Clinical Vignettes

A Case of Histamine Fish Poisoning in a Young Atopic Woman

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Histamine fish poisoning, also known as scombroid poisoning, is a histamine toxicity syndrome that results from eating specific types of spoiled fish. Although typically a benign syndrome, characterized by self-limited flushing, headache, and gastrointestinal symptoms, we describe a case unique in its severity and as a precipitant of an asthma exacerbation.

A 25-year-old woman presented to the emergency department (ED) with one hour of tongue and face swelling, an erythematous pruritic rash, and dyspnea with wheezing after consuming a tuna sandwich. She developed abdominal pain, diarrhea and hypotension in the ED requiring admission to the hospital. A diagnosis of histamine fish poisoning was made and the patient was treated supportively and discharged within 24 hours, but was readmitted within 3 hours due to an asthma exacerbation. Her course was complicated by recurrent admissions for asthma exacerbations.

KEY WORDS: histamine fish poisoning; scombroid; asthma.

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INTRODUCTION

Scombroid poisoning is a histamine toxicity syndrome that results from eating spoiled fish. When fish are not maintained at cool temperatures, bacteria metabolize histidine into histamine. When consumed, this exogenous histamine load results in the characteristic syndrome of tongue dysesthesias, flushing of the face and torso, and a throbbing headache. As scombroid toxicity is usually a benign, self-limited condition, many affected persons never present for medical care. Here, however, we present a case of histamine fish poisoning which placed the patient at serious risk.

Key points 1. Histamine fish toxicity is generally a benign, self-limited illness that does not require therapy.

2. Clinicians should recognize that a history of atopy can result in a prolonged and complicated course.

3. Severe cases should be considered in the differential diagnosis of anaphylaxis.

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Case report

A 25-year-old woman presented to the emergency department (ED) with a one hour history of tongue and face swelling with flushing and shortness of breath. Her illness began after eating a tuna sandwich made with a can of solid white tuna in water. The patient reported that the tuna had an odd taste and appearance. She removed portions that appeared discolored and went on to consume the remainder of the can. Immediately upon finishing the tuna, she noticed a burning sensation in her tongue. This was quickly followed by a sense of flushing and warmth that spread from her face to her neck and torso. She also described feelings of tongue, lip, face, and ear swelling. She then developed an itchy, bright red rash over her torso, shortness of breath, and wheezes. The patient's roommate, who also consumed a small amount of the tuna, had a similar but less severe syndrome not requiring medical attention. Her past medical history was remarkable for mild intermittent asthma, allergic rhinitis, eczema, and recurrent ovarian cysts. In addition, she reported a prior anaphylactic reaction to opiates. She had two previous ED presentations for such reactions; in neither case was she intubated nor admitted to hospital. Her medications included a budesonide-formoterol combination inhaler, a salbutamol (albuterol) inhaler when necessary, and a combination estrogen-progestin oral contraceptive. She denied the use of opiates, prescribed antihistamines, and regular over-the-counter medications.

In the ED, the patient was afebrile, had a heart rate of 150 beats per minute, blood pressure of 139/83 mmHg, respiratory rate of 26 breaths per minute, and intermittent oxygen saturations of 88% on 4 liters by nasal cannula. She had an erythematous, papular rash over her face, neck, and torso, decreased breath sounds bilaterally with expiratory wheezes, and increased work of breathing. Bedside bronchoscopy revealed normal vocal cord and proximal airway anatomy. During her ED stay, she developed severe headache, diffuse abdominal pain, diarrhea, and progressive hypotension, reaching a nadir of 86/53 mmHg.

Her laboratory results were remarkable for a white blood cell count of 11.9×10^9 cells/L with 11.5×10^9 neutrophils/L, a bicarbonate of 17 mmol/L, and an anion gap of 18 meq/L. Her serum electrolytes, D-dimer, lactate, chest and abdominal radiographs were within normal limits. A serum beta human chorionic gonadotropin confirmed that she was not pregnant.

Her syndrome was initially treated with a total of three intramuscular doses of 0.3 mg 1:1000 (1 mg/mL) epinephrine in the walk-in clinic and by emergency medical services (EMS) prior to arriving in the ED. In addition, she received normal saline, intravenous methylprednisolone, ranitidine, diphenhydramine, and nebulised salbutamol. Given her unique presentation and its clear association with the ingestion of tuna, the emergency physician consulted internal medicine to assist in the diagnosis and further management of suspected scombroid poisoning. With this therapeutic regimen, she recovered and was discharged the following morning. She was given a prescription for an EpiPen and advice to return if any symptoms recurred.

Because of concern regarding the potential contamination of other cans of tuna, the regional Medical Officer of Health was immediately consulted. Three of the patient's remaining unopened cans, and six cans obtained from retail, all from the same lot number, were sent to the Canadian Food Inspection Agency laboratory (Burnaby, British Columbia) for analysis of tissue histamine levels. As the culprit can was disposed of, any remnants could not be sent for analysis. Histamine levels in the analyzed cans were undetectable (i.e. <1 mg/100 g), implying that the affected fish was presumed to be isolated to the one particular can.

2nd presentation

Within three hours of her discharge, approximately 24 hours after the ingestion, she returned to the ED complaining of recurrent dyspnea and a sensation of facial, neck and torso warmth and flushing. At that time, she was noted to have diffuse, bilateral wheezes and hypoxemia, with an oxygen saturation of 86% on room air. She was admitted to the internal medicine service for observation and management. Her 5-day inpatient course was remarkable for intermittent dyspnea and hypoxemia. Pre- and post-bronchodilator peak expiratory flow rates were measured at 200 mL and 350 mL, respectively. She was treated with salbutamol, budesonide-formoterol, and was discharged with a 5-day course of prednisone to complete a ten day course of therapy.

In the following two months, she was admitted an additional four times for recurrent hypoxemic respiratory syndromes of uncertain etiology. During this time, the patient underwent extensive investigations, all of which were all unremarkable. Specifically, plasma levels of immunoglobulin E, C1 esterase inhibitor, and histamine, maximal static inspiratory and expiratory mouth pressures, and a CT pulmonary angiogram were all unremarkable. A transthoracic echocardiogram revealed a small patent foramen ovale that was deemed to be hemodynamically insignificant. The persistent hypoxemia was ultimately

attributed to recurrent asthma exacerbations, the precipitants for which are still not clear. It was hypothesized that the first hypoxemic episode represented an asthma exacerbation that was provoked by the histamine fish toxicity. The subsequent course of recurring asthma exacerbations could not be linked to the initial episode of histamine fish toxicity. With pulmonary consultation, daily montelukast, tiotropium, and cetirizine were added to her regular budesonide-formoterol therapy.

DISCUSSION

Clinical review

Scombroid was first described in 1799¹. It was so named because of the belief that fish of the Scombridae and Scomberesocidae family—namely tuna, mackerel, and bonitos—were the sole cause. It is now known that non-Scombroid fishes can also cause this condition. Because of this, and the understanding that the condition results from histamine toxicity², the more descriptive and accurate term 'histamine fish poisoning' has been used³.

Histamine fish poisoning classically manifests within minutes of ingesting spoiled fish^{1,2,4}. It begins with a burning sensation in the tongue that can be associated with a 'peppery' or metallic taste. Progressive flushing of the face, neck, and torso with a characteristic throbbing headache also occurs soon after ingestion. Anxiety, nausea, tachycardia, and abdominal pain are also common features. More sinister features, such as respiratory distress and myocardial dysfunction, are extremely rare, being limited to single case reports^{1,3}.

If spoiled fish is to produce histamine fish poisoning, three factors must be present: The ingested fish must be rich in the amino acid histidine, which is typically the case with dark-fleshed fish³. Secondly, colonizing gram negative enteric bacteria must contain histidine decarboxylase, the enzyme necessary to convert histidine into histamine³. Lastly, at some point after the catch, the fish must have been exposed to relatively warm temperatures to permit bacterial replication and histidine metabolism, ultimately leading to critical histamine levels. Whereas freshly caught fish have tissue histamine levels less than 1 mg/100 g, 20 mg/100 g is thought to be the level necessary to cause disease⁴.

Histamine fish poisoning is a clinical diagnosis. The diagnosis is based on the characteristic syndrome in close proximity to fish ingestion. Laboratory testing can be used to support the diagnosis. Elevated plasma histamine levels, taken within 4 hours of ingestion, have been proposed to be a specific finding in a small case series². In addition, suspect fish, either residual from a given incident or products from the same lot, can be sent to specialty laboratories to measure tissue histamine levels, with excess

levels supporting the diagnosis⁴. Importantly, tissue histamine levels vary significantly among even different body regions of the same fish. Indeed, there are reports of undetectable histamine levels in one part, and >100 mg/100 g in another part of the same fish known to have caused histamine fish poisoning².

Almost invariably, histamine toxicity follows a benign, self-limited course. The syndrome completely resolves within 6 hours in the vast majority of victims^{3,4}. However, atopic conditions, including two case reports of asthma, have been reported to extend course duration and severity^{1,2}. For example, in a small case series², the syndrome lasted 6 and 24 hours in small groups of non-atopic and atopic patients, respectively. More recently, there are case reports describing significant hypotension, ranging from that requiring aggressive fluid resuscitation⁵ to a biventricular assist device⁶. Treatment is supportive, consisting of H1- and H2-receptor antagonists. Health care providers should immediately inform their local public health officer in order to help prevent further cases. Local outbreaks have been reported.

Histamine fish poisoning is a foodborne intoxication that should be clearly distinguished from food allergy. True food allergy results in IgE-mediated mast cell activation with allergic reactions with subsequent exposures. In contrast, histamine fish poisoning does not require future abstention from dark-fleshed fishes. In this regard, it is important to inform the patient that a fish allergy does not exist and that future fish ingestion is safe. In severe allergy, epinephrine and glucocorticoids are used, in part, to specifically inhibit mast cell and basophil degranulation⁷. Due to the mast cell- and basophil-independent mechanism of histamine fish toxicity, these agents do not have a major role in the management of routine, non-severe histamine fish toxicity. Therefore, patients with recent attacks would not benefit from the routine prescription for an EpiPen.

Our case is unique because of the source (canned fish), duration, and hemodynamic consequence of the histamine fish toxicity. Moreover, it is also possible that it contributed to the provocation of a cascading and persisting asthma exacerbation. Histamine fish poisoning most often occurs after the ingestion of fresh, rather than canned fish⁸. Compared to fresh fish, canned fish that make it to market are relatively protected from histamine fish toxicity because of more stringent quality control regulations⁹. Specifically, fish destined to be canned are subject to frequent tissue histamine level analyses, with fish containing excessive amounts being discarded³. The fresh fish industry is not subject to this degree of scrutiny. In addition, whereas fresh fish are usually processed and consumed as a single fish fillet, canned fish is composed of multiple different fish; the limited contribution of any single fish helps to minimize the impact, or histamine load, of any spoiled fish that makes it

through the quality control process and into the can. The process of canning itself does not destroy formed histamine, though the procedure can kill the bacteria that produce it¹.

Our case further implicates asthma as an important modifying comorbidity. Our patient had a relatively severe course whereas her non-atopic roommate, after eating a portion of the same spoiled fish, did not require any medical attention. Previous authors have reported that atopic individuals may indeed have longer courses⁸. In addition to predisposing our patient to a prolonged course, the histamine fish poisoning may have also triggered an acute exacerbation of her asthma. We are not aware of any previous reports that have implicated histamine fish poisoning in the provocation of an asthma exacerbation. However, there is strong evidence for a direct causative link between histamine and bronchoconstriction in asthmatics^{10,11}. Specifically, histamine induces bronchial smooth muscle contraction (i.e. bronchoconstriction) directly and indirectly, via histamine receptors and acetylcholine receptors, respectively. Therefore it is possible that an exogenous histamine load could have precipitated an asthma exacerbation in this patient.

In conclusion, we report a case of severe histamine fish poisoning in a young atopic woman. Awareness of this condition may prevent unnecessary treatments or hospitalization and should prompt a public health investigation. Clinicians should recognize that the clinical course may be prolonged and of greater severity in patients with a history of atopy. Severe cases should be considered in the differential diagnosis of anaphylaxis.

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