肥大細胞胞膜穩定藥物減緩胃液吸入傷害相關肺移植病理變化-大鼠原位肺移植模型

張睿智

佛教花蓮慈濟醫院 心臟胸腔血管外科

Mast Cell Membrane Stabilizer Ameliorates Gastric Fluid Aspiration-Associated Pulmonary Allograft Pathology in Rat Orthotopic Lung Transplant Model

Jui-Chih Chang, MD, PhD[1,2,5], Jason Leung, BS[1], Tao Tang, MD[1,6], Zoie E. Holzknecht, BS[1], Matthew G. Hartwig, MD[1], R. Duane Davis, MD[1], William Parker, PhD[1], Soman N. Abraham, PhD[2,3,4], and Shu S. Lin, MD, PhD[1,2,3]

[1]Department of Surgery, [2]Department of Pathology, [3]Department of Immunology, [4]Department of Molecular Genetics and Microbiology, Duke University Medical Center, Durham, North Carolina, 27710, United States, [5]Division of Thoracic and Cardiovascular Surgery, Tzu Chi General Hospital, Hualien, Taiwan, [6]The Thoracic and Cardiovascular Surgery, The Second Xiangya Hospital, Changsha City, Hunan province, Peoples Republic of China

Purpose:

Obliterative bronchiolitis (OB) is the primary factor limiting long-term pulmonary allograft survival. Mast cells, the first responder of the innate defense system, have been associated with OB in human pulmonary allografts and might play a role in the pathogenesis of OB due to their ability to orchestrate innate and adaptive immune responses. In this study, the role of mast cells in pulmonary allograft rejection was evaluated using a heterotopic rat pulmonary allograft model which reliably leads to the development of OB that is dependent on the chronic aspiration of gastric fluid.

Materials and Methods:

The pulmonary allograft recipients (n = 35) were separated into three groups: chronic gastric fluid aspiration (GF), chronic gastric fluid aspiration plus treatment with a mast cell membrane stabilizer, cromolyn sodium (GF+C), or chronic aspiration with normal saline (NS) as a control.

Results:

The rats receiving cromolyn developed significantly fewer OB lesions than those treated with gastric fluid alone ($p<0.001$), with a mean reduction of 46 % of the airways affected. Further, the acute graft injury associated with long ischemic time in the model (6 hours total ischemic time, typical acute graft injury rate of ~30%) was apparently blocked by cromolyn ($p = 0.045$). The number of mast cells per small bronchiole significantly increased in all animals aspirated with gastric fluid, regardless of treatment with cromolyn (GF vs. NS, $p = 0.005$; GF+C vs. NS, $p = 0.024$). Further analysis demonstrated a positive correlation between the fraction of airways affected (OB lesions) and the number of mast cells per small bronchiole only in the allografts from the GF group, and not in the GF+C or NS groups.

Conclusion:

This result suggests that chronic exposure to gastric fluid increases mast cells in the

bronchioles of pulmonary allografts, and that the recruited mast cells play a critical role in the initial ischemia-reperfusion injury and the subsequent development of OB in this model. These findings suggest that further studies aimed at devising methods to block mast cell function in human pulmonary allografts may be worthwhile.