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SIBLINGS WITH ALLERGIC ANGIOEDEMA: A CASE SERIES ON ORAL ALLERGIC SYNDROME AND FAMILIAL ATOPY

Firstine Kelsi Hartanto[1),2)], Jeff Tjokro[3)], Vivi Angelina[3)], Maria Leny Raiyon[1),2)*]
[1)]Department of Oral Medicine, Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia
[2)] Oral Pathology for Diagnostics, Collaboration Research and Education (OPaDCoRE) Laboratory, Faculty of Dentistry, Jakarta, Indonesia
[3)] Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia

ABSTRACT
Background*: Oral Allergy Syndrome (OAS) is a localized IgE-mediated food allergy triggered by certain fruits and vegetables in patients with atopic history. This case report describes two siblings with Oral Allergy Syndrome (OAS) presenting as allergic angioedema triggered by specific food allergens.* ***Case Presentation****:* ***Case 1*** *involves a 25-year-old female who developed lip swelling, a burning sensation, numbness, multiple oral ulcers on the lower lip, and surrounding redness 30 minutes after consuming mint sauce in an Indian dish.* ***Case 2*** *details a 21-year-old male who experienced immediate lip and soft palate swelling with numbness after eating Chinese food suspected to contain nuts.* ***Discussion:*** *Both siblings share a history of childhood atopy, predisposing them to IgE-mediated reactions. Their symptoms were characteristic of localized allergic responses in the oral mucosa, consistent with OAS.* ***Case Management:*** *Management involved a combined therapeutic approach: topical corticosteroids were applied to the affected oral areas to reduce local inflammation and promote healing of the mucosal lesions, while oral corticosteroids provided systemic anti-inflammatory effects. Additionally, cetirizine, an H1 receptor antagonist, was administered to block histamine-mediated symptoms such as swelling and itching. Patients were also advised to avoid mint-containing and peanut-containing foods as predisposing factors.* ***Conclusion:*** *This report highlights not only the clinical presentation and successful management of OAS in individuals with familial atopy but also underscores the potential genetic predisposition contributing to food-induced allergic reactions.*

Keywords: *Allergic angioedema, Case report, IgE-mediated food allergy, Topical corticosteroid, Oral allergy syndrome*

***Correspondence:** Maria Leny Raiyon, Department of Oral Medicine, Faculty of Dentistry, Universitas Trisakti, Jakarta, Indonesia, leny.raiyon@trisakti.ac.id +62 81332922106.

INTRODUCTION

Oral allergy syndrome (OAS) is a food allergy presentation. Food allergy (FA) refers to an abnormal immune reaction and symptoms triggered by food antigens. OAS is a localized IgE-mediated food allergy triggered by certain fruits, vegetables, or nuts. Meanwhile, atopy is a genetically inherited phenotype characterized by an increased risk of IgE-mediated, non-IgE-mediated, and mixed hypersensitivity reactions. It is classified as a type-1 hypersensitivity reaction, which occurs minutes to hours after exposure to allergens. Clinical presentation of OAS might include pruritus (itching), tingling, and mild swelling localized to the oropharynx region, including the lips, tongue, palate, and throat. These symptoms occur due to histamine release following allergen exposure. In most cases, the reaction remains localized and self-limiting.[1]

Several allergens, such as peanuts, chestnuts, kiwis, mints, and cucumbers, are found to cause OAS. These allergens have proteins structurally similar to pollen homologs, such as Bet v 1-like proteins and profilins. Similarities in the protein structures may lead to cross-reactivity between pollen and specific foods, also known as Pollen Food Allergy Syndrome (PFAS).

In more severe cases, OAS might be accompanied by angioedema.[2] Angioedema is a vascular reaction that leads to swelling in deep dermal/subcutaneous or mucosal/submucosal tissues due to increased blood vessel permeability. The accumulation of extracellular liquid appears as oedema or tissue swelling. If this occurs in the throat region and is not treated quickly, it might pose life-threatening risks due to the restriction of the airway.

Besides, if the patient has severe reactions to the allergen, there is a risk of anaphylactic shock.[3] Therefore, management and prompt treatment of OAS are crucial to prevent potentially fatal outcomes. We present two cases of allergies involving siblings who sought treatment at our clinic on separate occasions.

Cases Presentations

Case 1

A 25-year-old female patient visited The Dental Hospital of Universitas Trisakti with complaints of swollen lips accompanied by burning and numbness, ulcers on the left lower lip, reddish spots on the upper left lip, and reddish spots around the mouth that appeared after lunch three days ago. The patient was a regular at an Indian restaurant. She developed swelling and a burning sensation on the lips after consuming mint in the sauce that accompanied the main dish approximately 30 minutes later. The patient noted that the burning sensation was most intense around the ulcer on the left lower lip, which had been accidentally bitten two days prior.

The working diagnosis is OAS, and primary treatment planning includes avoiding allergens. He was given Cetirizine Hydrochloride 10 mg once daily after meals, Methylprednisolone 40 mg twice a day, and topically Triamcinolone Acetonide 0.01% in orabase ointment.

Fig. 1. The upper pictures show clinical conditions on the first visit, while the lower pictures show the follow-up. Note the swollen upper and lower lips and yellowish crusts formed along the lower vermillion (A). The ulcer on the right lower lip appeared to be typical aphthous stomatitis (B). The swelling on the upper and lower lips subsided (C) on the follow-up, as did the ulcer (D).

The patient showed no oral lesion on the next follow-up visit, and all symptoms subsided. The patient was dismissed with a take-home note to avoid all suspected allergens.

Case 2

A 21-year-old male patient visited the Dental Hospital of Universitas Trisakti complaining of swelling of lips and posterior palate and feeling numbness in the affected areas. The complaints started 3 days ago, right after a meal. The patient had Chinese food, which was suspected to contain nuts. The history of similar symptoms was positive when he had food containing nuts and bamboo shoots. The patient had tried to medicate himself with allergic medication, which had some results, but the feeling of numbness stayed. In the examination, extra orally, we found an erythematous area of vermillion of the upper lip, soft in consistency, with no induration, with a clear margin. On the lower lip, widespread swelling or oedema is marked by shining lower vermillion, which lessens the texture of the lip surface and the tubercles. Intra-oral examination showed an oval-shaped ulcer lesion, measuring around 1 mm on the buccal mucosa, as high as the occlusal plane of teeth 16 and 46. It was whitish in colour and soft in consistency. The swelling was extended to the uvula, while the reddish mucosa extended to the soft palate. It was soft in consistency and without any induration on palpation. The working diagnosis of this patient was OAS. In this case, the treatment plan included avoiding allergens and taking Cetirizine hydrochloride once a day after meals and Methylprednisolone 40 mg twice daily after meals for five days.

Fig. 2. The pictures show the patient's conditions on the first visit in the upper pictures and the follow-up visit in the lower pictures. The lower lip was swollen, with redness of mucosa and vermilion, glossy, and edematous (A). Note the reduction in lateral dimension and reappearance of the natural crevice of the lower lips (C). The patient subjectively reported numbness on the palate, and on examination, the soft palate looked erythematous and slightly swollen, although clinically not significantly noticeable (B).

DISCUSSION

Oral allergy syndrome (OAS) is an IgE-mediated allergic reaction in the oropharyngeal region after consuming certain foods such as fruits, nuts, and vegetables.[4] This can happen due to the exposure of allergenic proteins in the class 1 or class 2 food allergens. Class 1 food allergens are those in which sensitization occurs in the gastrointestinal (GI) tract, involving proteins resistant towards digestion. Class 2 food allergens arise from prior sensitization to an inhaled allergen, usually pollen, leading to cross-reactivity.[5] When OAS occurs in patients suffering from pollinosis and are exposed to certain plant-derived foods, it is called pollen food allergy syndrome (PFAS or PFS).[6] Previous studies show that people with an allergy towards birch pollen might develop an allergy towards hazelnuts, almonds, walnuts, and peanuts due to the homologous proteins encountered through respiratory exposure.[4] Although less common, some reports of mint allergy occur due to prior pollinosis towards birch, mugwort, or grass pollen.[7]

The diagnosis of OAS in these cases was established based on a thorough evaluation of their medical history and clinical presentation. Both siblings reported experiencing lip swelling and numbness after ingesting specific foods. In the first case, mint was identified as the triggering allergen, whereas in the second case, the reaction was attributed to the ingestion of nuts.

The two cases reported in this study are still uncertain if there is any involvement of pollinosis. However, the familial atopy seems very likely due to the presence of OAS in both siblings. Atopy is a genetically inherited phenotype characterized by an increased risk towards IgE-mediated hypersensitivity reactions. Approximately 80% of individuals having atopy have a family history of allergies. Although still not fully understood, it is believed that atopy arises from the interaction of multiple genes, resulting in the overproduction of IgE.[8]

As it is an IgE-mediated allergy, also known as a type-1 hypersensitivity, the symptoms of OAS generally manifest within minutes after exposure towards the causing allergen. The symptoms observed in OAS are primarily due to histamine release from degranulated mast cells. Histamine binds to a specific receptor, triggering the release of various proinflammatory cytokines and arachidonic acid metabolites, resulting in increased vascular permeability and sensations of itching and pain.[9] Angioedema might occur due to the inflammatory response, as shown in these two cases, as well as the numb sensation on the posterior palate reported in the second case. While some had reported the tingling, burning and pricking sensations on the palate, the numbness reported in case two had not been recorded yet. As previously mentioned, the localized areas involved are lips, tongue, perioral and pharyngeal mucosa. However, an isolated swelling of one of these areas such as lips swelling or angioedema alone, is considered an indicator of OAS. The mild symptoms of OAS, such as itching of the tongue, could occur and be managed promptly. On the other hand, the involvement of the posterior oropharyngeal area should be treated cautiously for the possibility of respiratory blockage as severe implications.

The dose of allergen sufficient to trigger an allergic reaction varies between individuals and depends on the degree of sensitization, age, health status, and previous exposure history to the allergen.

Effective management of OAS involves identifying the primary allergens responsible and educating patients on the importance of avoiding them. Antihistamines and corticosteroids should be given as indicated to manage the symptoms. Cetirizine hydrochloride (an antihistamine) 10 mg daily and methylprednisolone (corticosteroid) 4mg twice a day were prescribed systemically as long as the symptoms were subdued for both cases. Additionally, for case 1, a topical triamcinolone acetonide in orabase (corticosteroid) was prescribed for the labial mucosa ulcer.

The prescribed drugs were antihistamine, and corticosteroids, worked synergically, to reduce the allergic cascade. Antihistamines block histamine from binding to H1 receptors, preventing the allergy cascade.[10] On the other hand, corticosteroids such as methylprednisolone and triamcinolone acetonide worked by suppressing the expression of proinflammatory proteins, including cytokines and matrix metalloproteinases (MMPs), and inhibits phospholipase A2 which results in reduced prostaglandin E2.[11] In addition to its anti-inflammatory properties, application of topical triamcinolone acetonide as shown in case 1 acts as a covering agent for ulcerated lesions, protecting them from further irritation.[12]

The differential diagnosis of OAS in these two cases included irritant contact dermatitis, angioedema as a part of hereditary angioedema and specific food allergies which involve systemic reactions. In both cases reported, the skin prick and patch test were non-compliant due to their unavailability in our clinic. The diagnosis of an allergy to mint leaves and nuts was made based on the patient's medical history and presenting symptoms. Challenge-proven food allergy diagnosis, while ideal for food allergy assessment, was not something patients were prepared for. The prognosis for both cases was excellent, providing the time-critical judgment for the treatment. The possibility of recurrence was preventable as long as the patients were aware of and avoided the allergens.

In conclusion, the main principle of OAS management was identifying and avoiding allergens. Ideally, identification can be achieved through the Skin Prick Test or Food Challenge Diagnosis. In the absence of an ideal test, thorough history taking, anamnesis, clinical examination, and the recognition of symptoms such as lips swelling or angioedema would be fundamental for diagnosis and the treatment followed. Prompt and appropriate medication, in this case, antihistamine and corticosteroid, would also benefit the patient.

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