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CASE REPORT

A Rare Case of Allergic Stomatitis Due to the Consumption of Boiled Cassava

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Introduction: Allergic stomatitis is an oral inflammatory disorder characterized by a painful, burning sensation, or itchiness in the oral cavity which clinically appears as erythematous plaques, vesiculation, ulceration, and/or hyperkeratosis. The causative agents include drugs, dental materials, and food ingredients. Allergic stomatitis might develop after a person eats, touches, or inhales food allergen which then triggers the hypersensitivity reaction. The most common types of food hypersensitivity generally involve type 1 and type 4 reactions or a combination of both.

Purpose: This case report aims to discuss a case of allergic stomatitis caused by one of the staple food ingredients in Indonesia: cassava.

Case: A 26-year-old woman came with complaints of burning pain from multiple ulcers on her right inner cheek. The ulcers appeared shortly after the patient ate boiled cassava, extending to the soft palate and causing pain when swallowing food. The patient has a history of asthma.

Case Management: The patient was referred for a total IgE examination with a result of 271.41 KIU/L (normal < 150 KIU/L). She was prescribed an antiseptic mouthwash and topical corticosteroids for palliative therapy. Additionally, multivitamins were also prescribed to speed up the healing process.

Conclusion: Allergic stomatitis can be caused by food ingredients, even those considered healthy or non-allergenic. A complete anamnesis, including the patient's food history, along with supporting examinations, must be carried out to confirm the diagnosis and select appropriate therapy.

Keywords: allergies, allergic stomatitis, hypersensitivity, cassava

Introduction

Allergic stomatitis is an allergic reaction in the oral cavity characterized by erythematous plaques, vesiculation, ulceration, and/or hyperkeratosis causing painful, burning sensation, or itchiness. The allergens are varied, such as drugs, dental materials, including restorative materials, prosthetics, orthodontic devices, mercury, acrylic, and cobalt, and also food ingredients, ie, cow milk, nuts, seafood, etc.[1–3] Among all races, Asians (10.5%), Hispanic (10.6%), and non-Hispanic Black (10.6%) have the highest rates of food allergy.[4] The predilection of allergic stomatitis is non-specific. It can occur throughout the oral cavity, but the most common locations are the labial mucosa, gingiva, lips, and tongue. The principles of therapy are the relief of pain, shortening the ulcer duration, and improvement of the normal function of the oral cavity. Treatment of allergic stomatitis can use topical or systemic corticosteroids.[1–5] A food allergy is a negative reaction to a food or component involving the immune system. Food allergies can follow different allergic reaction pathways, including type 1 (antibody-specific IgE), type 2 (antigen-antibody dependent cytotoxic reaction), type 3 is a reaction that occurs between an antigen and an antibody complex. On the other hand, type 4, also known as "delayed type", is a reaction that takes a longer time to appear. The most common reactions are a combination of type 1 and type 4, or just one of them.[2,6]

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Reports of this case are exceptionally uncommon in Indonesia, primarily because the causative allergen cassava is the third staple food commonly consumed. Cassava, also known as yucca, is a tuber belonging to the Euphorbiaceae family from Latin America, Africa, and the West Indies.[1,7,8] Indonesia's love for this staple food is only surpassed by their passion for rice and corn, making it the third most widely consumed food in the country. Cassava is used to make various processed products, such as cassava *tape*, cassava *eyek-eyek, opak*, cassava crackers, *gethuk*, and tapioca flour, which are widely consumed by the local community. The plant is a rich source of carbohydrates and offers many benefits, including the potential to replace or complement staple foods like rice and wheat.[9] This case report discusses how cassava can cause allergic contact stomatitis when consumed and highlights the mechanism behind it.

Case Presentation

A 26-year-old woman has multiple canker sores on her right inner cheek accompanied by a burning sensation. She needs medical help to alleviate her condition. She mentioned that it happened briefly after consuming boiled cassava sprinkled with palm sugar. The ulcers develop and extend to the soft palate causing pain during swallowing food. The patient has a history of asthma. The patient also admitted that she habitually chews only on their right side. She had experience when using rubber gloves, after removing them, his hands felt itchy. But according to her, maybe it was because of too long of use, not because of an allergic reaction. The extraoral examinations found no abnormalities, while from the intraoral examination, there were multiple papules with varying sizes, and irregular and diffuse borders, accompanied by areas of erythema in the right buccal mucosa (region 43–47) and soft palate (Figure 1A and B). The patient was then referred for routine blood tests and a total IgE test to confirm the diagnosis. She was instructed to rinse her mouth twice a day with chlorhexidine gluconate mouthwash and topical corticosteroids for palliative therapy. Additionally, multivitamins were provided to expedite the healing of lesions. During the control, which occurred five days after the first visit, she reported a decrease in the number of the canker sores, and that she felt less painful than previous (VAS score from 7 to 2). The right buccal mucosa and soft palate appeared to be almost normal in appearance. The total IgE examination results were 271.41 KIU/L (with a normal value of less than 150 KIU/L), and the results of routine blood tests can be seen in Table 1.

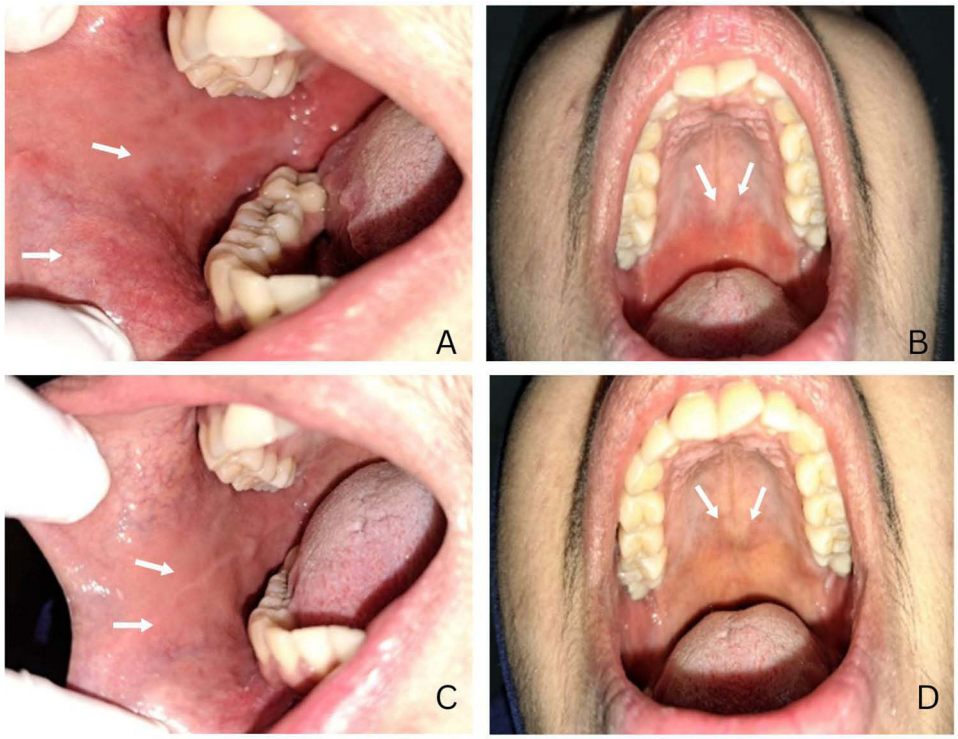

Figure 1 (A) The right buccal mucosa had multiple, irregular papules of varying sizes, accompanied by areas of erythema. (**B**) The soft palate had painful areas of erythema. (**C** and **D**) The right buccal mucosa and soft palate were healed.

Table 1 Results of Laboratory Examinations

	Result
Hematology	
Complete blood	
Hemoglobin	14.5 g/dl (normal 12.0–16,0)
Hematocrit	40.6% (normal 35–47)
Leukocytes	8.5 ribu/mm^3 (normal 4.4–11,3)
Erythrocytes	4.57 juta/uL (normal 4.2–5,4)
Platelets	301 ribu/uL (normal 150–450)
Mean Corpuscular Volume (MCV)	88.8 fl (normal 80–99)
Mean Corpuscular Hemoglobin (MCH)	31.7 pg (normal 27–32)
Mean Corpuscular Hemoglobin Concentration (MCHC)	35.7 g/dL (normal 35–36)
Immunology	
Total IgE	**271, 41*** KIU/L (normal < 150)

Note: * indicates a value above or below the reference value.

The patient was diagnosed with allergic contact stomatitis due to a high total IgE value. After 11 days of outpatient treatment, the ulcers on the buccal mucosa and soft palate were completely resolved following the second visit (Figure 1C and D).

Discussion

In 1994, Blanco et al coined "latex fruit syndrome" to describe the co-occurrence of latex allergies and fruit sensitivities in patients.[9,10] The top five fruits associated with this syndrome were avocado (36%), chestnuts (36%), bananas (28%), kiwi (20%), and papaya (12%). Many studies have confirmed this pattern of symptoms as diagnostic criteria using clinical history and skin tests. It is a well-established fact, based on studies since 1995, that latex cross-reacts with several foods. These foods include potatoes, tomatoes, mangoes, papayas, melons, figs, peaches, and eggplant.[9] In 2003, there were reports of three patients who were found to have a latex allergy and also showed cross-reactivity with cassava.[8] Cassava, a tropical plant with edible roots, was introduced to Africa by the Portuguese in the 16th century. Without a doubt, it is one of the most significant sources of energy in tropical diets.[7,8] Consuming cassava can cause allergic reactions that cross with latex allergies, according to Mikponsè et al.[11] It is a known fact that people who are allergic to latex may also develop allergies to boiled cassava.[11] Man e5, an allergen found in cassava, shows IgE cross-reactivity with Hev b5, the allergen responsible for latex allergies.[7,11–13] Data suggests that Hev b5 may be the primary cause of allergic reactions to cassava consumption in individuals who have not been previously exposed. Man e5 is a protein rich in glutamic acid and has a similar structure to hevein, a protein found in plants that play a role in plant defense. Hevein is an important allergen because it is not easily broken down by heat or processing, and can still cause allergic reactions.[7,12–14]

Consuming boiled cassava has been associated with allergic reactions, with the first cases being reported in Brazil and Mozambique. It is important to be aware of this potential risk and take necessary precautions to avoid any adverse effects. These incidents took place in two separate instances, one in 2004 and another in 2007. The patients affected were located in Brazil and Mozambique. It is crucial to take note of these events and learn from them to prevent future occurrences. In contrast, no cases of cassava-related food allergies have been reported in Benin.[7,8,14] In Indonesia, there are currently no reports of allergies to boiled cassava. Therefore, this case report is categorized as a rare case.

Cassava is a primary food source in Indonesia and is easily found in the West Java region. One village in West Java is famously known as the *Kampung Singkong* Cireundeu due to its large production of cassava. In Cireundeu village, 20 hectares of land are home to thousands of cassava trees that are vital for the community's food security. Our patient is originally from West Java and had been exposed to cassava before without experiencing any allergic reaction. This supports the theory of hypersensitivity reactions, which suggests that such reactions can occur following previous desensitization and may even occur upon initial exposure.[14]

A food allergy (FA) is a specific immune response that can occur when someone is exposed to a particular food. This can result in symptoms such as hives, angioedema, gastrointestinal issues, respiratory problems, and anaphylaxis, which is a potentially life-threatening condition. Food allergies are more common in children, with infants and toddlers being at the highest risk. There are two main types of food allergies: class I (traditional food allergies) and class II (pollen food allergy syndrome, PFAS). Class IFA is typically the most common food allergy in children, while class IIFA has rarely been studied in children, mainly because it is usually researched as a condition related to pollen allergies in adults.[15,16]

Research unequivocally demonstrates that environmental factors, in addition to food allergens and genes, significantly contribute to the prevalence of food allergies. It is firmly established that environmental exposures play a crucial role in the development of food allergies, aligning with the 'dual exposure hypothesis' of FA. While existing studies largely concentrate on the influence of outdoor environmental factors, there is indisputable evidence linking outdoor NO2 exposure to food allergies.[15] Food allergy is a complex mechanism that involves two stages: awareness and the proper reaction.[14] Upon initial contact with an allergen, the patient's immune system produces specific IgE antibodies, which then attach themselves to target cells throughout the body. During the first phase of an allergic reaction, the body does not show any clinical symptoms but prepares itself to respond quickly to a second exposure to the same allergen. When the person comes into contact with the allergen again, or with a similar substance in the case of cross allergies, the allergic reaction occurs. When IgE antigens lead the formation of immune complexes, it triggers the release of chemical mediators like histamine and pro-inflammatory cytokines. These mediators attract eosinophil granulocytes to the affected tissue and increase allergic responses. Atopic reactions occur when a person or their family tends to produce IgE antibodies in response to low doses of allergens, typically proteins. This can lead to the development of typical symptoms such as asthma, rhinoconjunctivitis, or eczema/dermatitis. In the case of this patient, they had a history of asthma. (Figure 2).[14,17,18]

Ventura et al characterized cassava immunogenic proteins by testing their reactivity with serum from cassava-allergic patients and recombinant FBA molecules. Cassava, a popular starchy root vegetable, contains three allergens that have been identified by researchers. These allergens are Fructose-Bisphosphate Aldolase (FBA), which has a theoretical molecular mass of 39.9 kDa; Glyceraldehyde-3-Phosphate Dehydrogenase (GAPDH), with a theoretical molecular mass of 36.8 kDa; and a glutamic acid-rich protein known as Man e5, with a theoretical mass of 30 kDa. These allergens can be harmful to individuals who are sensitive or allergic to them, and it is important to be aware of their presence when consuming cassava or products that contain cassava. It was shown that Man e5 partially reduced IgE reactivity to Hev b5, a latex allergen that has been identified. This suggests that sensitization to Hev b5 may have preceded IgE sensitivity to

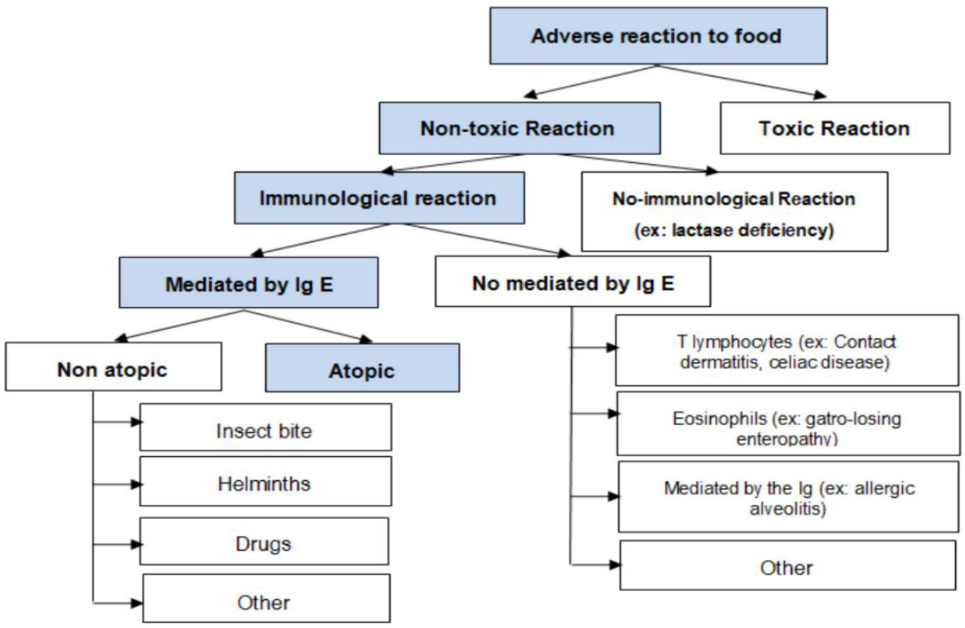

Figure 2 Detailed algorithm of the mechanisms of clinical manifestations of hypersensitivity.[13]

cassava.[19] The protein FBA is labile and possesses a natural tetrameric structure. Ingestion and inhalation are the principal routes of exposure to this chemical. The IUIS has identified FBA as an allergen present in several sources. It was first identified in cockroaches and has also been found in other sources such as shrimp, tuna, salmon, and cod. Physical activity can trigger anaphylaxis in response to this protein. FBA proteins from different sources are very similar. However, differences in allergenicity may be due to the cooking process and the presence of different food matrices. When molecules change such as denaturation, conformational, and structural changes, this can make foods more or less allergenic. The structure of allergens can also be affected by food matrix components, which can change the biological processes of allergen sensitization in the human body, ultimately affecting their allergenicity. During processing, physical-chemical interactions occur between components released from the food matrix and the allergens. These processes can promote the formation of aggregate between allergens and the matrix, limiting the destruction of the allergen epitope, but can also lead to the generation of new allergens. Further research is necessary to understand the mechanisms involved in this case FBA is recognized by the IUIS as an allergen that can be found in a number of sources. It was first discovered in cockroaches, but it has now been discovered in shrimp, tuna, salmon, and cod, among other foods. This protein has the ability to cause anaphylaxis in response to physical exertion. The FBA proteins found in many sources are quite similar. Nonetheless, variations in allergenicity could result from various food matrices and the cooking method. Foods can become more or less allergenic due to molecular changes such as denaturation, conformational, and structural alterations. Food matrix components can also modify the structure of allergens, altering the biological processes of allergy sensitization in the human body and eventually influencing the allergenicity of the allergens. Physical-chemical reactions take place between components emitted from.[19,20]

Moreover, studies have shown that females are at a higher risk of developing food allergies and experiencing more severe symptoms than males. This is also true for asthma, where estrogen has been found to worsen symptoms while testosterone has a protective effect. Additionally, the female skin and mucosa barrier is more permeable, and their metabolic capacity is lower, making it easier for disease-causing foods to be absorbed and stay in the body for longer periods, potentially leading to more severe symptoms.[19,21,22]

This patient's allergy may also be caused by palm sugar, but there is a slight difference in the symptoms that occur. They tend to target the respiratory or digestive systems.[23–25] The patient's signs and symptoms are more indicative of an allergy to cassava. In this case report, the patient did not undergo the prick test due to their fear of needles.

Patients are prescribed topical corticosteroids to reduce inflammation and suppress the immune system, providing relief from ulceration, erythema, and pain. Administering corticosteroids topically was preferred due to their minimal and localized effects, as opposed to systemic administration.[1] A multivitamin supplement including vital elements like vitamin E, vitamin C, B1, B2, B6, D, folic acid, pantothenic acid, zinc, and niacin has been prescribed to the patients. By enhancing immunity, supporting energy generation, promoting healthy skin, eyes, and nerves, and preventing numerous health issues, these vitamins and minerals are essential for keeping the body in good condition. Every mineral and multivitamin has a distinct purpose. Vitamins C and E build connective tissue, speed up wound healing, and strengthen the immune system in addition to acting as antioxidants. Niacin, vitamin B2 (riboflavin), and vitamin B1 (thiamine) are in charge of the metabolism of carbohydrates. Pyridoxine, or vitamin B6, helps with the metabolism of glycogen and proteins. Folic acid and vitamin B12 (cobalamin) are necessary for the production of red blood cells.[26,27]

Administering chlorhexidine mouthwash can improve oral hygiene, prevent secondary infections, and speed up healing. CHX acts as an antiseptic mouthwash that has anti-microbial effects on bacteria, fungi, and viruses responsible for various oral diseases.[9]

Conclusion

Allergic stomatitis can manifest due to food ingredients, even those considered healthy or non-allergenic. Confirming the diagnosis and determining appropriate treatment necessitates a comprehensive examination of the patient's food consumption history, complemented by relevant supporting tests.

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Consent Statements

The manuscript has been approved by the institution. The patient has filled in a written informed consent for the publication of this case including the images.

Disclosure

The authors declare no conflicts of interest in this work.

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