A recently established murine model of nasal polyps: similarities and differences with human nasal polyps

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Animal model systems are valuable for investigating human diseases and developing new therapeutic targets. Our laboratory recently established a murine model of nasal polyps (NP) and investigated similarities and differences between this murine model and human NP. It was previously demonstrated that B cell–activating factor of the TNF family (BAFF), a key B-cell survival factor, is highly expressed in NP tissue from patients with chronic rhinosinusitis with nasal polyps (CRSwNP). Several reports also have shown increased levels of various isotypes of immunoglobulins, including IgG, IgE, and IgA, in sinus tissue from patients with CRS. Therefore, we aimed to focus this investigation on B cell activation in this murine NP model.

Mice were sensitized with an intraperitoneal injection of PBS or 25 µg of ovalbumin (OVA; grade V; Sigma, St. Louis, MO) plus 2 mg of aluminum hydroxide gel (Alum) on days 0 and 7. After general sensitization, mice were locally challenged with PBS or 6% OVA into their nostrils daily from day 14 to day 20. To generate NP-like tissues, 6% OVA with Staphylococcus aureus enterotoxin B (SEB, 10 ng) was instilled into the nasal cavity of mice 3 times a week for 8 weeks after induction of an OVA-induced allergic rhinosinusitis. Negative control mice did not receive either OVA or SEB. The OVA group mice were challenged nasally with only 6% OVA without SEB. The development of NP was confirmed by hematoxylin and eosin staining. The mRNA and protein levels of various inflammatory cell markers and mediators were measured by real-time PCR in nasal tissue and by ELISA in nasal lavage fluid (NLF), respectively. Total immunoglobulin isotype levels in NLF were also quantitated using the Mouse Immunoglobulin Isotyping Multiplex kit (EMD Millipore, Billerica, MA) on a Luminex 200 instrument (Life Technologies, Grand Island, NY), and normalized to total protein.

The H & E staining of nasal tissue revealed that mice challenged with OVA plus SEB (NP group) developed multiple edematous polypoid lesions with heavy eosinophilic infiltrations, whereas mice challenged with only OVA (OVA group) showed eosinophilic infiltrations, but no polypoid lesions. Similar to human NP, there were significant increases in gene expression of inflammatory cell markers such as CD19 (2-fold), CD138 (3-fold), CD11c (9-fold), and MCP-6 (300-fold) in nasal tissue samples of the NP group compared with those of the control group ($P < 0.05$). In further investigations of B cell activation, mRNA expressions of BAFF (3-fold) and A Proliferation Inducing Ligand (APRIL, 2.5-fold) were found to be significantly increased in murine NP tissue ($P < 0.05$). BAFF protein concentration in NLF was significantly higher in the NP group than in the control group ($P < 0.05$). IgA and IgG levels in NLF were significantly higher in the NP group compared with the control group ($P < 0.05$).

In conclusion, this study demonstrated that the NP mouse model confirms enhanced B-cell responses, reminiscent of the activation of B cells in human NP. The value of mouse models in general, and this model of CRS in particular, is that genetically manipulated mice are available and can be used to test the importance of various therapeutic targets for therapeutic intervention, such as BAFF. Mouse models can also be utilized to explore pathogenic mechanisms and to identify novel biomarkers of disease.