Microanatomical evidences for potential of mesenchymal stem cells in amelioration of striatal degeneration

Edalatmanesh Mohammad Amin*, Bahrami Ahmad Reza*, Behnam Rasuli Morteza†, Moghaddam Matin Maryam*, Moghimi Ali† and Neshati Zeinab*

*Institute of Biotechnology, and †Department of Biology, Faculty of Sciences, Ferdowsi University of Mashhad, Mashhad, Iran

Huntington’s disease is an inherited neurodegenerative disorder, characterized by loss of spiny neurons in the striatum and cortex, which usually happens in the third or fourth decades of life. In advanced form of the disease, progressive striatum atrophy happens and medium spiny neurons, which occupy more than 80% of the striatum, become atrophic. Gradually, the atrophy expands to the neocortex and other regions of the brain. To our knowledge, there is no effective therapeutic strategy for diminishing the motor disorders of Huntington’s disease. In recent years, cellular transplantation has been an effective therapeutic method for neurodegenerative diseases. In the present study, the potential of bone marrow derived mesenchymal stem cells in amelioration of striatal degeneration was assessed in animal model of Huntington’s disease. After unilateral lesion in striatum was caused by quinolinic acid (QA), bone marrow derived mesenchymal stem cells, which were isolated and purified from 4–6 weeks old rats, were transplanted into the damaged striatum. After 9 weeks of transplantation, the volume of striatum, lateral ventricles and hemispheres were measured in control (normal) and test (QA injected + cell transplanted) groups. After volume determination, the atrophy percentage of both striatum and damaged hemisphere and volume extension of lateral ventricles were calculated. Histologic results showed significant difference in amount of striatum atrophy between sham (only QA injected) and test groups. These results confirm the potential of bone marrow derived mesenchymal stem cells in treatment of microanatomical defects in motor disorders of Huntington’s disease. According to our results, cell therapy by means of bone marrow derived adult stem cells could be considered as a good candidate for treatment of neurodegenerative diseases, especially Huntington’s disease. [Neurol Res 2008; 30: 1086–1090]

Keywords: Huntington’s disease; mesenchymal stem cells; cell therapy; quinolinic acid

INTRODUCTION

Huntington’s disease (HD) is an inherited neurodegenerative disorder caused by repeating of CAG bases in 5’ coding region of hd gene. Occurrence of more than 39 repeats of this sequence is abnormal and would results in HD. Naturally, the CAG repeats occur less than 36 times. In progressive state of this disease, devastating clinical consequences will appear in motor, cognitive and physiologic functions1–3 which finally leads to death ~18 years later. These clinical symptoms are accompanied with progressive degeneration of the GABAergic intermediate spiny neurons in striatum and deep layers of cortex. Other regions such as hippocampus and hypothalamus become atrophic later4,5.

The most prominent atrophy of caudate nucleus and putamen leads to significant expansion of the lateral ventricles. Reduction of total brain weight by 25–30% in advanced stages reflects the fact that the whole part of the brain becomes atrophic. This atrophy is more obvious in cerebral cortex, the underlying white matter and especially the basal ganglia6.

Different neuronal populations exist in striatum, which are differentially affected by HD. For example, the negative effect of disease on the projection neurons is greater than intermediate neurons7. Meanwhile, the most affected neurons by this disease are known to be the projection ones that secret γ-amino butyric acid (GABA) and enkephalin (ENK) or P substance. These neurons constituted more than 90% of striatum neurons8.

Neuronal loss is accompanied by reactive astrocitosis (gliosis). Atrophy occurs in other parts of the basal ganglia, especially the globus pallidus and subthalamic nucleus, although the amount of atrophy is less than striatum. Loss of neurons also appears in the cerebral cortex. The most severely affected neurons in this region