Does Omalizumab Cause Atopic Dermatitis Flare-Ups?

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To the Editor:

We read with interest the case reported by Yanovsky et al[1] (*Cutis.* 2023;112:E23-E25). We thank the authors for updating our knowledge about atopic dermatitis (AD) and omalizumab and improving our understanding of the various wanted and unwanted effects that may manifest with omalizumab. We wish to clarify a few points on omalizumab use.

First, Yanovsky et al[1] reported that their patient's AD flares occurred within a few days after omalizumab injections to control asthma, possibly because omalizumab may have caused a paradoxical increase in sensitivity to other cytokines such as IL-33 in basophils and increased IL-4/IL-13 production in the skin. The authors cited Imai[2] to explain that IL-33 plays a role in the pathogenesis of AD, increases itching, and disrupts the skin barrier. However, Imai[2] did not discuss a relationship with omalizumab. As a recombinant humanized IgG1 monoclonal anti-IgE antibody, omalizumab works by interacting with the high-affinity receptor Fc epsilon RI that typically is found on eosinophils, mast cells, and basophils and plays a critical role in preventing the allergic cascade.[3] We could not find any studies in the literature regarding omalizumab having a specific effect on the skin, causing cytokine imbalance, or increasing IL-4/IL-13 levels.

Second, the case report indicated that AD lesions improved with the biologic dupilumab,[1] which seems amazing. Dupilumab is a monoclonal antibody used in patients with moderate to severe AD that blocks IL-4/IL-13 signaling and thus inhibits receptor signaling downstream of the Janus kinase signal transducer and activator of transcription protein pathway.[4] It also has been shown to be beneficial in children with moderate to severe uncontrolled asthma.[5] In vivo studies are needed to learn about the effects of these biologics on asthma and AD, whose complex immunologic effects are increasingly well understood by real patient experience.

Third, omalizumab has been found to relieve AD, not exacerbate it, in our own experience with 7 patients (unpublished data, 2024) and randomized controlled trials.[6]

Fourth, Yanovsky et al[1] reported that the patient's lesions flared up within a few days after taking omalizumab, which suggests a non-IgE delayed reaction. Could this reaction be related to polysorbate 20 used as an excipient in the commercial preparation? When we examined both preparations, the presence of polysorbate 80 in dupilumab was noteworthy,[7] unlike omalizumab. We suggest the authors perform a patch test including polysorbate 20 and polysorbate 80.

Finally, the authors mentioned that omalizumab may cause a paradoxical exacerbation of AD in certain patients, as in tumor necrosis factor α inhibitor–induced psoriasis.[8] This has been reported,[8] but tumor necrosis factor α inhibitors are cytokine inhibitors and can lead to cytokine imbalance, while omalizumab is an IgE inhibitor.

Yanovsky et al[1] described AD flares as "triggered by omalizumab," which we believe was not the case. Because this patient had chronic AD, other causes of AD exacerbation in this patient could include stress or infection. Also, when they say that AD is triggered or induced, it implies that they are attributing the occurrence/development of AD in this patient to omalizumab. Of course, this also is not true.

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Author's Response

Thank you for your thoughtful comments. Although we agree that we cannot prove omalizumab was the cause of our patient's AD flares, the new onset of severely worsening disease that was exacerbated by each dose of omalizumab as well as subsequent resolution upon switching to dupilumab was highly suggestive for a causal relationship. Our goal was to alert physicians to the possibility of this phenomenon and to encourage further study.

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