Plasmablasts and antibody response to Haemophilus influenzae type B vaccine in patients with chronic lymphocytic leukemia

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Introduction

Bacterial infections are the most common cause of morbidity and mortality among **chronic lymphocytic leukemia** (CLL) patients. In some countries vaccination against encapsulated bacteria, such as **Haemophilus influenzae type B** (HIB), is recommended for this group. Vaccine effectiveness is usually measured by serum concentration by IgG anti-HIB, but the procedure requires a month interval between vaccination and antibody titers assessment. Moreover CLL patients are often started on immunoglobulin substitution therapy before antibody production is evaluated. In such a situation, it is difficult to segregate transferred from antigen-induced specific antibodies. The aim of the present study was to investigate plasmablasts and antibody response to HIB vaccine and to check if the response in plasmablasts correlates with increase of specific anti-HIB antibodies in vaccinated CLL patients.

Materials and Methods

Study and control group

This study included 30 previously untreated CLL patients and 15 healthy persons. All individuals received HIB conjugated vaccine.

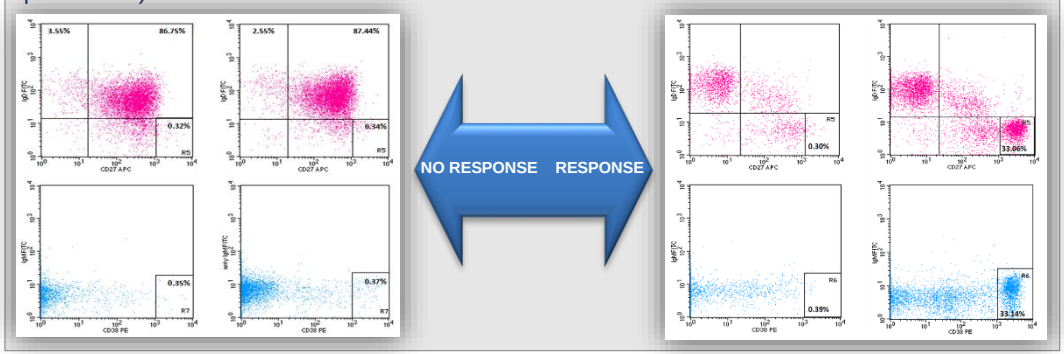
Flowcytometric immunophenotyping with directly labelled monoclonal antibodies (MAb) was used to determine the following lymphocyte subpopulations: T-lymphocytes (CD3+CD4+ and CD3+CD8+), B-lymphocytes (CD19+, including CD5+, CD20+ and CD38+ B cells), natural killer (NK), NKT-like cells (CD3-CD16+CD56+), naive B-lymphocytes (CD19+CD27-IgM+IgD+), natural effector B-lymphocytes (CD19+CD27+IgM+IgD+), IgM only memory B-lymphocytes (CD19+CD27+IgM+IgD-), switched memory B-lymphocytes (CD19+CD27+IgM-IgD-), transitional B cells (CD19+CD38++IgM++), and class-switched plasmablasts (CD19+ CD38+++IgM-). Plasmablasts were also checked in 7th day after vaccination with the use of HIB vaccine in order to assess patient's immune response. Aliquots were incubated for 15 min in the dark at room temperature with a mixture of optimally titrated, FITC-, PE-, PerCP-Cy-5.5- or APC-labelled MAbs [all Becton Dickinson (BD), San Jose, California USA], within 4 h after sampling.

HIB antibody titres

Anti-HIB antibody titers were measured before and after vaccination with o dose of HIB vaccine at monthly interval using the VaccZyme™ Hib IgG ELISA kit (The Binding Site, UK) in order to assess patient's immune response.

Results

Increase of plasmablasts and specific anti-HIB antibodies was noted in 11 **CLL patients** (**36.67%**) and all **healthy persons** (n=15, **100%**). The percentage of plasmablasts before and after vaccination, and postvaccination anti-HIB antibodies were lower in CLL patients than in healthy individuals (p=0.0023, p=0.0021, and p=0.0016, respectively). There was a positive correlation between the increase of anti-HIB antibodies and the percentage of plasmablasts after the vaccination in healthy subjects (r=0.721, p=0.00014), and CLL patients (r=0.692, p=0.00017).



Conclusions

- The majority of CLL patients fail to increase circulating plasmablasts following antigen challenge.
- Lacking response in plasmablasts correlates with lacking increase of specific anti-HIB antibodies in vaccinated individuals.
- Assessment of the differences in the amount of plasmablasts prior and after vaccination provides a rapid screening test to demonstrate defective antibody responses in CLL patients, even when on replacement immunoglobulin therapy.
- Moreover, CLL patients with adequate response to HIB conjugate vaccine had higher IgG concentrations and were younger than those without response (data not shown). According to these findings it would appear to be beneficial to vaccinate all CLL patients with conjugate vaccine at the presentation of the disease.

References

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