisted in genomic analysis to retrieve integrant sites.

2. The Second People's Hospital of Shenzhen team
(The First Affiliated Hospital of Shenzhen University)

The team was led by Professor Zhuo Jiacai, Clinical Profesor and the Head of Division of Hematology at the Second People's Hospital of Shenzhen, and performed hematopoietic stem cell mobilization and collection, auto-transplantation of genetically modified hematopoietic stem cells.

3. The National Taiwan University Hospital (NTUH) team
The NTUH team led by Professor Hwu Wuh-liang from the Department of Genetic Medicine at NTUH, assisted with some follow-up examinations including blood testing for ARSA biochemical activity, motor and cognitive assessments and MRI imaging, after the patient returned to Taiwan.