Clinical Characteristics of Cryptococcosis in Non-HIV Patients Associated with Anti-granulocyte-macrophage Colony-stimulating Factor (Anti-GM-CSF) Autoantibodies in Siriraj Hospital, Thailand

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Background: Cryptococcosis is an opportunistic fungal infection in immunocompromised, especially Human Immunodeficiency Virus (HIV)-infected patients. Granulocyte-macrophage colony-stimulating factor (GM-CSF) regulates the functions of phagocytes and pulmonary alveolar macrophages, which is crucial in cryptococcal control. Recently, a syndrome of anti-GM-CSF autoantibodies has been found to be associated with cryptococcosis in non-HIV individuals, but it has never been extensively described in Thai population.

Objective: This study aimed to investigate the clinical characteristics and the association of non-HIV cryptococcosis and anti-GM-CSF autoantibodies in Thais.

Methods: We performed anti-GM-CSF autoantibody assays in patient’s sera collected from our cohort of non-HIV-associated cryptococcosis. Clinical characteristics, immunological evaluation and treatment outcomes were analyzed.

Results: From 2008 to 2016, a total of 14 HIV-negative, immunocompetent patients who had cryptococcal diseases were included in the study. None of them had anti-interferon gamma autoantibodies. Seven patients (50%) had positive results for anti-GM-CSF autoantibodies. Mean age (±SD) of patients with positive and negative anti-GM-CSF autoantibodies were 54 (±8.3) and 66 (±14.7) years, respectively (p = 0.08). Male sex was 57.1% and 28.6% in those with and without anti-GM-CSF autoantibodies (p = 0.59). There was no difference in underlying diseases between the two groups. Patients with anti-GM-CSF autoantibodies were significantly associated with disseminated disease (85.7% vs 14.3%; p = 0.029). In the anti-GM-CSF autoantibodies group, 5 patients had central nervous system (CNS) and pulmonary diseases, while 1 patient had CNS and cutaneous diseases and 1 patient had isolated CNS disease. All 7 patients (100%) with anti-GM-CSF autoantibodies had CNS involvement; whereas, 3 out of 7 (42.9%) patients without anti-GM-CSF had CNS diseases (p = 0.07). There were 3 patients with isolated pulmonary cryptococcosis and all of them were anti-GM-CSF negative. The number of CD4 and CD8 cells and the mortality rate were comparable between both groups.

Conclusion: Anti-GM-CSF autoantibody is a new entity of immunodeficiency associated with CNS and disseminated cryptococcosis in Thai patients.

Keywords: Cryptococcosis, Anti-GM-CSF, Anti-granulocyte-macrophage colony-stimulating factor, Non-HIV, immunocompetent