An Outbreak of Histamine Poisoning after Ingestion of the Ground Saury Paste in Eight Patients Taking Isoniazid in Tuberculous Ward

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Abstract

Objective To determine the cause of outbreak mimicking food poisoning, we studied the toxic polyamine contents of the food and analyzed the clinical characteristics of the affected eight patients.

Patients and Methods Eight cases of histamine poisoning which occurred in tuberculous patients after dinner in our hospital were analyzed by clinical and biochemical methods. We examined the contents of four representative toxic polyamines, histamine, putrescine, cadaverine and tyramine, of each food of the dinner and their serum concentrations of the monoamine oxidase (MAO), one of histaminases, using radioimmunoassay.

Results The allergy-like symptoms such as flushing, headache, palpitation, itching, wheezing, dyspnea and diarrhea appeared from 20 minutes to two hours after ingestion in those eight patients taking isoniazid (INH), although the other 378 inpatients had no symptom. The histamine content of the ground saury paste was increased to 32 mg/100 g of food, however, the toxic level of food poisoning is less than 50 mg/100 g of food. All eight patients were taking INH, and their serum concentrations of MAO were decreased.

Conclusion We concluded that this accident was the histamine fish poisoning. We speculated that those allergy-like symptoms were due to both the increased histamine in the food made with the saury under poor storage conditions and the patients’ reduced histaminase activities due to INH. We should perceive possible adverse effects depending on the interactions between certain drugs and food.

Key words: isoniazid, histamine fish poisoning, outbreak, ground saury paste, histaminase

Introduction

Histamine is a vasoactive amine that can induce allergy-like symptoms in sensitive individuals. Its content level present in fish increases when fish is improperly refrigerated or refrigeration is delayed. The hazardous levels are thought to be 50 mg histamine/100 g of food or more (1), but lower levels also can induce symptoms in individuals whose histaminase activities, such as monoamine oxidase (MAO) and diamine oxidase (DAO), are decreased (2). Isoniazid (INH), an anti-tuberculosis drug, is known to inhibit these enzyme activities and can induce histamine poisoning. Although the hepatotoxic, hematotoxic and neurotoxic adverse effects of INH are well known, the potential for frightening and dangerous interactions with certain foods is less well recognized.

On October 2, 2003, all 386 inpatients had had dinner around 6 PM in our hospital. Eight patients out of 25 in the tuberculous ward developed allergy-like symptoms from 20 minutes to two hours after ingestion. To determine the cause of outbreak of mimicking food poisoning, we studied the toxic polyamines contents, including the histamine, of each food of the dinner and analyzed the eight patients’ clinical characteristics.

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Materials and Methods

Patients

The patients were four men and four women (mean age 53.8; ranged 24 to 81). We examined their serum levels of histamine and MAO 14 hours after ingestion. We analyzed the patients’ characteristics, clinical symptoms and signs, their intake of medicines and the duration of therapy, and the data of routine blood tests. We also studied the responses to
a questionnaire on meal habits given to all patients in the tuberculous ward on that day.

**Analysis of the toxic polyamine concentrations and microorganisms of the food**

The menu of the dinner on that day was rice, egg beancurd with a thick starchy sauce, sautéed broccoli, soup with a ground saury paste and potato with a sauce. Samples of the ground saury paste and egg beancurd were analyzed for the concentration of four representative toxic polyamines, histamine, putrescine, cadaverine and tyramine, by Environmental officers at Taihaku Ward Municipal Health Center in Sendai City using a radioimmunoassay method.

Samples of the ground saury paste and the egg beancurd were added to the medium and cultured for the detection of microorganisms.

### Results

**Patients’ characterization**

The eight patients had allergy-like symptoms such as facial or skin flush (8/8), headache (3/8), palpitation (3/8), itching (3/8), wheezing (2/8), dyspnea (2/8) and diarrhea (1/8) (Fig. 1), whereas the other 378 patients had no such symptoms. The frequency of skin flush was the highest. All their vital signs were normal. None had a past history of allergy or hypersensitivity to foods or drugs. Their eosinophil counts were normal, and the IgE level of only case 4 was slightly high (Table 1).

The symptoms were compatible with those of histamine intoxication. Corticosteroids and anti-histamine (H1-blocker) were given to all eight patients, and their symptoms were relieved within 3 hours.

Serum histamine levels, examined 14 hours after food ingestion, were normal in eight patients. The patients’ characteristics, clinical symptoms and the signs of these patients are summarized in Table 1. Eight patients were taking INH for between 15 and 167 days and their serum MAO levels were lower than the normal limits (0.5 IU/l).

Among 17 patients who had no allergy-like symptoms in the tuberculous ward, two new patients did not start the therapy with anti-tuberculous drugs, three patients stopped taking INH for the adverse effects, 12 patients did not eat the ground saury paste due to bad smell or bad taste. The serum MAO concentration of 4 of these 12 patients was found to be decreased to 0.1, 0.2, 0.3 and 0.4 IU/l, respectively.

**The toxic polyamine contents and microorganisms of the food**

A high level of histamine (32 mg/100 g of fish) was confirmed in the ground saury paste (Table 2). Tyramine was not detected. Although two other toxic polyamines such as putrescine and cadaverine were detected, their concentrations were under the toxic levels (Table 2). In the egg beancurd, the four toxic polyamines were not detected. No microorganism pathogens were isolated from the food samples.

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**Table 1. Clinical Patients’ Characteristics and Serum MAO Concentrations**

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Symptoms</th>
<th>Time to symptom occurring</th>
<th>Serum IgE (IU/l)</th>
<th>Serum MAO (IU/l)</th>
<th>Duration of therapy with isoniazid (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24 F</td>
<td></td>
<td>Flushing, headache, palpitation, wheezing, dyspnea</td>
<td>20 min</td>
<td>129</td>
<td>0.3</td>
<td>79</td>
</tr>
<tr>
<td>2</td>
<td>36 M</td>
<td></td>
<td>Flushing, palpitation, wheezing, dyspnea</td>
<td>20 min</td>
<td>–</td>
<td>0.2</td>
<td>121</td>
</tr>
<tr>
<td>3</td>
<td>38 M</td>
<td></td>
<td>Flushing, headache</td>
<td>20 min</td>
<td>113</td>
<td>&lt;0.1</td>
<td>78</td>
</tr>
<tr>
<td>4</td>
<td>65 M</td>
<td></td>
<td>Flushing, itching</td>
<td>1 h</td>
<td>534</td>
<td>0.4</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>71 M</td>
<td></td>
<td>Flushing</td>
<td>1 h</td>
<td>–</td>
<td>0.2</td>
<td>107</td>
</tr>
<tr>
<td>6</td>
<td>81 F</td>
<td></td>
<td>Flushing, itching, palpitation</td>
<td>1 h</td>
<td>21</td>
<td>0.2</td>
<td>34</td>
</tr>
<tr>
<td>7</td>
<td>82 F</td>
<td></td>
<td>Flushing</td>
<td>1 h</td>
<td>121</td>
<td>0.2</td>
<td>114</td>
</tr>
<tr>
<td>8</td>
<td>33 F</td>
<td></td>
<td>Flushing, headache, diarrhea</td>
<td>2 h</td>
<td>–</td>
<td>0.2</td>
<td>167</td>
</tr>
</tbody>
</table>
Outbreak of Histamine Poisoning by Isoniazid

Table 2. The Concentration of the Toxic Polyamines (mg/100 g of food)

<table>
<thead>
<tr>
<th></th>
<th>Histamine</th>
<th>Putrescine</th>
<th>Cadaverine</th>
<th>Tyramine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ground saury paste</td>
<td>32</td>
<td>0.5</td>
<td>2.5</td>
<td>ND</td>
</tr>
<tr>
<td>Egg beancurd</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND: not detected.

Discussion

We concluded that this accident was an outbreak of histamine poisoning caused by ingestion of ground saury paste in the tuberculous patients taking INH. The symptoms of histamine poisoning mimic those of an IgE-mediated food allergy: hives, itching, rash, flushing, urticaria, abdominal cramps, headache, palpitations, diarrhea, nausea and vomiting, and hypotension can occur within minutes to a few hours after ingesting the hazardous fish and last up to 24 hours (3, 4). Eight patients complained of some of these symptoms, and they were diagnosed as allergic-like symptoms and were treated with corticosteroid and antihistamine.

Histamine fish poisoning is a common worldwide seafood-borne disease. Ten percent of the infectious intestinal disease outbreaks reported to the Communicable Disease Surveillance Centre were associated with fish, and about half of those to histamine poisoning (5), but such outbreaks were rare in Japan.

The diagnosis is based on taking a good food history and ruling out other causes of the dramatic symptoms, and determined by a high histamine level of food. Histamine levels in freshly-caught fish are less than 1 mg/100 g of fish, but if the fish is left at room temperature, they can increase to up to 100 mg/100 g of fish within 12 hours (6, 7). Bacterial histidine decarboxylase, found in Escherichia coli, Proteus species and Klebsiella species, present in fish tissue, converts muscle histidine to histamine (8, 9). Bacterial activity is increased at an elevated temperature, therefore poor storage conditions exacerbate the problem (10). Red fish meat such as saury is more susceptible to allergy-like food poisoning because the histidine content of red meat is much higher than that of white meat (11). In ground fish paste, the contamination of enterobacteria can more easily occur than prior to mincing, and more histamine is produced. The bacteria dies during the cooking process, but the histamine that has accumulated in the fish is heat stable and cannot be destroyed, thus, cooking of hazardous fish will not reduce the risk of illness (12). Histamine spoilage levels are estimated to be 20 mg/100 g of fish, and the toxic levels are 50 mg/100 g or more (1, 3). In the present case, the histamine content was 32 mg/100 g of the ground saury paste, which may be a spoilage level to humans, but it was not a toxic level. The fact that no inpatient except for these eight developed such symptoms also suggests that the level was not toxic.

Histamine is readily metabolized by histaminases such MAO and DAO. INH is known to suppress both of MAO and DAO (13), resulting in a decrease of the histamine detoxification. There are a few case reports on histamine poisoning after ingestion of fish in tuberculous patients (14–18). In the present case, all the plasma MAO concentrations of eight patients were reduced, although the high serum histamine contents were not detected because the blood samples were taken 14 hours after ingestion of the dinner. Other patients taking INH also showed low serum concentrations of MAO, but they did not complain of symptoms, because they did not eat the ground saury paste due to a bad smell or a bad taste on that day. Therefore we conclude that the allergy-like symptoms were presumably due to the high histamine concentration in the food and the low histaminase activities actively suppressed by INH in the intestine.

It is also reported that histamine poisoning occurs more frequently in individuals with allergic inheritance (19, 20). Our patients had no prior history of allergic diseases, their eosinophil counts were normal, and the IgE level of only case 4 was slightly high (Table 1). The relationship between histamine poisoning and allergic inheritance is not clear.

Patients with allergy-like food poisoning are often misdiagnosed as having a true food allergy. We should perceive the possible adverse effects depending on the interactions between certain drugs and foods.

Acknowledgements: The authors thank Dr. Hiroshi Takahashi of the Department of Respiratory Medicine, Saka Hospital, for his critical suggestions.

References


