

IL-5/eosinophils are involved in acquisition of steroid resistance in severe asthma of mice

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It has been known that 5-10% of asthma patients are resistant to the steroid therapy. However, mechanisms underlying the acquisition of steroid resistance remain unclear. Objective of this study is to elucidate whether IL-5/eosinophils are involved in the acquisition of steroid resistance. Ovalbumin (OVA)-sensitized BALB/c mice were intratracheally challenged with OVA at 5 or 500 µg/animal 4 times. Infiltration of eosinophils into the lung, and development of airway remodeling and airway hyperresponsiveness (AHR) were evaluated 1 day after the 4th challenge. Dexamethasone and/or anti-IL-5 mAb was i.p. administered during the multiple challenges. AHR was evaluated by forced oscillation technique using FlexiVent. Infiltration of eosinophils into the lung, and the development of airway remodeling and AHR in the 5 µg OVA-induced model were significantly suppressed by dexamethasone, whereas those asthmatic responses to 500 µg OVA were not inhibited by dexamethasone. Under treatment with anti-IL-5 mAb, in which the eosinophil infiltration was strongly reduced, dexamethasone showed significant inhibition on the development of airway remodeling. However, the steroid resistance in AHR was not restored by the anti-IL-5 mAb. It was suggested that IL-5/eosinophils are involved in the acquisition of steroid resistance in the severe asthma.