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Systemic mobilization of mesenchymal stromal cells and cytokines and local cell differentiation after clinical transplantation

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Objective

To evaluate systemic mobilization of mesenchymal stromal cells and cytokines and local cell differentiation after transplantation of a tissue-engineered trachea.

Material and methods

Analyses were performed in the early post-operative period following 6 tissue-engineered trachea transplantations using synthetic scaffolds seeded with autologous mononuclear cells. Biologically active molecules in the patients' peripheral blood were analyzed by ELISA every 2 days for 2 weeks following transplantation. Flow cytometry was used for the analysis of peripheral blood mononuclear cells subsets and phenotyping by 2 days before surgery, and every 2 days for 2 weeks postoperatively. Bronchoscopy was performed with bronchoscopic alveolar lavage of the graft for cytological examination. The cytological specimens were assessed by Giemsa Stain.

Results

Concentrations of inflammatory cytokines demonstrated an increase in TNF- α , IL-1 and IL-2 in the first days after transplantation. A second increase in inflammatory cytokines occurred between 12 and 14 days after surgery. Levels of adhesion molecules ICAM, VCAM, E-selectin, and growth factors, such as VEGF and EPO, were elevated during postoperative period as compared to pre-operative levels with maximum concentrations 10 - 14 days after transplantation. Hematopoietic cells CD34⁺ were found the first day following transplantation and cells with phenotype CD34⁻CD45⁻CD105⁺CD73⁺90⁺, which were characterized mesenchymal stem cells, appeared between 6 and 14 days after transplantation.

The cytological examination defined the groups of mesenchymal stem cells, which proliferated and divided 3 days after transplantation. In subsequent studies of cytology samples, epithelial cells appeared between 6 and 13 days following transplantation.

Conclusion

These results indicate the activation of mesenchymal stem cells, and the proliferation and differentiation of epithelial cells. Examination of the dynamics of biologically active molecules and stem cells in the peripheral blood of patients after transplantation of tissue-engineered tracheae seeded autologous mononuclear cells indicated an activation of the regeneration process.