

## CLINICAL VIGNETTE

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# Scombroid Fish Poisoning

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A patient called to report facial flushing, headache and a non-pruritic erythematous rash predominantly on the face and chest. She had no fever, hives, dyspnea or diarrhea. She had eaten spicy tuna sushi at a restaurant 30 minutes before symptom onset. She eats sushi regularly without prior reactions. She is healthy, on no medications, and has no known allergies to medications or food. Her vital signs were stable other than mild tachycardia. Physical exam revealed a widespread erythematous rash involving face and chest. She was instructed to start antihistamines and symptoms resolved after a few hours. Of note, the patient's friend, who accompanied her to dinner, also developed similar symptoms.

### *Introduction*

Histamine fish poisoning, also known as scombroid poisoning, is the most common cause of ichthyotoxicosis worldwide and results from ingestion of histamine-contaminated fish in the Scombroideae and Scomberesocidae families. This includes mackerel, bonito, albacore and skipjack.<sup>1</sup> These scombroid fish all have high levels of free histidine in their muscle tissues.<sup>2</sup>

It is now known that non-scombroid fish species are also implicated in scombroid poisoning, such as mahi-mahi, sardines, pilchards, anchovies, herring, marlin, Western Australian salmon, sockeye salmon, amberjack, yellowtail and swordfish.<sup>2</sup> The first description of this syndrome dates back to 1799 in Britain, and it is now estimated to be responsible for about 5% of all reported food poisoning in the United States.<sup>3</sup> Histamine fish poisoning is an under-recognized disease and often misdiagnosed as an allergic reaction.<sup>1</sup> Proper handling and storage of the fish is the most important preventive measure.<sup>4</sup> Cooking of contaminated fish does not prevent histamine poisoning because the toxins are heat stable.<sup>4</sup>

The symptoms associated with histamine fish poisoning are similar to that of an allergic reaction.<sup>1</sup> However, scombroid poisoning is not an allergy. Allergic reactions typically affect one person who has a history of allergy to the implicated food item.<sup>5</sup> Fish allergy is an IgE mediated reaction because of the ingestion of fish, unrelated to its state of preservation and integrity.<sup>3</sup> An allergic-like reaction in unrelated persons after consuming the same fish should raise the suspicion of scombroid fish poisoning.<sup>4</sup> Scombroid fish poisoning is nonimmunologic and due to fish contamination.<sup>4</sup>

Scombroid poisoning occurs when fish are inadequately frozen, which allows bacteria located in the flesh of the fish to thrive.<sup>1</sup> In the process, bacteria convert histidine to histamine. Histamine does not change the smell or appearance of the affected fish.<sup>5</sup> Thus the fish may seem normal. Elevated histamine levels can occur in fish owing to improper refrigeration before processing or to storage of the fish at room temperature after cooking. The appearance, taste and smell of the fish are poor guides as to the presence of histamine.<sup>5</sup> Once histamine is formed, it is highly resistant to tampering, so cooking, smoking, freezing and canning cannot prevent histamine fish poisoning reactions.<sup>1</sup>

### *Epidemiology*

Since 1980, fish consumption in the USA has dramatically increased. Paralleling the rise in fish consumption, cases of histamine fish poisoning have increased. The states with the highest number of reported cases were California, Hawaii and New York. Tuna and Mahi-mahi alone make up more than 80% of scombroid fish poisoning cases in the United States.<sup>1</sup>

### *Clinical Features*

The onset of scombroid poisoning is typically from 10 minutes to one hour following consumption of poisonous fish.<sup>2</sup> Given that the symptoms result from excess amounts of histamine, the physical manifestations of histamine fish poisoning are similar to those of an allergic reaction. Symptoms include facial flushing, rash, headache, dizziness, sweating, burning of the mouth and throat and urticaria, generally widespread erythema lacking wheals, which can help distinguish scombroid poisoning and fish allergy. Gastrointestinal symptoms can include abdominal pain and diarrhea. Severe, but rare reactions can include hypotension, bronchospasm, respiratory distress and myocardial infarction. The rash can last 2-5 hours and the other symptoms usually disappear within 3-36 hours.<sup>5</sup> The variety of symptoms is because histamine action on its receptors varies in different tissues: skin, respiratory tract, cardiovascular system, gastrointestinal tract, central nervous system, and immunity cells.<sup>3</sup>

### *Pathophysiology*

Histamine is not normally present in fish.<sup>3</sup> It is produced by histidine decarboxylase present in the bacteria resident in fish gills and gastrointestinal tract.<sup>3</sup> This enzyme is formed after a

few hours of fish exposition at room temperature and is inactivated by temperatures of 0 degrees C or lower.<sup>3</sup> Storage at 0 degrees C should be performed immediately after fishing because once activated, histidine carboxylase still functions even after bacteria are not viable.<sup>3</sup> Diamine oxidase and histamine N-methyltransferase are displayed on human gastrointestinal mucosa and are usually able to degrade histamine. However, diamine oxidase and histamine N-methyltransferase inhibitors are also present, together with histamine, in the contaminated fish.<sup>3</sup> Consequently, an increased amount of histamine is absorbed and available to extraintestinal tissues.<sup>3</sup> In scombroid syndrome histamine receptors type 1 and type 2 regulate the cutaneous and cardiovascular manifestations whereas the histamine receptors type 3 modulate neurological symptoms.<sup>1,3</sup>

Histamine was first suggested as the implicated agent in scombroid poisoning in the 1940s. However, for half a century, studies suggested that histamine could not be absorbed via the gastrointestinal tract in sufficient quantities to reach an appreciable amount in the systemic circulation.<sup>1</sup> In 1991 volunteer subjects knowingly ingested spoiled marlin with subsequent measurement of urinary histamine levels. Researchers conclusively demonstrated excess histamine was the culprit for scombroid toxicity.<sup>1</sup>

### **Diagnosis**

Scombroid food poisoning diagnosis is primarily clinical. Attention should be given to type of fish ingested, whether the fish was cooked or raw, whether these reactions have occurred in the past and the time frame between fish ingestion and the onset of symptoms. Another important question would be to ask if anyone else ate the same fish and presents with the same symptoms.<sup>3</sup> This question can help distinguish between scombroid fish poisoning and food allergy. The patient must be asked about medications. Isoniazid and monoamine oxidase inhibitors inhibit histamine metabolism, and may increase risk for histamine fish poisoning.<sup>1</sup> Testing the fish helps definitively diagnose the toxic etiology. Fresh fish contain minimal amounts of histamine, less than 0.01mg/100g. Histamine poisoning only occurs when the histamine levels are orders of magnitude greater.<sup>1</sup> As a general rule, >50mg of histamine per 100 g of fish causes histamine poisoning. To ensure a wide margin of error, food regulations in the USA require histamine levels not exceed 5mg/100g of fish.<sup>1</sup> Determination of histamine levels in plasma can be useful to confirm diagnosis. Samples must be collected as soon as possible because of brief half-life which limits use in clinical practice.<sup>3</sup>

### **Treatment**

Most instances of scombroid poisoning are self-limited,<sup>5</sup> such as H1 receptor antagonists, like diphenhydramine or cetirizine are commonly used, along with supportive care tailored to the symptoms. Oral H2 blockers such as cimetidine, famotidine or ranitidine can be added. Symptoms should completely resolve in 6-8 hours.<sup>1</sup> Adrenaline and corticosteroids are not indicated.

To prevent further instances of poisoning public health authorities should be notified to investigate the source and remove the implicated product from distribution.

### **REFERENCES**

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