Abstract 1579

Effect of anti-CD20 antibody-mediated B-cell depletion on susceptibility to a Pneumocystis infection in mice

Type: Oral Presentation

Keyword: Disease Modifying Therapies – Mechanism of Action

Authors: G. Dai[1], G. Weckbecker[2], J. K. Kolls[1]; [1]Center for Translational Research in Infection and Inflammation Tulane School of Medicine, Tulane School of Medicine/New Orleans, LA/United States of America, [2]Novartis Pharma AG/Basel/Switzerland

Background

Pneumocystis species are heterogeneous atypical microscopic fungi. Immune response against *Pneumocystis* infections is thought to be mediated by B and T cells.

Objectives

To investigate the effect of subcutaneous (s.c.) anti-CD20 antibody-induced B-cell depletion on T-cell responses and antibody generation against primary and secondary *Pneumocystis* infection in mice.

Methods

C57BL/6 female mice were administered with the s.c. anti-CD20 antibody or control 3 days prior to a pulmonary challenge with *Pneumocystis murina* (2×10^5 cysts, primary infection) and continued weekly for up to 4 weeks. In another group, mice were infected with *P. murina* and allowed to clear the infection. Six weeks later, mice were administered with the anti-CD20 antibody or control and then re-infected with *P. murina* after 3 days (secondary infection) to determine if the anti-CD20 antibody affected the pre-existing anti-fungal antibody. Administration of the anti-CD20 antibody or control was continued weekly. In both cohorts, T- and B-cells in the lung were assayed by flow cytometry at Day 14 and Day 28 after infection, and lung fungal burden was determined by quantitative polymerase chain reaction (PCR). Serum immunoglobulin (IgG, IgE and IgM) levels were measured by the enzyme-linked immunosorbent assay (ELISA).

Results

In mice with primary *Pneumocystis* infection, anti-CD20 antibody treatment depleted both CD19+ and CD27+CD19+ cells, but not T cells, in the lung at Days 14 and 28. Although the anti-CD20 antibody treatment impaired fungal clearance at Day 14 post-infection, fungal burden in the lungs was substantially reduced at Day 28 in both depleted and control mice. Anti-CD20 antibody treatment did not alter antigen-specific serum immunoglobulin levels compared with control mice, and there were no significant differences in the numbers of lung interferon gamma (IFNg)+CD4+, interleukin (IL-4)+CD4+, IL-5+CD4+ and IL-17A+CD4+ cells between depleted and control mice after infection. In mice with secondary *Pneumocystis* infection, the lung fungal burden was comparable between depleted and control mice 14 days after re-infection.

Conclusions

Subcutaneous anti-CD20 antibody treatment may delay fungal clearance but it does not impair the ability of the host to clear a *Pneumocystis* infection, irrespective of primary or secondary infection.

Print