Consultant360 Multidisciplinary Medical Information Network

CASE IN POINT

PEER REVIEWED

Possible Omalizumab-Induced Arthritis

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A 68-year-old man with a history of hypertension and anxiety disorder had received a diagnosis of idiopathic urticaria and angioedema approximately 2 years prior. He initially had been treated with a second-generation H_1 antihistamine (cetirizine), 10 mg twice a day. Due to persistent symptoms, ranitidine, 150 mg twice a day, montelukast, 10 mg once a day, and hydroxyzine were added; he also required a short course of prednisone. These medications also were ineffective in controlling the urticaria and angioedema, so he was started on omalizumab, 300 mg subcutaneously once every 4 weeks. His urticaria then resolved, and he continued to do well.

Approximately 1 year after beginning treatment with omalizumab, however, the man developed pain and swelling in the small joints of his hands and wrists. He eventually received a diagnosis of seronegative inflammatory arthritis (rheumatoid factor and anticitrullinated protein antibodies were negative; levels of inflammatory markers were normal). He had bilateral synovitis of the metacarpophalangeal joints, the proximal interphalangeal joints, and the wrist joints.

He was started on a regimen of methotrexate, 15 mg once a week. He reported the development of a metallic taste, and the methotrexate was discontinued. He was then started on leflunomide, 20 mg a day. He also required a short course of prednisone. After 3 months of leflunomide therapy, his symptoms had been largely controlled. He did experience episodic flares requiring corticosteroids, however. He noticed that his symptoms worsened within 1 to 2 days after having received an omalizumab injection every month. Given the fact that his urticaria had resolved, a decision was made to stop the omalizumab.

After having discontinued omalizumab, he experienced no further arthritis flares. After another 4 months, leflunomide was stopped, and the patient had continued to do well, without a flare of arthritis, over the past 18 months since then.

The patient's clinical course suggests an inflammatory arthritis likely triggered by omalizumab. No reported cases of this association have been reported in the literature. While the prescribing information for omalizumab does not mention inflammatory arthritis as an adverse reaction, it does note that fever, rash, and arthralgias were reported in post-approval use of the drug.[1]

The mechanism of action of omalizumab in chronic idiopathic urticaria is that the drug binds to immunoglobulin E (IgE) and lowers free IgE levels. Subsequently, high-affinity IgE receptors (FcεRI) on the surface of mast cells and basophils down-regulate.[1] The mechanism by which these effects of omalizumab result in an improvement of chronic idiopathic urticaria symptoms is unknown. How this mechanism may trigger an inflammatory arthritis, if at all, also is unclear.

It is also possible that the patient's development of inflammatory arthritis was coincidental and not related to omalizumab. Nevertheless, the arthritis flare occurring within a few days of the subcutaneous injection, and the complete resolution of arthritis after discontinuation of the medication, raises suspicion that the arthritis was likely drug-induced.

Reference:

1. Xolair [prescribing information]. San Francisco, CA: Genentech; 2019. https://www.gene.com/download/pdf/xolair_prescribing.pdf. Accessed May 20, 2019.