The Laryngoscope

Letter to the Editor

In Reference to *Real-World Adverse Events After Type 2 Biologic use in Chronic Rhinosinusitis with Nasal Polyps*

Dear Editor,

With great interest, we read the article "Real-World Adverse Events After Type 2 Biologic use in Chronic Rhinosinusitis with Nasal Polyps" recently published in The Laryngoscope.[1] The authors investigated the safety of dupilumab (D) and mepolizumab (M) in real-life patients with Chronic Rhinosinusitis with Nasal Polyps (CRSwNP). They suggested that D is associated with a higher rate of adverse event (AE) than M, although only 6–8% can lead to discontinuation.[1] The commonest AE leading to discontinuation for D was rash, whereas for M was lightheadedness. Authors concluded that the differences in frequency and types of AE need to be considered when choosing a biologic for CRSwNP.[1] We would like to focus on a novel AE we observed in two patients following treatment with D for asthma and CRSwNP not previously reported in the literature: alopecia areata (AA). AA is an immune-mediated non-cicatricial hair loss disorder provoked by the local increase in the level of interferon-gamma (IFN-g) and CD8+ T cells, suggesting the key role of the Th1/Th17 immune response in its pathogenesis.

However, recent research has indicated a potential role of T helper 2 (Th2) upregulation in the immunopathogenesis of AA.

Interestingly, patients affected by Atopic Dermatitis (AD) have a higher risk of AA. These two skin diseases seem to share pathogenetic mechanisms as the overexpression of interleukin 4 (IL4) and interleukin 13 (IL13).

Although cases of AA healing during treatment with D for AD were reported, hair loss clinically resembling AA is, as well, reported after D therapy.

In type 2 inflammation, IL-4 stimulates further production of IL-4, IL-5, and IL-13 driving Th2 clonal expansion, whereas IL-5 is mainly involved in the differentiation of Th2 into eosinophils. So, IL-4 plays an upstream role in the type 2 inflammatory pathway, therefore blocking IL4 could have a greater effect on the immune system response compared to a downstream target such as IL-5. That may explain the differences in clinical efficacy and AE between D and M. While previous studies have reported AA as AE following D therapy for AD, both clinical trials and real-life studies for asthma and CRSwNP did not report cases of AA. This letter aims to focus attention on a novel AE occurring following 2 years of treatment with D for asthma and CRSwNP.

Likely, the widespread use of D for the treatment of CRSwNP has led to the observation of novel AE as justified by the heterogeneity of patients with respect to clinical trails' populations.

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