Abstract 1575

Effect of anti-CD20 antibody-induced B-cell depletion on the susceptibility to Streptococcus pneumoniae infections

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Background

Treatment with rituximab, an anti-CD20 chimeric monoclonal antibody, rapidly depletes >95% of CD20+ B cells from circulation. However, immunosuppression induced by B-cell depletion therapy is associated with an increased risk of respiratory tract infections.

Objectives

To investigate the effect of B-cell depletion on the antibody-mediated immunity to *Streptococcus pneumoniae* in mice.

Methods

B cells were depleted in 6-week-old CD57/BL6 female mice (n=6/group) by intravenously injecting the anti-CD20 SA271G2 antibody (50 µg/mouse) for evaluating the effect of B-cell depletion on *S.pneumoniae* colonization and vaccination. After depletion, mice were either colonized by intranasal administration of the *S.pneumoniae* 6B strain (10 µL/dose, 1×10^7 bacteria, Day 3) or vaccinated by intraperitoneal injections of two doses of Prevnar (20 µL/dose, Days 3 and 13). Intravenous (i.v.) and subcutaneous (s.c.) routes of administration of B-cell therapy were also compared by injecting anti-CD20 mIgG1 (50 µg/mouse) followed by Prevnar vaccinations (n=8/group). For both studies, B-cell repertoire and *S.pneumoniae*-specific IgG levels were measured using the whole-cell enzyme-linked immunosorbent assay (ELISA) and flow cytometry antibody-binding assay.

Results

B-cell depletion did not increase susceptibility to *S.pneumoniae* in naïve mice, indicating limited functional effects on natural IgM. When administered before colonization/vaccination, the treatment caused a significant decrease in circulating IgG levels to *S.pneumoniae*. Following the pneumonia challenge model, a decreased level of protection induced by these immunizations was also observed in the B-cell depleted mice. In contrast, vaccination-induced protection was preserved in the depleted group when treatment was administered after vaccination. Both i.v. and s.c. administration of the anti-CD20 antibody using an identical dose induced a large decrease in splenic follicular B cells, with relative preservation of marginal zone B cells.

Conclusions

The timing of B-cell depletion by anti-CD20 therapy critically affects the development of antibody-mediated immunity to *S.pneumoniae*. Clinical studies further confirm the negative effects of B-cell depletion on antibody responses to *S.pneumoniae* in patients treated with rituximab.

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