JKT2-I  Type 2 inflammatory diseases in the upper airway

Tsuguhisa Nakayama, MD, PhD
Department of Otorhinolaryngology and Head & Neck Surgery, Dokkyo Medical University, Japan

Chronic rhinosinusitis with nasal polyps (CRSwNP) is composed of diverse populations of phenotypes and endotypes, and there is emerging evidence of its heterogeneity. Among that heterogeneity, CRSwNP patients with high eosinophilic infiltration in nasal polyps and sinonasal mucosa are clinically refractory and characterized by type 2 inflammation. This type of CRS is understood by the disease concept of eosinophilic chronic rhinosinusitis (ECRS). In the middle ear, which is connected to the nasopharynx by the eustachian tube, there is the disease, similar to ECRS, is characterized by a remarkably viscous middle ear effusion and accumulation of numerous eosinophils in the middle ear effusion and mucosa. This disease is termed eosinophilic otitis media (EOM), and it often occurs in association with another type 2 inflammations of the upper and lower airways.

These type 2 inflammatory diseases of the upper airway are resistant to various therapies, but recently launched biologic medications have held promise as a new treatment option. Among these biologics, dupilumab, a humanized IgG4 monoclonal antibody that inhibits IL-4Rα which is a common receptor for IL-4 and IL-13, has shown efficacy in the treatment of ECRS and EOM. In this presentation, I will discuss the characteristics of type 2 inflammatory diseases in the upper airway and the efficacy of dupilumab as a treatment option.

Curriculum Vitae
Name: Tsuguhisa Nakayama, MD, PhD
2002 Department of Otorhinolaryngology, Jikei University School of Medicine, Japan
2012 Department of Otorhinolaryngology and Head & Neck Surgery, Dokkyo Medical University, Japan
2014 Laboratory for Respiratory and Allergic Diseases, Center for Integrative Medical Sciences, RIKEN, Japan
2016 Department of Otolaryngology and Head & Neck Surgery, Stanford University, USA
2022 Department of Otorhinolaryngology and Head & Neck Surgery, Dokkyo Medical University, Japan
**JKT2-2  Which is more meaningful to differentiate type 2 from non-type 2 CRwNP, tissue or blood eosinophilia?**

Chih-Jaan, Tai, MD, PhD
Department of Otorhinolaryngology, China Medical University & Hospital, Taiwan

**Introduction:** Chronic rhinosinusitis with nasal polyps (CRSwNP) are classified to type 1, type 2 and type 3 according to their inflammatory endophenotype. Type 2 inflammation accounts for the majority in Western countries’ studies. Most of the etiologies are nonspecific, but some are related to genetic, metabolic and immune diseases, such as aspirin-exacerbated respiratory disease (AERD), allergic fungal sinusitis (AFRS), central compartment allergic disease (CCAD), etc. The purpose of this study was to compare the difference of clinical manifestations between patients in type II and non-type II CRSwNP, based on different diagnostic criteria, tissue or blood eosinophilia.

**Method:** From February 2021 to July 2022, a total of 182 patients diagnosed with chronic rhinosinusitis and received FESS were included. Among which, 55 (30.22%) were CRSwNP, 127 (69.78%) were CRSsNP. According to the pathological tissue and blood eosinophil count, they were divided into type 2 and non-type 2 groups. Patient characteristics, allergic comorbidities, nasal polyps score (NPS), CCAD, CT L-M score, preoperative and postoperative olfactory and SNOT-22, and intraoperative blood loss surgical bleeding amount were analyzed.

**Results:** The average age of 55 patients with CRSwNP was 45.7 years (24 to 66 years), and 37 (62.27%) were male. When based on histological diagnostic criteria, 43 cases (78.2%) are type 2 CRSwNP. However, when based on blood diagnostic criteria, 31 cases (56.4%) are type 2 CRSwNP. When based no histological diagnostic criteria, NPS, CCAD, CT L-M score, and intraoperative blood loss were higher in type 2 group than those in non-type 2 group. When based on blood diagnostic criteria, there was limited difference in NPS, CT L-M score, and intraoperative blood loss between the two groups.

**Conclusion:** The patients with CRSwNP are mainly middle-aged male and their age is lower than that of the patients with CRSsNP. Whether based on histological diagnostic criteria or blood diagnostic criteria, more than half of the CRwNP were type 2 inflammation, which is different from the traditionally believe that the prevalence of type 2 CRSwNP is not high in Asian patients. The histological diagnostic criteria showed more differences between type 2 and non-type 2 CRSwNP in clinical manifestations, than the blood diagnostic criteria.

---

**Curriculum Vitae**

Name: Chih-Jaan, Tai, MD, PhD
Professional positions:
1. Professor, School of Medicine; Dual appointment, Department of Health Services Administration, China Medical University, Taiwan
2. Director of Rhinology, China Medical University Hospital, Taiwan
3. Deputy Chairman, Committee of Medical Ethics, CMUH, Taiwan
4. Secretary General, Taiwan Rhinology Society
5. Surveyor, Hospital Accreditation, Ministry of Health and Welfare, Taiwan
Introduction: *Staphylococcus aureus* enterotoxin (SAE) superantigens are detected in nasal polyps (NPs), and SAE-specific immunoglobulin E predicts asthma comorbidity in patients with NPs. However, roles of SAE superantigens and superantigen-related T-cell responses remain to be elucidated in non-asthmatic patients. We investigated the presence of SAEs and SAE-related T cell receptor (TCR) Vβ in non-asthmatic NPs, the phenotypes and functions of SAE-related T cells, and the clinical implication of SAE-related T-cell expansion.

Method: Sinonasal tissues were obtained from patients with non-asthmatic chronic rhinosinusitis (CRS) with (CRSwNP) or without NP (CRSSNP) and control subjects. SAE genes were detected by polymerase chain reaction and the TCRVβ distribution and T-cell phenotypes examined by flow cytometry.

Results: Various SAE genes were detected not only in NPs but also in sinonasal tissues of CRSSNP patients and controls. The *S. aureus* enterotoxin I (SEI) gene was detected in all NPs. The fraction of SEI-responsive TCRVβ1 and Vβ5.1+ CD4+ T cells was significantly increased only in NPs and ethmoidal mucosal tissues from CRSwNP patients, indicating superantigen-induced expansion. The expanded TCRVβ5.1+ CD4+ T cells expressed proliferation marker Ki-67 and the Th2 transcription factor GATA3. Furthermore, TCRVβ5.1+ CD4+ T cells in NPs highly expressed Th2 markers, including IL-17RB, TSLPR, and CRTH2, with a potent Th2 cytokine-producing ability. Moreover, the expansion of TCRVβ1+ or Vβ5.1+ CD4+ T cells was associated with the Lund-Mackay CT score, indicating disease extent.

Conclusion: In non-asthmatic CRSwNP patients, superantigen-related expansion of CD4+ T cells with Th2 differentiation was associated with the disease extent.

---

Curriculum Vitae

**Name:** Dae Woo Kim, MD, PhD

**Education**

1993 - 1999: M.D., Seoul National University College of Medicine, Seoul, South Korea

2002 - 2008: M.S., Otorhinolaryngology, Seoul National University Postgraduate School, Seoul, South Korea

2008 - 2011: Ph.D., Immunology, Seoul National University Postgraduate School, Seoul, South Korea

**Postgraduate Training**

May, 1999 - February, 2000: Rotating Internship, Seoul National University Hospital

March, 2000 - February, 2004: Residency, Department of Otorhinolaryngology, Seoul National University Hospital

**Positions Held & Faculty Appointment**

Assistant Professor, Department of Otorhinolaryngology

Gyeongsang National University, College of Medicine, Jinju, South Korea

May, 2012 - present

Professor, Department of Otorhinolaryngology-Head and Neck Surgery, Seoul National University, College of Medicine, Boramae medical center, Seoul, South Korea

March, 2015 - February, 2016

Visiting scholar, Department of Internal Medicine, Division of allergy and immunology, University of South Florida Morsani College of Medicine, Tampa, FL33617

**Licensure and Certification**

Licenced to Practice Medicine in Korea, 1999

Korean Board of Otolaryngology, 2004

**Memberships**

Korean Society of Otorhinolaryngology

The Korean Society of Rhinology

The Korean Academy of Asthma, Allergy, and Clinical Immunology

American Academy of Asthma, Allergy, and Immunology

---

---