

Session: OS185 Immunity and immunogenetics of infections in immunocompromised hosts

**Category: 10a. Host genetics: infection susceptibility & immunodeficiency**

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**Epidemiological and clinical characteristics of patients with anti-interferon-gamma autoantibodies associated with opportunistic infections in Hong Kong**

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**Background:** The adult-onset immunodeficiency syndrome due to autoantibodies against interferon gamma (anti-IFN- $\gamma$  autoantibodies) is associated with disseminated and/or recurrent opportunistic infections, including non-tuberculous mycobacteriosis, non-typhoidal salmonellosis, burkholderiosis, penicilliosis, and herpes zoster. The condition appears to have an ethnic predilection among Asians including Chinese residents in Hong Kong, Taiwan, and mainland China, but the seroprevalence rate of anti-IFN- $\gamma$  autoantibodies is undetermined. Moreover, it is unknown whether anti-IFN- $\gamma$  autoantibodies are associated with other infective and non-infective conditions. This retrospective case-control analysis aimed to investigate the epidemiology, seroprevalence rate, and clinical manifestations of this emerging immunodeficiency syndrome in Hong Kong.

**Material/methods:** The study was approved by the Institutional Review Board of The University of Hong Kong / Hospital Authority Hong Kong West Cluster. Archived serum samples from subjects aged  $\geq 18$  years, with or without opportunistic infections, were tested by a screening enzyme immunoassay and an IFN- $\gamma$  spiking assay for detection of anti-IFN- $\gamma$  autoantibodies. The clinical data of the patients were retrieved from the Electronic Patient Record (ePR) system of the Hospital Authority and entered into a predesigned database. Comparison between groups of data was evaluated by the Chi-square test for categorical variables and Mann-Whitney U-test for continuous variables. All statistical analyses were performed using SPSS 18.0 for Windows. P-values $<0.05$  were considered statistically significant.

**Results:** A total of 3198 serum samples from 3198 patients were tested. Overall, we detected serum anti-IFN- $\gamma$  autoantibodies by the screening enzyme immunoassay in 34 serum samples (34/3198, 1.1%). These included 11 samples from patients with opportunistic infections including non-tuberculous mycobacteriosis, penicilliosis, non-typhoidal salmonellosis, burkholderiosis, and/or herpes zoster (11/133, 8.3%), 4 from subjects aged >65 years without these opportunistic infections (4/783, 0.5%), 14 from patients with autoimmune diseases without these opportunistic infections (14/753, 1.9%), and 5 from patients with chronic HBV or HCV infection without these opportunistic infections (5/764, 0.7%). The seroprevalence rate of anti-IFN- $\gamma$  autoantibodies in subjects without opportunistic infections was ~1%, which was significantly lower than that of the patients with opportunistic infections (8.3%,  $P < 0.001$ ). Some patients with high-titer serum neutralizing anti-IFN- $\gamma$  autoantibodies also developed reactive (Sweet's syndrome and lobular panniculitis) and infective dermatoses. Anti-IFN- $\gamma$  autoantibodies were strongly associated with HLA-DR\*15:02/16:02 and HLA-DQ\*05:01/05:02 among the affected patients.

**Conclusions:** These findings helped to optimize the diagnostic and treatment protocols for this emerging immunodeficiency syndrome. The long-term outcome of these patients and their clinical response to antimicrobial and immunomodulation therapies should be monitored in future studies. Routine screening for anti-IFN- $\gamma$  autoantibodies in asymptomatic patients is unlikely warranted. A working algorithm for the diagnosis and treatment of patients with dermatoses associated with anti-IFN- $\gamma$  autoantibodies was established. Our non-laborious screening enzyme immunoassay could be adopted by clinical laboratories.