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CORRESPONDENCE

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Idiopathic anaphylaxis due to SARS-CoV-2 mRNA vaccine?

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Dear Editor,

I have read the article titled "A case with recurrent idiopathic anaphylaxis episodes starting soon after COVID-19 mRNA vaccination" by Korkmaz et al. with great interest.[1] While reading the case report, I had a few questions about the case that, if clarified, would be useful to the reader.

The occurrence and/or exacerbations of chronic spontaneous urticaria (CSU) after such COVID-19 BioNTech® mRNA (messenger ribonucleic acid) vaccines have been frequently reported in the literature.[2,3] The occurrence of idiopathic anaphylaxis (IA) in these patients after or with chronic spontaneous/idiopathic urticaria is known in the literature due to cases also reported by us.[4] Additionally, in the evaluation of 73 patients with IA by Boxer et al., 23/73 patients had chronic idiopathic angioedema, urticaria, or both before the development of IA.[5] It has even been reported that these patients were resistant to treatment and that their urticaria and anaphylaxis could be controlled successfully with omalizumab.[4,6,7] The clinical effectiveness of omalizumab in such patients should be through the deactivation of flowing immunoglobulin E (IgE) by omalizumab, performing on both type I autoallergy and type IIb autoimmunity mechanisms and decreasing histamine release from mast cells and basophils.[8,9]

Three doses of BioNTech® SARS CoV-2 vaccine are administered for 3 months in the patient.[1] Urticaria attacks started 4 days after the first dose of the SARS CoV-2 vaccine. Signs of anaphylaxis occurred four days after the third dose of vaccine administration. Then, urticaria and angioedema continued to occur daily after the second dose, and anaphylaxis attacks recurred approximately once a month.[1] Therefore, how can it be idiopathic if it is known to occur after BioNTech® vaccine administration? There seems to be a certain trigger here because, even if it is not possible to explain neatly the pathogenesis of urticaria and anaphylaxis, it developed after vaccination and no other logical reason has been found to explain this situation.

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Some comments on the pathogenesis of CSU and then IA in this patient would have been useful to the reader. Currently, two autoimmune mechanisms (two major endotypes) for origination of CSU have been proposed. The first possibility is mast cell activation by IgG autoantibodies against IgE or FcεRI. Both IgG antibodies cause cross-linking FcεRI to trigger mast cell activation (type IIb autoimmunity).[8] The second possible mechanism is autoimmunity dependent on IgE itself, with the theory that the patient with IgE reacts with autoallergens (type I autoallergy).[8] Again, these mechanisms recently proposed for CSU may be involved in the occurrence and development of IA in this patient. We think that these presumed autoimmune mechanisms may be stimulated by different environmental and individual triggers (e.g., stress, infection, vaccination, etc.) as well as autoallergens from time to time, and IA episodes may occur in this patient as in exacerbations of other autoimmune diseases.

Biomarkers that can help endotyping CSU patients and to select the most appropriate treatment have recently started to be reported in the literature—for instance, for autoallergic CSU, serum high total IgE level and IgE against autoallergens, and for autoimmune CSU, low serum IgE level, low basophil cell counts, and IgG against autoantigens like thyroid peroxidase and a positive autologous serum skin test.[10] Would the pathophysiology in this patient have been better understood if the basophil count in the sample complete blood count and the results of the autologous serum skin test had been given? Also, was CSU in this patient accompanied by chronic inducible urticaria? The good response of this patient to omalizumab indicates an autoallergic endotype, but does it not seem contradictory to the low IgE value in this patient? Can the authors comment on whether this patient's CSU is autoimmune or autoallergic type? If we could understand the endotype of CSU, the pathophysiology of IA episodes in this patient would be more understandable for us.

In conclusion, I thank the authors for this beautiful and high-quality case report and its implications for understanding the pathophysiology of CSU and IA in us.

AI Declaration

No artificial intelligence (AI) tools or systems were used in the development, writing, analysis, or any other aspect of this manuscript.

Author's Consent for Publication

All authors approved the submission.

Author Contributions

ÖÖ has done everything.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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