IMSUT Hospital

Department of Rheumatology and Allergy
アレルギー免疫科

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Our department is founded in 2001 to tackle systemic autoimmune inflammatory diseases including rheumatoid arthritis, systemic lupus erythematosus, vasculitic syndromes, and IgG4-related disease. We provide patients personalized and evidence-based medical service. Moreover, we challenge cutting edge science of autoimmune, rheumatic and allergic diseases and novel treatments for patients with these disorders. As part of an elite teaching hospital, we also contribute to preparing the next generation of leading academic physicians, scientists and clinician-educators.

1. Clinical activities in IMSUT Hospital

Tomonao Tanaka, Satsuki Aochi, Masaaki Uehara, Motohisa Yamamoto

Rheumatologists at our division provide state-of-the-art diagnosis and treatment for systemic autoimmune diseases (the total number of patients was approximately 3,000 per year). Our physicians have active basic and clinical research projects and also are involved in the training of rheumatology specialists.

Rheumatologic services offered at IMSUT Hospital include:

- Outpatient consultations
- Outpatient specialty care for patients with rheumatic diseases
- Hospital consultations
- Education on rheumatologic diseases and treatments
- Training of residents and young doctors for rheumatologists
- Clinical trials
- Community medicine

2. Establish of new registry for patients with IgG4-related disease and develop novel diagnostic and therapeutic approaches for IgG4-related disease

Tomonao Tanaka, Satsuki Aochi, Masaaki Uehara, Motohisa Yamamoto

IgG4-related disease is a new disease concept, established this century. As a chronic fibro-inflammatory disorder, IgG4-related disease is characterized by elevated serum levels of IgG4 and abundant infiltration of IgG4-bearing plasma cells into and fibrosis of the involved organs. Whether the disorder is an autoimmune disease remains unclear; nevertheless, consultation with rheumatologists regarding patients with IgG4-related disease is increasing owing to the various organ dysfunction involved and the abnormal immune responses observed. We tackle elucidating the pathogenesis of IgG4-related disease and developing novel treatments. At first, we established a new registry system for the patients with IgG4-related disease (TOMORROW registry), and started to enroll IgG4-related disease patients. We cooperate with national policies and also provide the data to the Rare Disease Data Registry of Japan (RADDAR-J), which was established by AMED. We will organize the clin-

ical figures of IgG4-related disease and develop a more accurate diagnostic and therapeutic approach by a TOMORROW registry.

Furthermore, using the obtained blood and tissue samples, we will carry out a multi-omics analysis. We will link the results to the individual clinical data, and promote personalized medicine that predicts therapeutic response and prognosis using artificial intelligence. To achieve this, we are currently conducting RNA-Seq of both salivary gland specimens and peripheral blood mononuclear cells, microbiome analysis of saliva, and analysis of the relationship between therapeutic response and HLA.

3. Development of AI-based diagnostic, therapeutic methods, and prognostic algorithms for rheumatic diseases

Tomonao Tanaka, Masaaki Uehara, Motohisa Yamamoto

Rheumatic diseases are currently diagnosed using patterned diagnostic criteria based on a combination of physical, hematological, and imaging findings. In addition, the therapeutic strategy for rheumatic diseases is decided after carefully considering the distribution and degree of disability. We have developed a diagnostic algorithm for IgG4-related disease based on clinical data collected in a multicenter collaboration. The subjects were 602 patients with IgG4-RD who visited the Institute of Medical Science, The University of Tokyo (IMSUT) Hospital, The University of Tokyo Hospital, Kanazawa University Hospital, Shinshu University Hospital, Kyoto University Hospital, and Sapporo Medical University Hospital. The analysis was performed using a decision tree and a random forest model. A dataset including two basic patient characteristics and 29 laboratory findings was created for each case at the first visit. Both analysis showed good accuracy, sensitivity, and specificity of the algorithm. Algorithms for predicting response to therapy, complications, and prognosis are currently being developed for rheumatoid arthritis and other rheumatic disorders.

4. Development of preventive methods for glucocorticoid-induced myopathy and osteonecrosis

Masaaki Uehara, Motohisa Yamamoto

The administration of glucocorticoids to patients with rheumatic diseases often results in glucocorticoid-induced myopathy. We previously found that administration of branched-chain amino acids (BCAA) to such patients improves the loss of skeletal muscle, especially slow-twitch muscle. We also found that the serum concentration of the specific amino acids reflects the slow-twitch muscle improvements. Based on this, we propose the need for separate muscle recovery methods for slow- and fast-twitch muscles and investigate the best method for each.

On the other hand, when a large amount dose of glucocorticoid is used for remission induction, the risk of osteonecrosis of the femoral head occurs. Currently, osteonecrosis of the femoral head is one of the complications that there is no way to prevent. In collaboration with the Department of Orthopaedic Surgery, Sapporo Medical University School of Medicine, we are working to develop a method to prevent osteonecrosis of the femoral head. Currently, several candidate drugs have been identified and clinical trials have been completed.

5. Establishment of pathogenesis and prevention of rheumatic diseases after COVID-19 vaccine

Satsuki Aochi, Masaaki Uehara, Motohisa Yamamoto

The onset of rheumatic diseases after COVID-19 vaccination has attracted much attention in recent years. It has also been experienced that patients with rheumatic diseases suffer exacerbation of the primary condition when receiving the vaccination. For this reason, we are urgently working to elucidate the pathogenesis of this disease and to establish a prophylactic method.

Publications

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