Adipose-Derived Mesenchymal Stem Cells Reduce Lymphocytic Infiltration in a Rabbit Model of Induced Autoimmune Dacryoadenitis: Some Discussions

We read with great interest the recently published article by Xue Li and colleagues1 that investigated the immunoregulatory roles of adipose-derived mesenchymal stem cells (ADSCs) in a rabbit model of induced autoimmune dacryoadenitis. In their study, the authors performed much research and demonstrated that allogeneic ADSCs are effective for treating autoimmune dacryoadenitis in rabbits1; however, we believe that some results and conclusions presented in their article deserve further discussion.

First, the authors used the rabbit model of autoimmune dacryoadenitis via intravenous injection of activated autologous peripheral blood lymphocytes (PBLs). In this model, the onset of ocular surface disease is supposed to be 2 weeks, indicating the secure establishment of autoimmune dacryoadenitis and keratoconjunctivitis.2 In this study, the authors began to administer their first treatment at 12 hours after adoptive transfer of activated PBLs when there had not been any signs of ocular surface compromise. Because there is also no evidence showing that autoimmune dacryoadenitis has been present 12 hours after PBL injection, the beneficial effect of ADSC administration on the autoimmune dacryoadenitis may be claimed only as a prevention effect instead of therapeutic one. In addition, there is a possibility that ADSCs work by inhibiting the activity or number of the injected PBLs from the very beginning. Then, fewer activated PBLs may result in a less-severe animal model of dacryoadenitis, which could also yield a beneficial effect in the end, but this effect is not a result of the inhibition of inflammation or autoimmune response by such therapy. It would be more appropriate for their conclusion if the authors gave the treatment at least 2 weeks after disease induction, as others did with other therapy in a similar animal model.3

Second, the authors confirmed that the ADSC-treated rabbits showed decreased autoimmune responses, and the secretory function of their lacrimal gland was restored significantly by some clinical evaluations. Looking carefully at the results, one can note that some clinical evaluations did not show so much significance between groups. Regarding comparison in tear production, there is only approximately 1 mm difference between the untreated and ADSC-treated groups for various time points (2, 4, 6 weeks). The minimum scale in the Schirmer strip used for evaluation of tear production is 1 mm. So, although the statistical difference is significant, it is difficult to tell if the improvement is actually due to reading error, and it is also difficult to say if this kind of minimal improvement is clinically visible. The same condition exists with fluorescein staining, which shows approximately 1.2 to 1.5 score changes. Based on our own experience, there is always slight fluorescein staining in the normal rabbit cornea; one to two score changes may not reflect clinical meaningfulness. Difference in break-up time between groups looks good because it is approximately 2 seconds, which may reflect clinical improvement. In this study, clinical severity may exhibit some improving tendency, but it may not be appropriate to conclude that the clinical severity has been attenuated.

Another set of data which should be treated carefully is the mRNA expression of inflammatory mediators. The authors compared the treated with untreated groups, revealing significant reduction in expression of some inflammatory cytokines, and enhanced expression of some anti-inflammatory cytokines, such as IL-10. The data would look better and more complete if the authors included the normal control in their study because there are no baseline values for the expression levels of these cytokines.

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References

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