Extended Abstract Journal of Psychiatry 2021
Vol.24 No.4

Allogenic Mesenchymal Stem cell Therapy for CADASIL patient

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CADASIL, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, is an inherited small vessels disease that characterized by central nervous system dysfunctions caused by mutations in the Notch-3 gene. Clinical manifestations accrue due to brain's vasculopathy, neurodegeneration, and immune system reaction. We describe here an effective method for treatment of CADASIL by using mesenchymal stem cell therapy. A CADASIL case, 36 years old man, neuroimaging and genetic analysis for Notch-3 confirmed the diagnosis, is reported. In the present case, two stem cell injections have been performed at intervals of three weeks. The patient had no significant complications in the post-transplant period. No immediate or delayed side effects following MSC infusion were observed. He developed neither malignancy nor unwanted cells or any infectious complications 18 months after the transplantation, we performed a Cerebral MRI showed stable cerebral lesions and his gate and balance improved. Anti-HLA Antibody measurement confirmed that the patient's immune system was not stimulated by injected cells.With regard to his neurological symptoms, Scale for the assessment and rating of ataxia (SARA), The Multiple Sclerosis Functional Composite measure (MSFC), Quality of Life Assessment (QOL), and Cognitive Functioning Status (ACE-R), the patient did not has further deterioration of his previous clinical status in the follow up period of 18 months. Further studies need to be performed to show the generalizability of the results.

Keywords: CADASIL, Notch3, cognition, neuropsychology

Introduction:

Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) is a hereditary early-onset vascular disease that causes recurrent ischemic subcortical infarcts, generally accompanied by migraine, cognitive impairment, psychiatric symptoms and progressively severe neurologic deficits.

There are several methods for diagnosing CADASIL. The first method is Magnetic Resonance Imaging (MRI) characteristics of CADASIL were described in 1991. Generally, they reveal areas of T1 hypointensity and hyperintensity on T2 and FLAIR (Fluid Attenuation Inversion Recovery) images in subcortical white matter, initially affecting temporal lobes and external capsules and spreading to the other regions also, as well as the presence of lacunar infarcts. Practically all patients manifest the condition before the age of 60 years, while changes on MRI have been detected in individuals that are younger than 35 years. In addition to this the presence of Granular Osmiophilic Material (GOM) in capillary blood vessels of the skin and muscle on biopsy and genetic studies play a key diagnostic role. Biopsy exams have high specificity that are up to 100% yet low sensitivity that are less than 50%. Notch 3 testing has been proposed as the primary diagnostic approach, allowing the detection of 90% of affected individuals.

Results:

The Gesture Imitation tests have revealed the presence of constructional and ideomotor apraxia. Some studies have reported that ideomotor apraxia in 15% of individuals with lesions are confined to the thalamic or lenticular region. Individuals with CADASIL have found executive dysfunction in almost 90% of the individuals under the age of 50 years. These finding may be explained by a decline in attention and memory performance consistent with some degree of frontal subcortical dysfunction. The mechanisms underlying the cognitive dysfunction in CADASIL remain unclear. These mechanisms may be related to the disruption of corticosubcortical or corticocortical connections due to the progressive damage to the white matter and that the cognitive decline in CADASIL is likely related to the accumulated lacunar infarcts and augmented ventricular volume but not to the brain atrophy.

Conclusion:

The Neuroimaging pattern was diagnostically confirmed by Notch-3 gene analysis. The neuropsychological findings were consistent with those reported in the literature, most notably the presence of apraxias, seldom mentioned in the specialized literature. It is hoped that this individual and the other members of can benefit from the future development of protocols for pharmacological intervention and cognitive rehabilitation.