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Prevention of Pancake Syndrome

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ABSTRACT

Pancake syndrome is a severe form of allergic reaction caused by the consumption of foods prepared from mite-contaminated wheat flour or flour-containing cooked powder. It is also known as oral mite anaphylaxis. A case of pancake syndrome was first reported in the United States in 1993 by Erban *et al*. Since then, several cases have been reported overseas due to the presence of mites in wheat flour-containing cooking powder such as pancake flour. By contrast, the first two cases of pancake syndrome in Japan were reported by Matsumoto *et al*. in 1996: one was due to the consumption of food prepared from a pancake mix, while the other was due to the consumption of food prepared from okonomiyaki flour. Among the domestic cases, consumption of food prepared from okonomiyaki flour has been reported in the majority of these cases. This study aimed to report some of the cases of pancake syndrome that occurred in Japan and summarize their characteristics and the methods used to prevent the development of this condition.

INTRODUCTION

Pancake syndrome is a severe form of an allergic reaction triggered by the ingestion of foods prepared from mite-contaminated wheat flour or flour-containing cooked powder[1)]. It is also called oral mite anaphylaxis[2),3)]. A case of pancake syndrome caused by contamination with house dust mites (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, and *Tyrophagus putrescentiae*) was first reported in the United States in 1993 by Urban *et al*[2),4)]. The causative food was fried bread (beignet) using wheat flour containing cooking powder[5),6)]. Since then, several cases have been reported overseas caused by mites generated in wheat flour-containing cooking powder such as pancake flour. By contrast, the first two cases of pancake syndrome in Japan were reported in 1996 by Matsumoto *et al.*: one was caused by ingestion of food prepared from pancake mix, while the other was caused by ingestion of food prepared from okonomiyaki flour[5),7)]. Since then, dozens of cases have been reported. Among the domestic cases, consumption of food prepared from okonomiyaki flour has been commonly reported in the majority of these cases. This study aimed to report some of the cases that occurred in Japan and summarize their characteristics and the methods used to prevent the occurrence of this condition.

Disease characteristics

The disease characteristics are listed in Table 1. Wheat flour containing cooking powder is frequently used as a raw material to prepare food at home; when the flour is not used, it is usually kept at room temperature for a longer period after opening it[5)]. Mites propagate in the storage container; the dead mites and their feces remain in the flour and cause allergic reactions when ingested. Symptoms frequently develop within 1 h after ingestion of contaminated food[8)]. According to Matsumoto *et al*., the inhalation sensitization rate of mite allergens has increased because of the recent closed indoor environment. By contrast, food hygiene management practices have improved. The different opportunities for oral ingestion of mites were reduced, but the oral immune tolerance to mite allergens was disrupted[9),10)]. In other words, Japan lost the opportunity to come in contact with insects as a result of daily sterilization. Hence, occasional contact with insects has led to serious illness[11)]. However, if an individual's room remains dirty regularly, the risk of mite infestation in this area will relatively increase[6)]. Mites that have entered the packaging/container can rapidly reproduce if the temperature is low (20°C–30°C), the level of humidity is high (60%–80%), and suitable places for spawning are available[12)]. The number of tick eggs/insects and allergens increased

within a period of 3.5 months[1]. The reference value for sensitization in allergy patients is 1–2 mg/g for allergens, the number of mites is 500/g, and the amount of allergen that can cause seizures is 10 mg/g[1]. Ticks can cause anaphylaxis, even at lower numbers. Although the conditions are different, it takes 6 weeks for a tick to grow and for anaphylaxis to occur[13]. As shown in the introduction and Table 1, allergens (thought to be enzymes such as cysteine protease and serine protease[10]) are not inactivated even when treated with hot oil[12),14]. Regardless of whether the tick is alive or dead, if the residual amount of allergen produced is relatively high, allergic symptoms may occur. In Japan, many patients develop allergy symptoms immediately after ingesting foods that contain wheat flour, such as okonomiyaki, takoyaki, and pancakes, and foods that are half-baked. On the contrary, some patients develop pancake syndrome after ingestion of foods that are fried at high temperatures such as donuts and tempura[12]. A few studies reported that wheat flour alone causes anaphylaxis. Mites tend to breed and grow faster in okonomiyaki flour than in wheat flour. This is because this type of flour contains animal-derived ingredients (in addition to starch, amino acids, and umami ingredients) and can be a good source of food for predatorymites[12]. Moreover, the okonomiyaki flour is only used in small amounts and a limited number of dishes; hence, it takes time to use all the powder[5]. Therefore, this condition induces the invasion and proliferation of mites as the powder is stored for long periods.

Examination and treatment method

The following clinical examination methods are performed in the hospitals. 1) Mite antigens/antibodies are detected using the patient's serum[1),8),10),12]. 2) The pathogens (allergens) or insects (mites) are detected from the foods consumed (tempura clothes) and ingredients used in cooking (okonomiyaki flour or wheat flour)[1),5),8),12]. 3) The patient is examined to assess for the presence of antibodies after the onset of illness using a prick test or a similar testing method[8),10),12]. The prick test is a method used to detect allergies, such as skin allergies. Allergic reactions are examined by placing a drop of an allergen extract on the skin and lightly piercing the site with a needle to allow the allergen to absorb on the skin. Scratch tests, intradermal tests, and patch tests were also performed.

1) A prick test is currently performed relatively often in Japan. It is thought that this is because Japanese people (especially infants) use many antibacterial products and their immune tolerance to mites is significantly reduced[10]. The test is often performed to assess for skin symptoms (red swelling, rash), which are triggered as fleas and mites burrow under the

skin causing skin infection. As ectoparasites, the mites often infest the skin surface and pores. 2) Microscopic examination is widely used to detect insects. This method is more preferable and error-free as it involves chemical measurements. If it matches the symptoms, the discovery of insects will be a definitive diagnosis[12]. As a method of increasing the sensitivity, a sample containing mites is suspended in saturated saline solution, and the mites are separated from other substances based on the density[1),3)]. However, in Japan, medical personnel other than pathologists and laboratory technicians are less likely to use microscopes for examination purposes, and the number of doctors who can diagnose the results of microscopic examinations is decreasing[11]. In some cases, it may be better to ask an institution such as an external laboratory center or a clinical laboratory technician who is accustomed to performing similar tests to detect the body of the insect alone or to detect the allergen chemically. A simple mite allergen test kit called Dani Scan (test paper based on immune chromatography) has also been developed[3),12)]. Several similar methods and patch tests for detecting resistance to alcohol detoxification have been frequently used. Since this method also examines the amount of antibodies in the same manner[1)], it can also determine previous infections. Strong positive results reflect the current state of illness; however, if the results are within the borderline between low positives and negatives, a comprehensive judgment is made in combination with other test results and interview information.

By contrast, general allergic symptom relief methods have been used for treatment. Adrenaline is administered if the symptoms are severe and cause anaphylaxis[5]. Oral antihistamines are often administered as a radical treatment for allergies. When skin or asthma symptoms are prominent, anti-inflammatory drugs, asthma drugs, or antihistamines may be applied to the skin as symptomatic treatments.

Prevention method

Simply put, the only preventive method is to hinder the invasion of mites into foodstuffs. According to previous research, an unopened package of the powder product contains a small number of mites [2),13)]; therefore, it is necessary to devise ways to prevent further increase and invasion of these mites from the outside. A small number of mites can be found in an unopened flour as they can get in during packing or have adhered to crops long ago. In the prick test, a negative result is obtained if the number of mites is small[2)]. Hence, a cooking powder is used to measure the number of mites[12)]. As time passes, proliferation and invasion progress. If the powder needs to be stored long-term, it is necessary to properly seal the

container to prevent the invasion of mites and to store them in an environment where mites do not easily grow, such as the refrigerator and in places with low humidity[12]. Some containers contain labels that indicate the need for refrigerated storage, as mites usually invade and multiply while the powder is stored at room temperature[5]. Additionally, for patients suspected of having mite allergies, the medical personnel needs to guide food preservation methods daily, which will lead to the prevention of this disease[2]. In cases 1 and 2 in Table 1, the doctor recommended the proper sealing of opened foods that are stored in the refrigerator; however, recurrence of allergic symptoms was not reported[10].

After identifying the cause, the specific drug treatment may be decided, or measures to prevent disease recurrence may be taken. Pancake syndrome should not be confused with wheat allergy[8], and doctors should consider the possibility of this disease based on the patient's response to the interview[2]. Since this disease does not occur after consuming foods prepared from wheat flour alone, patients with allergic symptoms don't need to refrain from ingesting wheat flour products.

CONCLUSION

Pancake syndrome is a very familiar illness, but this illness is difficult to assess. As mentioned in Table 1, if severe symptoms occur within a short time, the disease can be diagnosed by undergoing examinations at a hospital. If the skin and respiratory symptoms are mild, they may be left unattended at home without going to the hospital, and the cause may remain unknown. Therefore, the number of case reports may be less compared with the actual number. When deciding to reopen and use wheat flour that has been stored for a long time, if the flour is infested with large insects such as cockroaches or turns brown, it should not be used. However, if the appearance remains unchanged, many consumers end up using it. Mites are small insects that are difficult to visually identify and can be overlooked. On the contrary, the storage condition of powder is considered to be different for each household, and the differences in the indoor environment should also be considered. Therefore, certain situations make it difficult for distributors and countries to issue guidelines, such as the duration in which the product should be used to prevent illness. If measures are to be considered uniformly, for the time being, the cooked powder should be stored at a low temperature after opening its package. At the same time, if the symptoms seem unlikely, it is necessary to keep in mind that the mites in the cooking powder are the potential causes[2]. This can lead to prompt treatment when the patient is admitted to the hospital and prevents the severity of the

disease. If possible, the cooking powder should be stored and examined by medical personnel.

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Table No. 1: Investigation Cases of Pancake Syndrome

Case (reference number)	Patient age and gender	Symptoms	Causative substance	Inspection results	Treatment and guidance
1 (10)	32-year-old female	After ingesting okonomiyaki, itching, dyspnea, and wheals on the face occurred after 30 minutes. She has a history of airway allergies such as asthma and allergic rhinitis.	Okonomiyaki flour that has been stored at room temperature for several months after opening	Serum-specific IgE and prick tests showed mite allergies.	Taking anti-allergic drugs. For flour products, the doctor instructs to pay attention to the storage environment and storage period of food; i.e., these products should be stored in a closed container after opening it and placed in the refrigerator.
2 (10)	37-year-old female	Immediately after ingesting okonomiyaki, he noticed a feeling of discomfort in the pharynx and dyspnea, and a wheal appeared on his face and spread to the whole body. She has a history of airway allergies such as asthma and allergic rhinitis.		Serum-specific IgE and prick tests showed mite allergies. *Dermatophagoides farinae* was detected in the old powder brought.	
3 (2)	A 60-year-old	After taking okonomiyaki, the patient had difficulty breathing	Okonomiyaki flour that has	Positive for specific IgE-specific antibody	Improves physical condition

	female (mother of case 4)	and lost consciousness; so, she was transported to the emergency department. Generalized flushing and decreased blood pressure were noted.	been opened for >3 years	against house dust mite and *Dermatophagoides farinae*. Mites were detected in the okonomiyaki powder.	with adrenaline and antihistamines
4 (2)	A 32-year-old man (son of case 3)	Son eats okonomiyaki made by his mother and comes to the hospital with the mother. Wheezing and dyspnea occurred while her mother was waiting for medical treatment.		The prick test using the okonomiyaki flour showed positive results.	
5 (5)	Older brother and sister in their late teens	When the family ingested fried tempura for dinner, the younger sister developed itchy eyes, facial swelling, nasal congestion, and dyspnea, and was eventually brought to the emergency department. Her older brother, who returned home late and was unaware of the incident, also ingested the remaining tempura, and showed similar symptoms. He was also	Tempura flour was opened once and stored at room temperature for 2–3 months.	The serum was positive for tick-specific IgE antibody titers. When the leftover tempura was observed under a microscope, mites were found on the batter.	It improved with treatment such as adrenaline.

		transported to the emergency department.			

Summarized based on the contents of references 2), 5), and 10).