The NTM Host Research ConsortiumInternational workshop 2023

Disseminated NTM disease

"Understanding the spectrum of NTM disease across the human lifespan"

January 14 2023

Time schedule : Japan Time

10:00 am opening remarks
Naoki HASEGAWA, *Keio University, Japan*

Part1 Chair : Ho NAMKOONG, *Keio University, Japan*

10:05 Anti GM-CSF related diseases
Hélène SALVATOR, *Saclay University, France*

10:30 Disseminated NTM disease with anti-IFN-γ autoantibodies; as an autoimmune NTM disease
Takuro SAKAGAMI, *Kumamoto University, Japan*

11:00 Disseminated NTM in non-HIV infected patients in Thailand
Ploenchan CHETCHOTISAKD, *Khon Kaen University, Thailand*

11:30-35 short break

Part2 Chair : Ho NAMKOONG, *Keio University, Japan*

11:35 Mendelian susceptibility to mycobacterial diseases
Satoshi OKADA, *Hiroshima University, Japan*

12:05 Immunomodulatory Treatment of NTM and Other Opportunistic Infections in Patients with Altered Immunity : Hits and Misses
Yi Ann Louis CHAI, University Medicine Cluster, *National University Health System, Singapore*

12:30 Neutralizing anti-IL23 autoantibodies and their role in pulmonary and disseminated mycobacterial disease
Aristine CHENG, *Taiwan National University, Taiwan*

12:55 Closing Remarks
Ho NAMKOONG, *Keio University, Japan*

Abstracts

Part1

10:05～

Anti GM-CSF related diseases

Dr Hélène Salvator
Foch Hospital, Saclay University, France

Anti GM-CSF autoantibodies are supposed to lead to pulmonary macrophages dysfunction and they are recognized as the main cause of acquired pulmonary alveolar proteinosis (PAP). Recently, they also have been related to severe infections such as cryptococcocal meningitis and disseminated nocardiosis, linking these antibodies to relatively narrow immunodeficiencies. The phenotypes induced by anti-GM-CSF autoantibodies are variable and not necessarily overlapping. Why nominally the same anti-GM-CSF autoantibody may cause distinct phenotypes in different hosts remains to be elucidated. More globally, these observations question the pathogenic role of anti GM-CSF antibodies, according to the targeted cellular subtype.

10:30～

Disseminated NTM disease with anti-IFN-γ autoantibodies
; as an autoimmune NTM disease

Dr. Takuro SAKAGAMI
Kumamoto University, Japan

We have established methods for the detection of anti-IFN-γ autoantibodies (IFNγ-Ab) in sera and have accumulated cases in Japan. A total of 331 cases with mycobacterial infection was analyzed and 30 cases with IFNγ-Ab (positive rate 80.1%) among 37 disseminated NTM cases with no apparent background immunodeficiency. Clinical phenotypic analysis showed that the clinical manifestations differed significantly from that of cases with NTM disease commonly found in clinical practice. Strongly suggested association between the autoimmune mechanism of autoantibody production and the development of severe NTM disease was suggested in this disease, which should be recognized under the new concept of 'autoimmune NTM disease'.

11:00～

Disseminated NTM in non-HIV infected patients in Thailand

Professor Ploenchan Chetchotisakd
Khon Kaen University, Thailand

Before the year 2000 disseminated NTM (DNTM) infections were rare in Thailand. In 2000, we reported 16 patients whose disease manifestation was a hitherto unrecognized clinical entity characterized by chronic bilateral lymphadenopathy as a result of rapidly growing mycobacteria (RGM). We later reported 129 cases of DNTM in non-HIV infected patients, mostly infected with RGM. These patients had co-infection with other intracellular pathogens. They often involved concomitant reactive dermatosis. We later enrolled these patients into a study of adult onset immunodeficiency in Thailand and Taiwan. Most of them (88%) tested positive for anti-interferon gamma autoantibodies (IFN-• Ab). When comparing these patients from Thailand with the US, most Thai patients infected with *M. abscessus* while in the US patients infected with MAC. The natural history of these patients from a long term follow up, 24% of Thai patients died, 57% of them with no active disease and off therapy. IFN-• Ab levels decreased over time. Treatment of DNTM in IFN-• Ab is troublesome; they may need adjuvant therapy. Rituximab is not accessible in Thailand. We used intravenous cyclophosphamide as an alternative treatment with moderately successful.

Part2

11:35～

Mendelian susceptibility to mycobacterial diseases

Dr. Satoshi Okada
Hiroshima University, Japan

Mendelian susceptibility to mycobacterial disease (MSMD) is characterized by a selective predisposition to infections caused by intracellular pathogens, such as mycobacteria, due to impaired IFN-γ immunity. To date, 18 different genes associated with MSMD have been reported. BCGitis is often the first symptom of this disorder in countries where BCG vaccination is administered. The other representative symptom is multifocal osteomyelitis due to mycobacteria. Impaired inhibition of osteoclast differentiation and bone resorption owing to a poor response to IFN-γ has been shown to be in association with multifocal osteomyelitis in MSMD. The lecture introduces recent update of MSMD.

12:05～

Immunomodulatory Treatment of NTM and Other Opportunistic Infections in Patients with Altered Immunity : Hits and Misses

Dr. Yi Ann Louis CHAI,
University Medicine Cluster, National University Health System, Singapore

Our understanding in the immunological pathways involved in host pathogen interaction in the recent decade has enabled us to elicit situations whereby host immune response may be deficient or inappropriate in non-tuberculous Mycobacteria infection. Especially in complex difficult-to-treat cases, the prospect of using immunomodulatory agents to complement with conventional antimicrobials is an attractive one. Here, we discuss the clinical experience gained anecdotally to date against the backdrop of elicited altered immunity.

12:30～

Neutralizing anti-IL23 autoantibodies and their role in pulmonary and disseminated mycobacterial disease

Dr. Aristine CHENG,
National Taiwan University Hospital
and National Taiwan University College of Medicine, Taiwan

Neutralizing autoantibodies to IL-23 (23–28%) are a distinctive feature of patients with thymoma. In addition, they have been identified in three individuals of Southeast Asian descent with opportunistic infections. We discuss the possible impact of neutralizing autoantibodies to IL-23 on infection susceptibility particularly in the context of mycobacterial or fungal lung disease.