Unusual Lysozyme-induced anaphylaxis in an egg-allergic child

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Abstract

A nine-year-old egg allergic child developed anaphylaxis after ingesting the lysozyme-containing over-the-counter-drug Lysopaine(**R**). He complained of a sore throat without fever or cough. His mother administered him one sublingual tablet of the over-thecounter drug Lysopaine(**R**), containing 20 mg lysozyme hydrochloride. A few minutes after intake of the drug, he developed anaphylaxis and received 300 mg intramuscular epinephrine. HE was not exposed to other allergens. The responsibility of lysozyme was confirmed by positive skin prick tests for Lysopaïne(**R**) and the presence of specific IgE against lysozyme. When giving this treatment to her son, his mother had no idea that it could contain egg protein and she did not perceive lysozyme as an allergenic protein. However, the box mentioned the presence of lysozyme and also specified "contains lysozyme extracted from egg". Lysozyme, a minor egg allergen, may induce anaphylaxis in egg-allergic patients. Lysozyme can be found in many commonly consumed industrial food and drug products and its labelling may be misleading. Our observation highlights the importance of properly educating allergic patients to recognize allergens, even minor ones.

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Lysozyme (gal d4) is a minor allergen of hen's eggs, with sensitization to lysozyme demonstrated in up to 35% of children with hen's-egg allergy¹. Specific IgE (sIgE) against lysozyme is generally not useful in clinical practice for the diagnosis of egg allergy or to monitor its evolution. Indeed, sIgE against egg white or ovalbumin is a better predictor of hen's-egg allergy². The labelling of lysozyme in packaged food products as an egg allergen may be misleading and its recognition may be difficult for patients, as it appears as the additive "E1105 (lysozyme)", "conservator (lysozyme)", or "lysozyme (egg protein)". Lysozyme is also present in numerous drugs, including antiseptics and nasal sprays. Thus, egg-allergic patients may be frequently unknowingly exposed to small amounts of lysozyme in various industrial food products, including cheese, pesto sauces, and pre-packed dishes, such as pizza, ravioli, or salads, or in drugs, without such exposure evoking an allergic reaction³. Here, we report an unusual case of anaphylaxis induced by the lysozyme-containing over-the-counter-drug Lysopaine(**R**) in a nine-year-old child with hen's-egg allergy. A nine-year-old poly-allergic male child developed anaphylaxis after ingesting Lysopaine(\mathbb{R}). He was followed in our department for an IgE-mediated hen's egg allergy, confirmed by a positive open oral food challenge (OFC) to baked egg, associated with sensitization to eggs (Table 1). He is also allergic to wheat and fish, both allergies having been confirmed by the presence of sIgE and a positive open OFC. In addition, he has allergic rhinitis to birch pollen and has presented with asthma and atopic dermatitis in the past. He now tolerates cow's milk but previously presented with an IgE-mediated cow's milk allergy, to which the resolution was confirmed at the age of four years by a negative open OFC to fresh milk. At the time of the reaction, he was following oral immunotherapy to baked egg. He was avoiding fish, wheat, and eggs in his diet and, despite being tolerant to cow's milk, he was avoiding dairy products because of an aversion to such products.



In May 2021, he complained of a sore throat without fever or cough. His mother administered him one sublingual tablet of the over-the-counter drug Lysopaine \mathbb{R} , containing 20 mg lysozyme hydrochloride and 1.5 mg cetylpyridinium chloride. A few minutes after intake of the drug, he developed edema of the lips and tongue, associated with dysphonia (Figure 1), without dyspnea, wheezing, urticaria, or vomiting. His mother administered 5 mg of the oral H1-antihistamine mequitazine and 20 min later, he took a 20 mg tablet of prednisolone, because the symptoms persisted, before finally visiting the emergency department. The initial examination showed a breathing rate of 17/min, oxygen saturation of 98% in ambient air, a heart rate of 93 bpm, and a blood pressure of 92/49 mmHg. He showed no wheezing or dyspnea. He was administered another 20 mg tablet of prednisolone and was monitored. Two hours later, he started vomiting and developed abdominal pain, without dyspnea. He was administered 300 mg intramuscular epinephrine (Anapen \mathbb{R}) and the symptoms resolved within a few minutes. He was then kept under observation for 8 h and subsequently discharged.

The allergy workup was conducted six weeks later. Skin prick-tests (SPTs) were performed with Lysopaine $(ALK(\mathbb{R}))$. Lysopaine (\mathbb{R}) was crushed and mixed with a physiological saline solution and one drop of the mixture used for prick-testing. Circulating sIgE against lysozyme was measured using the ImmunoCAP System (Phadia, Uppsala, Sweden). Results of the tests, including previous sIgE against egg white and ovomucoid, are shown in Table 1 and Figure 2.

Table 1. Results of the allergy work-up.

06/06/2021	06/06/2021
3	3
0	0
2	2
8	8
08/06/2021	12/10/2020
29.4	-
76.8	30.8
26.3	23.1
4376	4794
	06/06/2021 3 0 2 8 08/06/2021 29.4 76.8 26.3 4376





For this child, the initial presentation and evidence for sensitization against lysozyme, in the context of an egg allergy, are compatible with the diagnosis of anaphylaxis to lysozyme. Within the hours before the reaction, he did not ingest any food containing eggs, wheat, fish, or milk and had a usual meal for dinner two hours before intake of the drug. When giving this treatment to her son, his mother had no idea that it could contain egg protein and she did not perceive lysozyme as an allergenic protein. However, the box mentioned the presence of lysozyme and also specified "contains lysozyme extracted from egg". Previous reports have described anaphylaxis attributable to lysozyme. One case of anaphylaxis following the ingestion of Lizipaina® for a mild respiratory infection was reported for a 15-year-old egg-allergic patient sensitized to lysozyme⁴. The SPT was positive for Lizipaina® and sIgE against lysozyme was detected. Another case of anaphylaxis to Lizipaina® was described in a 54-year-old patient sensitized to lysozyme. The SPT was positive for lysozyme (commercial extract) and sIgE against lysozyme was detected. This patient experienced similar symptoms 3 to 4 times after the ingestion of cured cheese or raw egg⁵. A six-year-old egg-allergic child presented with anaphylaxis 5 mins after the first use of a deodorant containing lysozyme hydrochloride, but no lysozyme sensitization was demonstrated, either by SPT or sIgE measurement⁶. Other cases of allergic

reactions potentially related to lysozyme were described for women using vaginal suppositories containing lysozyme, among whom three were known to be allergic to egg. However, these suppositories contained other egg proteins, which may have been involved in the occurrence of the allergic reactions, and none of these patients was sensitized to lysozyme⁷. In the child of the case presented here, symptoms may have been worsened by the presence of a concomitant infection. Despite the presence of lysozyme in various industrial food products, our patient may have not been previously exposed because of his large food restrictions and his aversion to dairy products. It is also possible that he may simply not have reacted to previous exposure because the amount of lysozyme contained in food products is too low to induce an allergic reaction compared to the 20 mg contained in Lysopaine($\mathbf{\hat{R}}$).

In summary, lysozyme may induce anaphylaxis in egg-allergic patients, especially when aggravating factors, such as infection, are present. Lysozyme can be found in many commonly consumed industrial food and drug products and its labelling may be misleading, exposing patients to potentially severe reactions. Indeed, lysozyme is not necessarily perceived by egg-allergic patients as an allergenic protein. Our observation highlights the importance of properly educating allergic patients to recognize allergens, even minor ones.

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Table 1. Results of the allergy work-up.

Skin prick-tests (mm)	06/06/2021	
Positive control	3	
Negative control	0	
Egg white	2	
Lysopaine®	8	
Specific IgE (kUA/L)	08/06/2021	12/10/2020
sigE lysozyme (gal d4)	29.4	-
slgE egg white	76.8	30.8
slgE ovomucoid	26.3	23.1
Total IgE (kU/L)	4376	4794

mm: millimeters, slgE: specific lgE, positive control = histamine dichlorhydrate (10 mg/mL).