

Transplantation of human adipose tissue-derived stem cells delays clinical onset and prolongs life span in ALS mouse model.

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Abstract

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that selectively affects motor neurons in the cortex, brain stem, and spinal cord. The precise pathogenic mechanism remains unknown and there is no effective therapy. We evaluated the therapeutic effects of human adipose tissue-derived stem cell (ASC) in an animal model of ALS. Human abdominal subcutaneous fat tissues were obtained by simple liposuction from donors, and ASCs were isolated from the fat stromal vascular fraction. ASCs were found to differentiate into adipocytes, chondrocytes, osteocytes and neurons. SOD1G93A ALS mice were divided into three groups of sham, intravenous (IV) and intracerebroventricular (ICV) group. Human ASCs were transplanted in the ALS mice at 70 postnatal days before the appearance of clinical symptoms. Behavior of transplanted animals was assessed by rotarod test, paw grip endurance (PaGE) and reflex index. Mice in every group were sacrificed after 4 weeks post-transplantation. Transplanted ASCs were identified in the lumbar spinal cords were with an anti-human mitochondria antibody, and cell type specific markers for neurons or astrocytes. Delayed onset of clinical symptoms (26 days) and extended survival of animals (24 days) were observed in ALS mice transplanted with ASCs via ICV route. ASCs were found to secrete high levels of neurotrophic factors such as NGF, BDNF, IGF-1 and VEGF, and reduction of apoptotic cell death by these factors was confirmed in cultured CNS cells and in the ALS spinal cord. These results indicate that transplantation of ASCs in ALS mice provides neuroprotective effects by production of cytokines/growth factors, delays disease progression, and prolongs life span of ALS mice.

PMID: 24070071 [PubMed - as supplied by publisher]