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Can patients with epilepsy become bone marrow donors? A case report of allogeneic hematopoietic stem transplantation from child with seizures

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Introduction

Hematopoietic stem cell transplantation (HSCT) is an important treatment option for malignant and non-malignant hematopoietic disorder in adults and children.

The use of matched sibling donors (MRD), unrelated volunteer donors (MUD), unrelated cord blood or haploidentical donors makes HSCT feasible for most of the patients and the number of HSCTs continues to increase each year *(fig.1)*.

Hematopoietic stem cells sources are bone marrow (BM), granulocyte colony-stimulating factor-(G-CSF)-primed peripheral blood (PB) and cord blood (CB); they are used according to different diseases, type of transplant and donor/center preference [1].

Pretransplant donor assessment and testing are very important issues affecting the quality and safety of donation. Several international regulatory bodies, such as European Directives for Donation of Tissues and Cellular Therapy products, published recommendations for donor assessment and suitability. For long time epilepsy was temporary exclusion condition to voluntary BM and PBSC donation, and donors had to be medication or seizure free. It is still unclear if people with history of epilepsy are indeed potential eligible donors, even if a significant increased risk of adverse events in these donors has not been demonstrated. HSCs collection from BM requires general anesthesia, while PBSCs collection requires a treatment with G-CSF mobilization followed by apheresis [1]. Both procedures could be contraindicated in epilepsy.

Case report

This 10-year-old boy was born at 29th week of gestation after in vitro fertilization (IVF); he had two twin brothers (one monozygotic and one heterozygous) in good health. The mother

received two doses of betamethasone before delivery. In family history, two second-degree relatives of the mother had epilepsy. Auxometric parameters of the child were adequate for gestational age. APGAR scores were six and eight at 1 and 5 minutes.

In the first month of life he had respiratory distress syndrome that was managed with exogenous surfactant treatment, oxygen and caffeine therapy, and transient jaundice that required phototherapy *(fig.2).* Brain ultrasonography at 2 months showed bilateral subependymal cystic area and left parenchymal anechogenic area; brain Magnetic Resonance Imaging (MRI) at 3 months showed poroencephalic areas in posterior deep white matter of both cerebral hemispheres, greater on the left side, where 7 mm paratrigonal cystic cavity and ectasia of the lateral ventricle were observed.

At the age of 18 months, the child had epileptic seizures, characterized by repeated jerking movements of the right limbs, both in wakefulness and sleep.

The patient came to our attention at the age of 23 months, due to the appearance of daily atypical absences and swallowing automatisms, in wakefulness, and right-version of the head, repeated jerks of the limbs and drooling, in sleep.

He exhibited double spastic hemiplegia; no notable dysmorphic features were observed. Interictal electroencephalogram (EEG) showed poorly organized background activity, and multifocal epileptic abnormalities, more prominent in the right fronto-temporal region. Two focal seizures were recorded by video-EEG, with jerks of the upper limbs and head version, associated with atypical spike-wave complexes in the right fronto-temporal area. According to these electro-clinical features, a diagnosis of symptomatic focal epilepsy was made.

A further MRI examination, at the age of 28 months, revealed dilatation of supratentorial ventricular system, especially in the left fronto-parieto-insular region, a thin corpus callosum,

and an increased paraventricular and peritrigonal fronto-parietal white matter signal on T2 weighted images, probably related to perinatal hypoxic-ischemic brain injury.

Valproic acid therapy was started, with slow but progressive clinical control, reaching a seizure-free period of approximately 2 years at the end of follow-up (9.7 years of age).

At the age of 7 years, his monozygotic twin suffered from acute lymphoblastic leukemia (ALL). The flow cytometry analysis of the leukemic cells revealed a B-lineage ALL and the multiplex Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) assay identified the presence of *BCR-ABL1* p190 e1a2 isoform, a rare leukemia subtype at this age. He showed a resistance to the first-line chemotherapy and HSCT became the best change for his cure. Our patient with epilepsy, monozygotic brother, was the only available donor. He was evaluated for suspected syndromic pathology by karyotyping and SNP-arrays searching for micro deletions and/or micro duplications, and the RT-PCR for *BCR/ABL1* p190 was also evaluated: all tests were negative and the child showed a normal male genomic profile. Involved physicians (neurologist and anesthesiologist) regarded the child suitable for donation of HSCs from BM.

A total of 3.39 x 10^8/kg HSCs were collected from the BM and all reinfused to the leukemic brother after conditioning treatment.

At the end of follow-up, our epilepsy patient had no consequences and his brother is in complete remission of the disease at 3 years from the transplant procedure.

Discussion

Currently, people suffering from epilepsy can become voluntary donors just in case of well controlled seizures, and if they are certified to have the fitness to drive (such a marker for unrestrictedly healthy) [2]. These limitations are based on a potential increased risk for perioperative seizures due to the pre-existent condition or the proconvulsant effect of

anesthetic drugs, and, also due to electrolyte changes experience during apheresis [3]. Anticonvulsant medications may cause abnormalities in blood counts, which may exacerbate after PBSC [3].

However, these limitations are based on both donor and recipient safety protection principles but are poorly supported by clinical evidence [2]. Similarly, health policies of different countries apply more restrictions to people with epilepsy for blood donation, not always based on scientific support [4]. Blood donation can caused convulsive syncopes misinterpreted as epileptic seizures and the antiepileptic drugs could give negative effects to the recipient, but actually they undergo a strong dilution in the recipient's blood with low risk of undesirable effects and hypersensitivity reactions [4].

In the present case, in absence of clear scientific evidence of medical risk for the donor, we have chosen as donor our child with epilepsy for transplantation urgency with adequate results both for the donor and the receiver.

In conclusion, our observation confirms that a patient with epilepsy can be a donor, without consequences for himself and for the recipient. However, further studies are needed to better define any risk factors related to specific clinical conditions and the role of antiepileptic drugs.

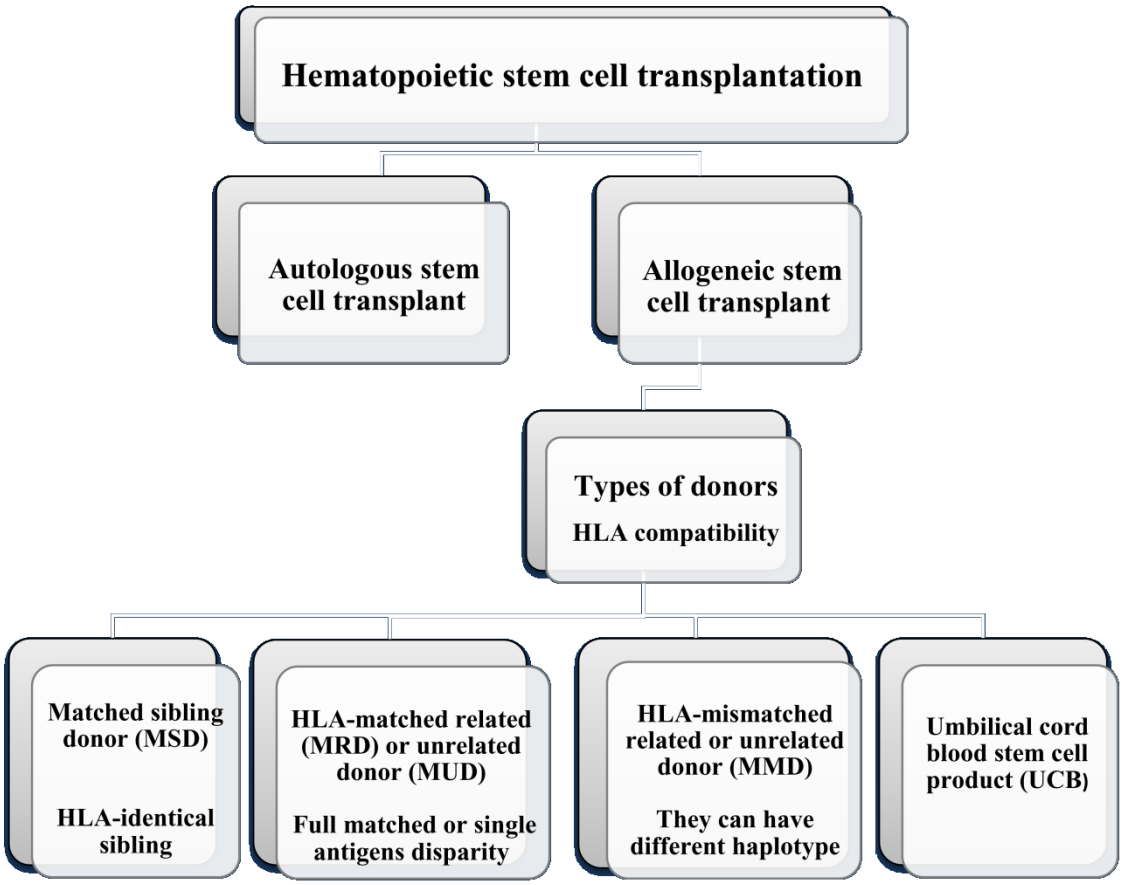

Figure 1 Types of hematopoietic stem cell transplantation

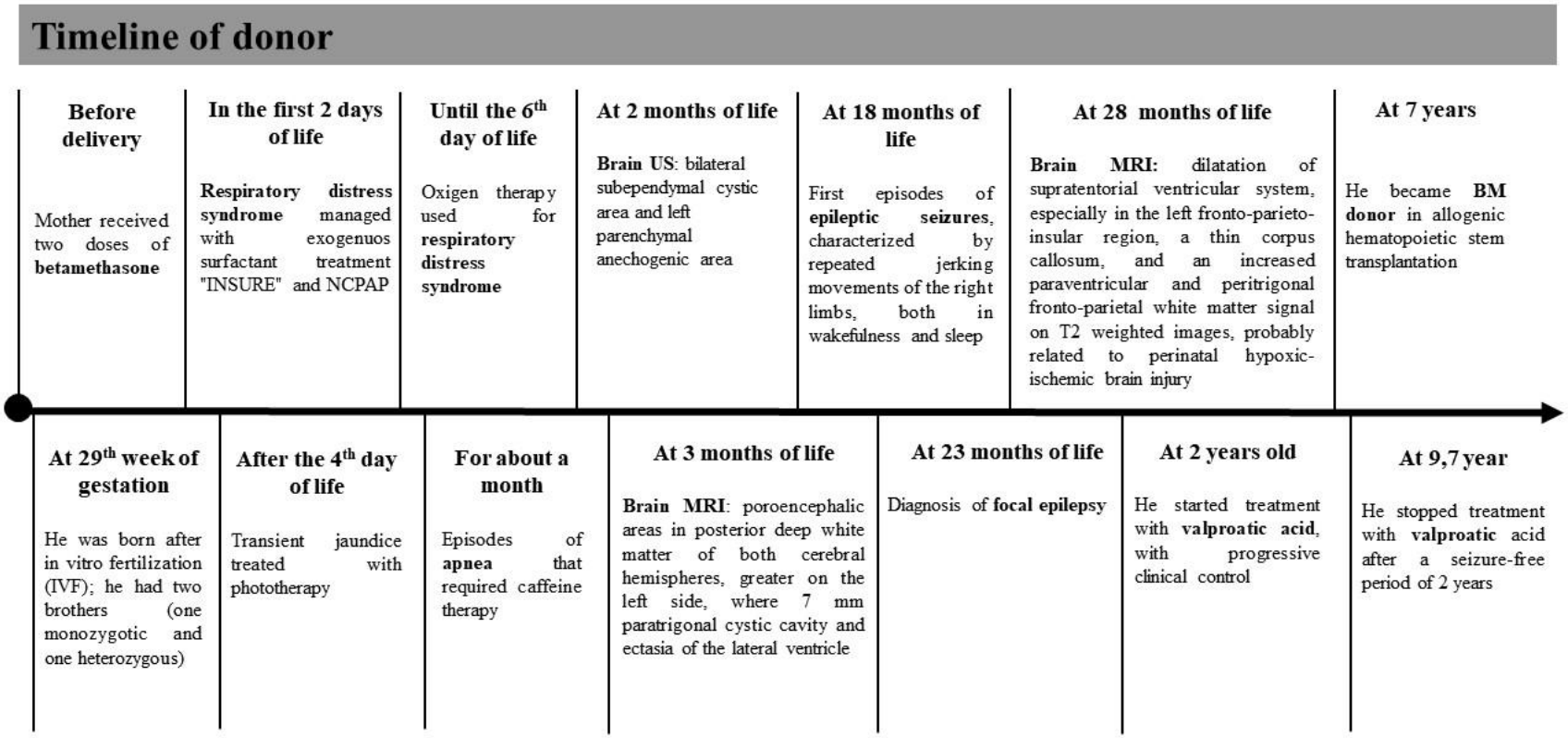

Fig.2 IVF: in vitro fertilization; INSURE (IN tubing, SURfactant, ES tubing); NCPAP (Nasal Continuous Positive Airways Pressure; US: ultrasonography; MRI: magnetic resonance imaging; BM: bone marrow

Figure 2: timeline of donor's history

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Standard protocol approvals, registrations, and patient consents

Informed consent has been obtained from patient's parents.

Ethical publication statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Declaration of Competing Interest

None of the authors has any disclosure in regard to this publication.

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