Histamine-Induced Allergic Outbreak in among Junior / Senior High School Students - A Case-Control Study

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Abstract

On January 13, 2009, several students at X Junior/Senior High School in Kaohsiung City started to show allergic symptoms of flushed faces, irregular heart rates, dizziness, and vomiting and were sent for medical assistance. Epidemiological case-control investigation is conducted in order to determine the scale of the outbreak, the cause, and the food responsible for the episode.

According to the 818 questionnaires distributed and collected from

• Received : February 20, 2009. • Accepted : March 12, 2009.
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the classes with students showed allergic symptoms, a total of 777 students consumed the school lunch on January 13. Among these 777 persons, 71 fit the case definition, with 32 males (45.1%) and 39 females (54.9%), showing an attack rate of 9.14%. The case symptoms were (in order) dizziness (67.6%), flushed faces (63.4%), increase heart rates (50.7%), nausea (45.1%), abdominal pains (32.4%), headache (43.7%), chillness (29.6%), short of breath (19.1%), vomiting (18.3%), and fever (15.5%). The incubation period was between <1 and 8 hours with a medium of 1 hour. Test results show that the histamine found in a fried sailfish fillet specimen was 377.4 ppm. Results of the logistic regression analysis of the single dish and multiple dishes of the school lunch on January 13 showed that the risk factor of the outbreak was the fried sailfish fillet which induced the histamine fish poisoning outbreak (OR: 2.987, 95% CL: 1.268-7.036).

According to the case symptoms, incubation period, results of both statistical analysis of the school lunch contents and food residual (from the fried sailfish fillet) tests, we can conclude that the allergic symptoms in the students were a histamine-induced fish poisoning outbreak. The cause of the outbreak was histamine which originated from the fried sailfish fillet.

Keywords: food poisoning, allergic symptoms, histamine, outbreak, case-control study

Introduction

According to the statistic data from the Food Information Registry [1], food poisoning incidents occur in Taiwan every month between the years 1981 to 2007. Among these, incidents occur most often between the months of May and October. This is due to the fact that the temperature is higher in these months. The locations where such incidents occur most

common (in order) is at restaurants, caterers, food production factories, homes, schools, and shops. The most common pathogen found is bacteria (*Bacillus cereus*, enterotoxic *Staphylococcus aureus*, *botulinum* toxin, *Enteropathogenic E. coli*, *Salmonella enteritidis*, *Vibrio parahaemolyticus*). Other origins include chemical toxins and natural toxins. Due to the fact that Taiwan is an island country, a main source of food is seafood. When consuming seafood, not only whether the food contains anti-bacterial drugs (such as Malachite Green) [2] or not, but also the freshness of the food needs to be taken into consideration. Seafood that is not fresh will likely produce histamine which will lead to allergic reactions [3]. Therefore, this study will describe the incident and discoveries of the outbreak induced by consumption of seafood that was not fresh by students in X Junior/Senior High School in Kaohsiung City.

On January 13, 2009, tens of students (among 3,500 students and faculty members) of X Junior/Senior High School in the Cianjhen District of Kaohsiung City started to experience flushed faces, irregular heart rates, dizziness, vomiting, and rash symptoms after consuming catered lunch. The sick students were sent to the Kaohsiung Armed Forces General Hospital, Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung Branch of Chang Gung Memorial Hospital, Yuan's General Hospital, Kaohsiung Municipal Min-Sheng Hospital, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Municipal United Hospital (Datung District), and other hospitals for medical assistance. Due to the fact that sick students were epidemiologically related each other with respect to their onset time of symptoms and places, we can determine that the cluster of allergic symptoms in X Junior/Senior High School is an

allergic outbreak. Therefore, the Field Epidemiology Training Program, Centers for Disease Control (CDC) and Department of Health of Kaohsiung City Government jointly dispatched a field investigation team to study the incident. The purposes of the investigation are to asses the scale of the outbreak and confirm the transmission route, pathogen, and contaminated food.

Materials and Methods

Investigated subjects :

The investigated subjects are the students of X Junior/Senior High School which showed symptoms of flushed faces, increased heart rates, dizziness, vomiting, and rash.

Case definition :

A food poisoning case was defined as whoever had the school lunch on January 13, and developed any two of the following symptoms of abdominal pain, nausea, vomiting, flushed faces, irregular heart rates, dizziness, and headache.

Study methods :

Due to the fact that not all of the students at X Junior/Senior High School were included as the investigated subjects, the method used in this investigation is the case-control study. Among the investigated subjects, whoever fits the case description are categorized as the case group whereas those that also consumed the school lunch on January 13, but did not show symptoms are categorized as the control group.

Questionnaire :

A semi-structural questionnaire was designed for the classes with

students showed allergic symptoms. The content includes the basic information (gender, birth date, grade, class, and seat number), information about the lunch on January 13 (whether or not they consumed the lunch, time of consumption, and the contents of lunch), and the physical reactions after consumption (whether there symptoms or not, time and date, the symptoms, medical assistance, whether or not they were kept for observation, hospitalization, and recovery process). All of the students were instructed on how to fill in the questionnaires and were collected.

Specimen collecting and testing :

The Department of Health of Kaohsiung City Government collected a total of 46 rectal swabs from the students and sent them to Center for Research and Diagnostics located at the Fifth Division of CDC in Kaohsiung City for further testing. The tests include those for *Staphylococcus aureus* (including enterotoxin), *Bacillus cereus*, *Vibrio parahaemolyticus*, *Enteropathogenic E. coli*, *Salmonella Enteritidis*, and *Shigella dysenteriae*. In addition, food residual specimens from the lunch boxes on January 13 with the fried sailfish fillet were collected and sent for testing for *Staphylococcus aureus* (including enterotoxin), *Bacillus cereus*, *Enteropathogenic E. coli*, *Vibrio parahaemolyticus*, and *Salmonella Enteritidis*. The fried sailfish fillet was also tested for histamine. In addition, hand swabs were also taken from the 3 cooks and tested for *Staphylococcus aureus* (including enterotoxin). All of the residual food specimens and hand specimens were sent to the Laboratory of Department of Health of Kaohsiung City Government for testing.

Data processing and analysis :

All of the collected questionnaires were keyed into the database using

the software Epi-Info and were entered into the database after verification and confirmation. Afterwards, data description and analysis was conducted. Data description is the calculation of frequency and percentage, including number of cases, overall attack rate, class attack rate, case symptom distribution, and medical assistance rate. The medium and range, including the incubation period, were also calculated. The definition of the incubation period starts from the consumption of the school's lunch on January 13 until the appearance of the allergic symptoms. In addition, the epidemic curve of disease onset date was also drawn in order to show the transmission route of this outbreak. Data analysis includes the simple and multiple logistical regression analysis of the lunch box contents. The association index between lunch contents and food poisoning are shown with Odds Ratio (OR). If certain lunch content has an OR > 1.0, the content is a risk factor. If the OR < 1.0, the lunch content is a protective factor. Whether certain lunch content is statistically a risk factor or a protective factor is determined by the 95% Confidence Limits (CL). If the 95% CL does not include 1.0, that certain lunch content is statistically related to the disease, otherwise it is not.

Results

Scale of outbreak :

A total of 818 effective questionnaires were collected from classes with students who showed allergic symptoms. Among these, 777 students had consumed the school lunch on January 13. In these 777 persons, 71 students fit the case description with 32 males (45.1%) and 39 females (54.9%) with an attack rate of 9.14%. The distribution of the cases in each

class and attack rate is shown on Table 1. The case symptoms are similar to those of allergic symptoms with (in order) dizziness (67.6%), flushed faces (63.4%), increase heart rates (50.7%), nausea (45.1%), abdominal pains (32.4%), headache (43.7%), shivering (29.6), short of breath (19.1%), vomiting (18.3%), and fever (15.5%), weakness in limbs (14.1%), diarrhea (5.6%), and rash (2.8%). Among the 71 cases, 63 started to show symptoms on January 13, 2 on January 14, and no further cases appeared after the 15th of January (see Figure 1). The appearance of the cases had an incubation period of <1 ~ 8 hours with the medium and mode as 1 hour. A total of 51 students sought medical assistance (7 in private clinics) with a rate of medical assistance of 71.8%. 38 cases (53.3%) stayed for further observation, whereas 3 (4.2%) were hospitalized.

Results of analysis of lunch box contents :

A total of 777 cases consumed the school lunch on January 13. The lunch box contents that day included wheat germ rice, fried sailfish fillet, braised peanut pork leg, stir-fried garlic choy sum, lettuce and tofu stew, and pudding. Results of logistic regression analysis in analyzing the single lunch box contents (Table 2), the fried sailfish fillet shows a statistical relevance (95% CL: 1.253 ~ 6.933, 95%CL not including 1.0) and is concluded as the risk factor (OR: 2.947) of this allergic outbreak. In addition, the pudding was also tested to be statistically related (95%CL: 0.273 ~ 0.963). However, it was not a risk factor in this allergic outbreak and is a protective factor (OR: 0.513). The other 4 kinds of contents were all statistically unrelated to the allergic outbreak and their ORs and 95%CLs are as following: wheat germ rice (OR: 1.061, 95%CL: 0.442-2.547), braised peanut pork leg (OR：1.354, 95%CL：0.767-2.390),

stir-fried garlic choy sum (OR: 0.868, 95%CL: 0.533-1.414), lettuce and tofu stew (OR: 1.167, 95%CL: 0.711-1.916).

Table 1. Number of cases, number of students that consumed the lunch box on January 13, number of students answered the questionnaire, and attack rate for X Junior/Senior High School by grade and class.

Grade/Class	Case No.	Lunch Consumed No.	Questionnaire No.	Attack Rate* (%)
Junior High				
1/3	1	28	35	2.86
1/5	5	38	38	13.16
1/6	3	32	38	7.89
1/12	2	35	38	5.26
1/13	1	39	39	2.63
1/19	2	33	36	5.56
2/1	2	31	31	6.45
2/3	1	33	35	2.86
2/8	3	34	36	8.33
2/14	6	34	36	16.67
2/16	9	35	35	25.71
2/17	1	33	35	2.86
2/19	1	33	34	2.94
3/2	1	35	36	2.78
3/7	1	29	31	3.23
3/9	1	35	35	2.86
3/12	3	34	34	8.82
3/13	5	37	37	13.51
3/15	10	32	34	29.41
3/20	1	36	37	2.70
Senior High				
4/1	10	43	43	23.25
4/6	2	38	39	5.13
4/9	0	20	26	0.00
Total	**71**	**777**	**818**	**9.1**

* Attack rate = case no. / lunch consumed no.

The results of multiple logistic regression analysis for the lunch box contents show that both the fried sailfish fillet and pudding are statistically significant relevance. The former is the risk factor that induced the allergic outbreak (OR: 2.987, 95%CL: 1.268-7.036), whereas the latter is a protective factor (OR: 0.503, 95%CL, 0.267-0.948).

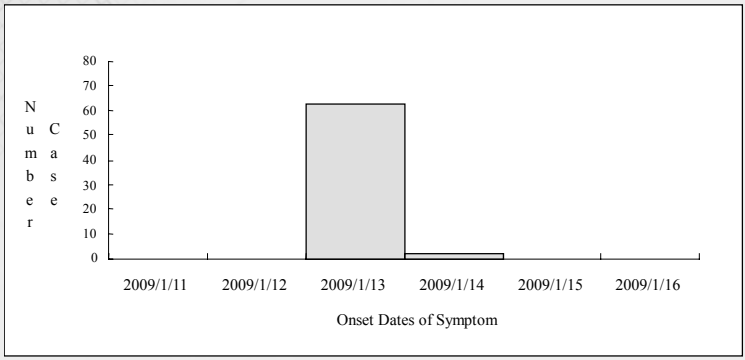

Figure 1. Distribution of onset dates of symptom for food poisoning cases in Kaohsiung City A High School

Table 2. Results of lunch box contents analysis of Kaohsiung City X Junior/Senior High School on January 13.

Contents	Sick		Not Sick		OR (95% CL)
	Consumed	Not consumed	Consumed	Not consumed	
Wheat germ rice	65	6	643	63	1.061 (0.442-2.547)
Fried sailfish fillet*	65	6	555	151	2.947 (1.253-6.933)
Braised peanut pork leg	54	17	495	211	1.354 (0.767-2.390)
Stir-fried garlic choy sum	35	36	373	333	0.868 (0.533-1.414)
Lettuce and tofu stew	42	29	391	315	1.167 (0.711-1.916)
Pudding*	57	14	627	79	0.513 (0.273-0.963)

* shows statistically significant at 95% CL not including 1.0.

Results of laboratory tests :

Apart from one specimen of the fried sailfish fillet which 377.4 ppm histamine was found, the rest of the food residual specimens and the 46 anal swab specimens showed no signs of *Staphylococcus aureus* (including

enterotoxin), *Bacillus cereus*, Enteropathogenic *E. coli*, *Salmonella enteritidis*, and *Shigella dysenteriae*.

Conclusion and Discussion

According to the leave record of the students at Kaohsiung City X Junior/Senior High School, starting from January, no record of 63 students took leave on one single day (January 13) due to allergic reactions. Due to the fact that the number of sick students exceeded the average number of sick leaves a day, we can conclude that a sudden outbreak has occurred in A Junior/Senior High School. The distribution of disease onset date shows a single peak curve (Figure 1). The cases distribution among many the classes (Table 1) also proves that this sudden outbreak's infection route is through a common source transmission. Common source transmission routes are through food [4], drinking water [5], air [6], shared utensils [7], and a single infected person [8]. No further cases appeared after January 15 and the drinking water was not processed. Thus the drinking water was eliminated from the possible contamination sources. The case symptoms were mostly allergic reactions and with only a 9.14% (in comparison with the 3,500 school lunches provided, the attack rate was lowered by approximately 2.00%). If air were the cause, the attack rate would not be so low; thus air borne transmission can also be ruled out. Due to the fact that the students consumed lunch boxes provided by the school and not a catered meal, it is almost impossible for the students to have shared utensils. Therefore we can also eliminate the possibility of shared utensil contamination. Because of the short latent period (< 8 hours) and the 22 classes located on different floors, it is impossible for a single patient to

infect so many students in such a short period of time. Therefore, the only left cause is food. Food is a possible source of contamination that can result in many different class students to become infected in such a short time. Therefore, the school lunch provided on January 13 is a reasonable explanation for the outbreak among 71 students, why the outbreak spread so quickly, and why no new cases appeared after January 15.

According to the allergic symptoms that appeared in the cases, the short incubation period (a few minutes to several hours), and the fried sailfish fillet specimen that showed traces of histamine, our preliminary conclusion is that the allergic symptoms shown in the students fits the description of histamine fish poisoning. Although the histamine found in the fried sailfish fillet only showed 377.4 ppm, a high percentage of cases showed allergic symptoms of dizziness (67.6%), flushed faces (63.4%), increase heart rates (50.7%), nausea (45.1%), abdominal pains (32.4%), headache (43.7%), shivering (29.6), short of breath (19.1%), vomiting (18.3%), and fever (15.5%) among the 71 cases of food poisoning at X Junior/Senior High School. We can confirm the cause is histamine according to (1) the fact that the histamine found in 100g of suspected fish, cheese, and other foods exceeds 50mg. Using ppm to calculate the amount of histamine, the amount found in suspected fish, cheese, and other foods must exceed 500 ppm; or (2) the consumption of fish that may cause allergic reactions (such as tuna, mackerel, jack mackerel, etc.) and showed symptoms (1996.7.16. Document No. 85036794 issued by Bureau of Food Safety, Department of Health) [9]. Therefore, we can conclude that the histamine in the fried sailfish fillet consumed at Kaohsiung City X Junior/Senior High School is this outbreak's main cause. In other words,

the allergic outbreak indeed is a histamine induced fish poisoning outbreak. Food and Drug Administration (FDA) also states that 50 mg of histamine (500 ppm) in 100g of fish will induce histamine fish poisoning [10]. However, the immunity of the human body towards histamine differs greatly from person to person according the gender, age, and state [11]. According to Gilbert et al, each 100g of fish, if contains less that 20 mg can still induce histamine fish poisoning [12]. Shalaby's study found that 8-40 mg /100g fish will induce severe histamine fish poisoning [13]. Therefore, even if only 377.4 ppm was found in the fried sailfish fillet specimen, we cannot eliminate its possibility as the cause of this allergic outbreak.

In addition, the results of statistical analysis for the lunch box contents and histamine found in the fried sailfish fillet specimen indicate that the fried sailfish fillet with histamine is the main cause of this outbreak. From 1987 to 2007, a total of 48 food poisoning incidents occurred in Taiwan with sailfish as the main cause, followed by mackerel with only a few were induced by tuna. A total of 1,922 cases were diagnosed but with no casualties [14-35]. Histamine is most commonly found in mackerel type fish such as tuna, mackerel, bonito, etc. and often causes histamine fish poisoning. These fish is an amphidromous type of fish with red meat which contains a higher amount of histidine. If not properly stored, it is very likely to be histamine accumulated by enteric bacteria (i.e. *Morganella morganii*, *Klebsiella pneumoniae*, and *Hafnia alvei*) or marine bacteria (i.e. *Photobacterium* spp., *Pseudomonas* spp., *Vibrio* spp., *Plesiomonas shigelloides*, *Aeromonas* spp.)[36]. The histidine, if contaminated will start to produce the decarboxylase effect and produce

histamine. Once histamine is produce, it is difficult to eliminate using freezing, cooling, or heating measures.

According to Article 11, subparagraph 3, of Act Governing Food Sanitation, and Article 2, of Enforcement Rules of the Act Governing Food Sanitation [9], foods contain histamine over 500 ppm and are harmful to the human health are categorized as hazards for the human health (2000.10.17. Document No.0890016378 issued by Bureau of Food Safety, Department of Health). This interprets that poisonous or those containing dangerous contents cannot be made, mixed, packaged, transported, stored, sold, imported, exported, sent, or sold publicly. Although the fried sailfish fillet specimen was only detected with histamine of 377.4 ppm, it did not violate the regulation of not selling, according to Article 11 of Act Governing Food Sanitation. But, histamine is still the main cause of this outbreak according to Article 2 of Enforcement Rules of the Act Governing Food Sanitation.

Histamine is a target standard for determining whether a fish supply is fresh or not. It is becoming important in international seafood products and many countries have regulations regulating the amount of histamine that can be found in seafood products [37]. Starting from the source, companies should be concerned with the management of temperature. If it is on a fishing boat, then there must be suitable equipment to preserve the fish. When selling the fish, the time should be shortened as much as possible in order to decrease the chances of the fish stock being contaminated by the environment, personnel, and ground. When transporting, the storage temperature must also be controlled. When preparing fish, defrosting should be done with flowing water. If unable to

prepare immediately, the fish should be preserved in temperatures lower than 4℃ in order to prevent spoiling under high temperatures. In addition, when selling fish, the repetition of freezing and defrosting should be avoided. Thus, the chances of contamination or production of histamine can be lowered.

Acknowledgments

This investigation would like to thank Research and Diagnostic Center located at the Fifth Branch of CDC in Kaohsiung City and the Department of Health of Kaohsiung City Government for assisting in testing. We would also like to thank the entire staff of Department of Health of Kaohsiung City Government in assisting with the collection of questionnaires, providing investigation records, and test reports; thus allowing for this investigation to proceed smoothly.

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