

**Chronic nasal carriage of Staphylococcus aureus does not increase the risk of relapse and severe infections in granulomatosis with polyangiitis patients when receiving rituximab maintenance treatment.**

**Background:**

Chronic nasal carriage of Staphylococcus aureus (SA) has been shown to increase the risk of relapse in patients with Granulomatosis with polyangiitis (GPA). B cell depletion with Rituximab (RTX) is effective in inducing and maintaining remission in GPA. However B cell depletion and hypogammaglobulinemia during RTX could increase the risk of chronic SA nasal carriage.

**Objective:**

To investigate the effect of long-term RTX treatment on chronic SA nasal carriage, the risk of relapses, severe infections and hypogammaglobulinemia in GPA patients.

**Methods:**

Cohort study with prospectively collected nasal swab data in 29 GPA patients on RTX (median RTX dose of 9 g) treatment for a median period of 49 months. Patients (52 % men, median age 50 (19-75) at RTX initiation, 86 % PR3-ANCA positive, 3 % MPO-ANCA positive and 10 % ANCA negative, 66 % and 59 % with respectively pulmonary and renal involvement) had received a cumulative dose of cyclophosphamide of 17 (0-250) g. Nasal swabs were collected prior and during RTX for a median of 3 and 9 swabs respectively. Persistent SA nasal carriage was defined as the presence of SA in more than 75 % of nasal swabs.

**Results:**

The frequency of persistent SA nasal carriage did not change before (20 %) and after RTX (28 %) ( $p=0.562$ ).

Persistent SA nasal carriage did not increase the risk of relapses ( $p=0.646$ ), severe infections ( $p=0.357$ ) or hypogammaglobulinemia ( $p=1.00$ ), but reduced the risk of chronic infections ( $p=0.033$ ) during RTX.

Patients without nasal SA carriage during RTX maintenance were at increased risk to discontinue RTX due to hypogammaglobulinemia ( $p=0.048$ ) (Figure). They had less lung involvement ( $p=0.032$ ), more disease activity at baseline ( $p=0.010$ ), lower CD4 cell count after RTX 2 g ( $p=0.023$ ) and larger decline of total Ig after RTX 2g ( $p=0.045$ ) and at last visit ( $p=0.021$ ).

**Conclusion:**

Long-term RTX maintenance therapy in GPA patients did not influence SA nasal carriage status. Persistent SA carriage during long-term RTX treatment did not increase the risk of relapses and infections and was associated

with a lower risk of developing hypogammaglobulinemia. Our results suggest that long-term RTX treatment is better tolerated in GPA patients with chronic SA nasal carriage.

Figure

Kaplan-Meier analysis of the probability of developing hypogammaglobulinemia according to nasal carriage of Staphylococcus aureus during rituximab maintenance

