Heterologous mesenchymal stem cells used in the treatment of sequela of encephalomyelitis caused by canine distemper virus (CDV) in dogs naturally infected

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Abstract

Canine distemper is a highly contagious infectious disease caused by a virus, which affects domestic dogs. Manifestations on epithelium, optic nerves and central nervous system may be presented. The neurological infection may affect the brain and spinal cord, leading to encephalomyelitis. There is no effective treatment that has been proven yet. Depending on the immune response created by the infection, the clinically affected dog may ultimately die or develop a neurological sequel of encephalitis such as paraplegia or quadriplegia, paraparesis or tetraparesis, hyperesthesia, compulsive movements, tremors, vestibular signs, focal and generalized seizures, myoclonus and more. We aim to develop an alternative treatment for dogs, which develop neurologic encephalomyelitis caused by canine distemper virus. The treatment consists on the transplantation of heterologous mesenchymal stem cells (MSC) collected from adipose tissue of healthy young dogs. To evaluate the efficacy of the treatment, 20 dogs naturally infected with CDV presenting neurological sequelae were used. The animals were divided into 3 groups, according to their age and time of sequela onset. In group A, animals were up to 18 months old and had sequela for up to 12 months (n=6). In group B, animals were older than 18 months old and had sequelae of up to 12 months (n=7). In group C, all animals were over 18 months old and had sequelae for more than 12 months (n=7). MSC were obtained by enzymatic digestion of an adipose tissue fragment taken from a donor, a healthy young dog during surgical castration procedure. The adipose tissue was brought to the laboratory to collect the MSC and then cultured in vitro. MSC were applied intravenously in 2 to 4 doses, with an interval of 30 days between the applications. By the end of the application cycle, the animals were evaluated for the presence or absence of normal gait recovery. The results showed that in group A, the gait was recovery in 83.33% of the animals. In group B, the gait recovery rate was 85.71%, while in group C was 14.29%. The results suggest that when the neurological sequela is treated before it completes 12 months onset, the treatment with MSC demonstrates to be very effective. Either in young animals (group A) as in adult animals (group B), the gait recovery rate was remarkable. However, if the neurological sequela is treated with more than 12 months onset, the treatment efficiency is significantly lower (group C) compared to early developed sequelae. Additional studies are still undergoing, in

order to increase the number of animals evaluated and an efficient induction protocol, even though the procedure have demonstrated the safety of the heterologous transplantation of MSC, as no dogs had presented any form of reaction from the applications or tumor formation, even after a year of treatment. The results also demonstrated high efficiency of MSC in the treatment of neurological sequela of distemper.