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CASE IN POINT

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Anaphylactic Reaction Induced by Inhaled Fluticasone Propionate

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CITATION:

Grayson CJ, NeSmith J. Anaphylactic reaction induced by inhaled fluticasone propionate [published online January 23, 2020]. Consultant360.

A 76-year-old man with a history of hypertension, aortic stenosis, transient ischemic attacks, and anemia presented to the emergency department with concern for tongue swelling. The patient stated that he had awoken during the night and noticed that his tongue was swollen and that he was not able to articulate properly. The patient had taken his first ever dose of fluticasone propionate nasal spray for allergic rhinitis earlier that afternoon.

On physical examination, the man's tongue was swollen, which altered his speech, and the pharynx was not visible. There was no associated lip swelling or stridor. The patient was treated with epinephrine, methylprednisolone, diphenhydramine, and famotidine, after which he reported mild improvement. The patient was then given dexamethasone and another dose of famotidine, which resulted in complete resolution of his tongue swelling and poor articulation.

The patient reported having had a very similar reaction to an angiotensin-converting enzyme inhibitor (ACEI) 6 months prior to this presentation; the medication had subsequently been discontinued. He had no history of asthma or atopic dermatitis.

The patient followed up in clinic 1 week later and reported feeling well. He denied having any further episodes of tongue swelling or speech difficulty after having discontinued intranasal fluticasone propionate.

DIFFERENTIAL DIAGNOSIS

This patient's angioedema and difficulty swallowing after exposure to a potential allergen is consistent with anaphylaxis.[1] Food, insect bites and stings, and medications are among the most common triggers of anaphylaxis.[2] The patient had not consumed any new foods that day, nor had he been bitten or stung by any insects, making food and insect envenomation unlikely causes. The only new introduction had been the intranasal fluticasone propionate.

The differential diagnosis also included idiopathic angioedema, hereditary angioedema, and angioedema caused by an ACEI. Idiopathic angioedema and hereditary angioedema would have caused recurrent episodes of angioedema and likely would have presented earlier in life. Since both cases of this patient's angioedema had been associated with medication use, tests for tryptase, C1 esterase inhibitor, and C4 levels were not explored. The patient confirmed having discontinued his ACEI 6 months prior to this presentation, making this cause very unlikely.

Given that the episode had occurred within several hours of administration of fluticasone propionate, and the complete absence of symptoms following discontinuation of this medication, the most likely diagnosis was fluticasone propionate hypersensitivity.

TREATMENT AND OUTCOME

Strict avoidance of intranasal fluticasone propionate was advised. He was advised to try alternative therapies for his seasonal allergic rhinitis.

Skin-prick and patch testing to determine sensitivity to fluticasone propionate and its vehicles was not performed since there is no established protocol. Given the resolution of symptoms following treatment and no recurrence of symptoms within the next 6 months, intranasal fluticasone propionate was determined to be the likely cause of this anaphylactic reaction, and the patient was advised to avoid the medication.

DISCUSSION

Medications such as aspirin, nonsteroidal anti-inflammatory drugs, and antibiotics are common culprits of anaphylaxis.[1] Anaphylaxis typically occurs within seconds or minutes of exposure to the offending agent but can also be delayed for several hours. Angioedema is one of the most common signs of anaphylaxis.[1] Treatment of anaphylaxis includes subcutaneous or intramuscular administration of epinephrine, intravenous fluid resuscitation, β-adrenergic agonists for respiratory tract symptoms, antihistamines, and corticosteroids.[1] The US Food and Drug Administration reports that rare hypersensitivity reactions such as anaphylaxis, angioedema, and contact dermatitis can occur following administration of fluticasone propionate nasal spray. However, only 2 such cases have been reported in the literature.[3] The improvement of our patient's angioedema following

administration of epinephrine, β-adrenergic agonists, antihistamines, and corticosteroids support the conclusion that this was an anaphylactic reaction.

Two cases with immediate hypersensitivity reactions following the use fluticasone propionate have been reported, both by the same authors.[3] One case was a 29-year-old man with a history of seasonal rhinoconjunctivitis who became diaphoretic and developed facial flushing 2 minutes after a dose of fluticasone propionate. His symptoms resolved after administration of epinephrine and antihistamines.[3] The other patient was a 23-year-old woman with a history of rhinitis and sinusitis without asthma. She received 3 doses of fluticasone propionate and developed flushing and chest pain within 5 minutes. Her symptoms resolved spontaneously.[3] A case has also been reported of a hypersensitivity reaction resulting in urticaria, maculopapular rash, and pruritus due to inhaled budesonide in an 8-year-old boy.[4]

Inactive ingredients in the fluticasone propionate preparation include microcrystalline cellulose, carboxymethylcellulose sodium, dextrose, benzalkonium chloride, polysorbate 80, and phenylethyl alcohol. One group of authors reported 2 cases of contact hypersensitivity reactions resulting in inflammatory plaques from polysorbate 80 used as an agent in vitamin A injections for dermatologic conditions.[5] Another group of authors reported 2 cases of anaphylaxis following injection of a corticosteroid that contained carboxymethylcellulose.[6] In both of these cases, skin testing showed immediate reaction to pure carboxymethylcellulose.[6] Carboxymethylcellulose has been identified as a cause of anaphylaxis in numerous other case reports.[7-11]

In a literature review on immediate hypersensitivity reactions to corticosteroids, 28.3% of reactions were due to pharmacologically inactive ingredients.[12] This highlights the importance of considering vehicle ingredients as a potential cause of anaphylaxis in corticosteroids.

In our case, fluticasone propionate was the only new medication the patient had introduced. Although the presentation was not immediate, it is believed that the dose of intranasal fluticasone propionate taken earlier that afternoon was the cause of this patient's anaphylaxis. The improvement of symptoms following standard anaphylactic treatment supports the hypothesis that this was an anaphylactic reaction.

THE TAKE-HOME MESSAGE

Fluticasone propionate and other corticosteroids should be prescribed in caution in patients with a history of anaphylaxis, since these patients might be more susceptible to hypersensitivity reactions. A thorough history of previous medication allergies and reactions should be reviewed prior to prescribing any medications, especially those with potentially life-threatening adverse reactions. Further research and possible patch testing should be conducted to determine whether the hypersensitivity reaction to intranasal fluticasone propionate is due to the active ingredient itself or to

hypersensitivity reaction to intranasal fluticasone propionate is due to the active ingredient itself or to one of the vehicle ingredients, especially given the numerous reports of anaphylactic reactions to carboxymethylcellulose. Standard treatment of anaphylaxis is important in cases such as this one. Physicians should be able to recognize the potential for anaphylaxis from inhaled fluticasone propionate, administer prompt treatment, and provide preventive recommendations.

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