ARSR Symposium 4

ARSR-S4-1  Keynote Lecture: Recent advances of macrolide therapy for the treatment of chronic rhinosinusitis and other airway inflammation

Takeshi Shimizu
Otorhinolaryngology-Head and Neck Surgery, Shiga University of Medical Science, Otsu, Japan

In 1984, the effectiveness of low-dose, long-term erythromycin treatment (macrolide therapy) for diffuse panbronchiolitis (DPB) was first reported in Japan. The 5-year survival rate for DPB improved from 62.9 to 91.4% after implementation of macrolide therapy. The usefulness of this treatment has since been demonstrated in patients with other chronic airway diseases, such as chronic bronchitis, cystic fibrosis, bronchiectasis, and chronic rhinosinusitis (CRS). The new 14-membered macrolides clarithromycin and roxithromycin and the 15-membered macrolide azithromycin are also effective for treating these inflammatory diseases. The mechanism of action of the 14- and 15-membered macrolides may involve anti-inflammatory rather than antibacterial activities.

Macrolide therapy is now widely used for the treatment of CRS in Japan; it is particularly effective for treating neutrophil-associated CRS and is useful for suppressing mucus hypersecretion. However, macrolide therapy is not effective for eosinophil-predominant CRS, which is characterized by serum and tissue eosinophilia, high serum IgE levels, multiple polyposis, and bronchial asthma. Recent reports have described new antiviral activities and the clinical efficacy of macrolides in treating chronic obstructive pulmonary disease (COPD), influenza virus infection and severe pneumonia.

We demonstrated that orally administered CAM attenuates the severity of avian influenza A virus (H5N1, H7N9) infection in monkeys by inhibiting the infection and reproduction of viruses and by suppressing the cytokines responses of infected lung. The therapeutic value of macrolides in treating severe airway inflammation may be caused by inhibition of the “cytokine storm” associated with the dysregulation of host immune responses, which causes respiratory distress in severe pneumonia.

Curriculum vitae
Takeshi Shimizu
Professor and Chairman
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Prof. Shimizu graduated from Mie University School of Medicine in 1983 and spent his fellowship at the Department of Otorhinolaryngology, Mie University (Prof. Yasuo Sakakura). He worked at the Department of Pulmonary Pathobiology (Prof. Paul Nettesheim), National Institutes of Environmental Health Science, U.S.A. in 1988-1991. Prof. Shimizu has been a chairman of Department of Otorhinolaryngology-Head and Neck Surgery, Shiga University of Medical Science, Otsu, Japan, since 2004. Prof. Shimizu’s major research interest is airway inflammation (Allergy and Immunology) in Rhinology, and he received the award of Japan Rhinologic Society in 1996.
Central compartment atopic disease (CCAD) is one of the phenotypes of the chronic rhinosinusitis with nasal polyp recently discovered by John M. DelGaudio in 2017. However, the mechanism and possible risks factors of CCAD has not yet been fully understood. The aim of this study is to unveil the clinical presentations and risk factors of CCAD in mid-Taiwan.

We retrospectively collect patients with CRS who underwent FESS in China Medical University Hospital from September, 2015 to September, 2020. Based on pre-operation CT and sinoscopy, the patients were divided into: “CCAD”, “non-CCAD” and “Equivocal” groups. Patients’ demographics, systemic disorders and comorbidity (hypertension, diabetes mellitus, allergic rhinitis, ectopic dermatitis, aspirin-exacerbated respiratory disease and asthma), preop and postop 3 month SNOT-22, surgical outcomes were analysed.

784 patients with CRS underwent FESS were included. 133 was excluded due to previous FESS or incomplete data. 73 were classified into CCAD group and 496 into non-CCAD group. There was a strong relationship between asthma and CCAD (19% versus 4%, p<.00001), but relatively weak relationship between allergic rhinitis (37% versus 28%, p=0.06) and CCAD. Furthermore, more 2nd look FESS could be found in CCAD group (29% versus 20%, p=0.04)

CCAD is related to particular types of allergic diseases. The prevalence of allergic comorbidities might exist racial or regional difference. The prevalence of asthma was higher in our CCAD patients. Clinical symptoms of CCAD were more severe than other types of chronic rhinosinusitis with nasal polyps and the symptoms relieved well after surgical intervention.
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**ARSR-S4-3 Keynote Lecture: Introduction of hands-on seminar on basic research for clinicians in the Japanese Rhinologic Society**

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As both clinical and basic research have been revealing the precise mechanisms about rhinologic disorders in this decades, it is important for otolaryngologists to understand the disease from the point of both clinical and basic research. However, clinicians may encounter some problems when they start up and continue the basic research.

The Japanese Rhinologic Society has launched “Hands-on Seminar on Basic Research for Clinicians” since 2014. The aims of the seminar are to raise the motivation and research skills of basic research for all clinical otolaryngologists, and to encourage inter-disciplinary collaboration through research with universities. So far, the seminar had been held by showing several basic experiments such as isolation of single cells from nasal samples, ELISA, Western blot, PCR, immunohistochemistry, cell culture, CRISPER-Cas9, and so on. Based on the questionnaire from the participants, they had a high need and satisfaction of these research seminars. Because this seminar has a great opportunity for all otolaryngologists to find new idea to expand the avenue of basic understanding of rhinologic disorders, we believe this seminar should be continued as long as possible.

In this session, we would like to introduce about this seminar and show some experimental method including the isolation of mononuclear cells from peripheral blood, nasal polyps, and tonsils.

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**Curriculum vitae**

2003 University of Fukui Faculty of Medical Sciences
2013 Post graduate course, University of Fukui Faculty of Medical Sciences

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