Comparison of Treatments with Local Mesenchymal Stem Cells and Mesenchymal Stem Cells with Increased Vascular Endothelial Growth Factor Expression On Irradiation Injury of Expanded Skin

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INTRODUCTION: Radiation injury results in chronically ischemic tissue. Radionecrosis can be encountered in severe cases. ^{1,2} Mesenchymal stem cells (MSCs) have a therapeutic effect on ischemia-related lesions. ^{3,4} In here, effects of bone-marrow derived MSC and vascular endothelial growth factor (VEGF) gene-transfected MSC (VEGF-MSC) treatment on expanded skin with irradiation injury is investigated.

MATERIALS AND METHODS: Silicone tissue expander (50cc) was placed subcutaneously and expanded weekly up to 60cc in 24 Sprague Dawley rats. Single fraction (30Gy) radiotherapy was applied to the 2x2cm area of the expanded skin. Dulbecco's Modified Eagle Medium (DMEM) without cell component, MSCs, and VEGF-MSCs were injected subcutaneously at the irradiation-expansion sites. Skin samples were evaluated by histomorphometry and immunohistochemistry. Perfusion rate of the samples were assessed by scintigraphy.

RESULTS: Epidermal thickness of irradiated-expanded skin was increased after MSC and VEGF-MSC treatment whereas dermal and capsule thicknesses did not change. MSC and VEGF-MSC treatments were effective in preserving respectively CD31 and VEGF expressions at a similar level as expanded skin after irradiation injury. VEGF-MSC treatment significantly elevated CD31 levels in the irradiated tissue. Skin perfusion results were consistent with the CD31 and VEGF expressions. MSC and VEGF-MSC treatments were effective in increasing PCNA expression in irradiation zone. VEGF-MSC treatment was efficient in reducing both expansion- and irradiation-related apoptosis.

CONCLUSION: Vascular impairment and dermal insufficiency due to tissue expansion and irradiation injury can easily result in a wound hard to repair. MSCs and VEGF-MSCs can promote neo-vascularization, reverse the effect of irradiation, and provide more durable soft tissue for expansion/implant reconstruction.

REFERENCES:

1. Bentzen SM, Thames HD, Overgaard M. Latent-time estimation for late cutaneous and subcutaneous radiation reactions in a single-follow up clinical study. Radiother Oncol. 1989;15:267-74.

2. Perbeck LG, Celebioglu F, Danielsson R, Bone B, Aastrup M, Svensson L. Circulation in the breast after radiotherapy and breast conservation. Eur. J. Surg. 167: 497, 2001.

3. Rafii S, Lyden D. Therapeutic stem and progenitor cell transplantation for organ vascularization and regeneration. Nat Med. 2003;9:702-12.

4. Öksüz S, Ülkür E, Öncül O, Köse GT, Küçükodacı Z, Urhan M. The effect of subcutaneous mesenchymal stem cell injection on statis zone and apoptosis in an experimental burn model. Plast Reconstr Surg. 2013;131:463-71.