46-Year-Old Man With Abdominal Pain and Hypotension

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A 46-year-old man with a history of type 2 diabetes, tetralogy of Fallot, and a bioprosthetic pulmonary valve replacement presented to the emergency department feeling generally unwell after eating a meal at a restaurant. The patient was in his usual state of health until starting dinner at the restaurant. The meal included cooked seafood, which consisted of different types of fish, shrimp, and scallops. A few minutes into his meal, he was overtaken by a sudden onset of severe back pain and cramping that radiated to his abdomen, mainly in the periumbilical region. He rated the pain as 8 of 10 on the severity scale. The pain was followed by progressively worsening dizziness and blurry vision. He also experienced intense palpitations, giving him the sensation of "wanting to pass out." The patient had no known allergies to fish, seafood, or iodine. He had never experienced any of these symptoms before. None of his colleagues who ate with him had any similar symptoms. He had not recently traveled.

On arrival at the emergency department, he became nauseated and vomited 6 times. He appeared to be moderately distressed. He was afebrile, his heart rate was 115 beats/min, and his blood pressure was 78/56 mm Hg. Physical examination yielded unremarkable findings except for erythema on his cheeks and mild wheezing on pulmonary examination. Laboratory tests, including complete blood cell count, metabolic profile, and liver function tests, revealed normal values except for a lactate level of 2.1 mmol/L (reference range, 0.6-2.3 mmol/L). Electrocardiography detected sinus tachycardia, and computed tomography of the abdomen with contrast medium revealed diffuse small-bowel wall thickening, edema, and mesenteric fluid with engorgement of the vasa recta. He was admitted to the hospital for further evaluation and treatment.

1. Which *one* of the following should be the *initial step* in the management of this patient's presenting symptoms?

a. Broad-spectrum antibiotics
b. Intravenous fluids
c. Stool studies for *Clostridium difficile*, ova and parasites, and bacterial culture
d. Colonoscopy with biopsy
e. Stress-dose corticosteroids

Broad-spectrum antibiotics should be considered in a patient who presents with evidence of hemodynamic compromise; however, antibiotics alone will not restore a normodynamic state. At this time, rapid hemodynamic stabilization with intravenous crystalloids should take precedence. The patient should be treated with fluids while the etiology of shock is investigated. In most cases, it is safe to start empiric antibiotics after fluids are administered if septic shock is high on the differential diagnosis. Once septic shock has been ruled out, antibiotics should be discontinued.

Stool studies will have low yield in this setting because the patient has neither diarrhea nor constipation. Even if enteric infection is present, rapid stabilization is more important than performing other diagnostic studies. Similarly, colonoscopy has no benefit in the patient's immediate care. Initially, there is no indication for stress-dose corticosteroids. The patient has no history of adrenal insufficiency, and there is no compelling evidence of adrenal crisis. Adrenal crisis should be considered in patients who have not responded to fluid resuscitation or in those who present with severe lethargy, weight loss, salt craving, hypoglycemia, and pigmentation of the skin, which are all indicative of adrenal crisis. In cases of shock refractory to fluids, the phenomenon of relative adrenal insufficiency can be explored, and stress-dose corticosteroids would be beneficial, especially if the patient has a recent history of corticosteroid use.

See end of article for correct answers to questions.

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On further questioning, the patient recalled that a piece of fish tasted "funny." At this point, when compared with initial presentation, the patient's flushing and wheezing had worsened.

2. Given the rapid clinical progression, which *one* of the following is the *most likely* etiology of the patient's symptoms?

a. *Staphylococcus aureus* preformed toxin
b. *Vibrio vulnificus*
c. Scombroid poisoning
d. *Bacillus cereus*
e. Ciguatoxin

The rapid onset of the patient's symptoms suggests that a preformed agent (possibly preformed toxin) is likely responsible for his symptoms. Food handlers who are colonized with *Staphylococcus* frequently contaminate food supplies. If food is then left at room temperature, the bacteria can multiply and produce a heat-stable toxin that can cause gastrointestinal symptoms such as nausea, vomiting, and occasionally diarrhea in as little as 6 hours after ingestion. These foods usually include high-protein or fatty foods such as dairy, meat, fish, eggs, and salad. However, *Staphylococcus* does not cause the severe flushing and wheezing observed in our patient.

Vibrio species including *V vulnificus* and *Vibrio parahaemolyticus*, often contracted by consumption of raw shellfish, usually produce symptoms approximately 48 hours after ingestion. Our patient was indeed consuming seafood, but the rapid progression of his symptoms does not correlate with *Vibrio* infection.

Patients with scombroid poisoning generally experience symptoms within minutes of consuming the affected fish product. Symptoms include facial flushing, abdominal pain, nausea, and hypotension in more severe cases. Our patient's symptoms were most representative of scombroid poisoning.

Bacillus cereus most commonly presents after consumption of rice that has remained at room temperature for a prolonged period. This incubation period would also be extended beyond the time of onset of our patient's symptoms, and he did not report rice consumption. Therefore, *B cereus* is an unlikely etiology.

Ciguatera fish poisoning is caused by a ciguatoxin produced by *Gambierdiscus toxicus*. These single-celled dinoflagellate organisms grow on coral reefs, and the toxin becomes concentrated in the muscle and organs of fish that consume them. This toxin does not cause harm to the fish but will readily affect humans who consume the contaminated fish. Symptoms usually begin in just a few hours after consumption of reef fish (snapper, barracuda, amberjack, parrotfish, moray eel, and certain types of grouper). Gastrointestinal and cardiac symptoms can be present as in scombroid poisoning but are less prominent; however, neurologic symptoms are a distinguishing feature. Neurologic symptoms include paresthesia, painful dentition, metallic taste in the mouth, painful urination, blurred vision, and the pathognomonic temperature-related dysesthesias (cold stimuli are misinterpreted as hot or as an abnormal and unpleasant sensation). Treatment is supportive.

Scombroid food poisoning was suspected, antibiotics were discontinued, and treatment was directed at the underlying cause.

3. In view of these findings, which *one* of the following would be the *best* treatment option at this time?

a. Ranitidine
b. Diphenhydramine
c. Prednisone
d. Epinephrine and an H_1-blocker
e. Vasopressin

Histamine is the mediator of symptoms in scombroid poisoning, and medications that reduce the effects of histamine are needed in this patient. Most cases of scombroid toxicity are indolent and self-limiting, characterized by headache, urticaria, nausea, vomiting, and abdominal pain. Patients usually recover in 1 to 2 days without treatment. However, when symptoms are severe enough to require treatment, the mainstay treatment consists of antihistamines. H_2-blockers, such as ranitidine, are usually effective, but their effects can be coupled with H_1-blockers, such as diphenhydramine. A synergistic effect can be achieved with such a combination; however, these agents should not be the initial treatment in a patient presenting with shock, as in this case.

Corticosteroids can sometimes be used as adjuvant therapy in very severe cases of scombroid poisoning, especially if a concomitant allergic reaction is suspected. However,

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because of this patient's instability, it would not be the initial treatment in this case.

When shock is a major feature, which is rare, acute anaphylaxis should be managed aggressively, and epinephrine should be administered immediately. In our patient with wheezing, extreme dizziness, and severe hypotension, epinephrine is the first-line treatment and would contribute to a more rapid resolution of symptoms.

Vasopressin is a vasoactive substance used to improve systemic mean arterial pressures in septic shock. In this patient with anaphylactic shock due to excessive histamine intake from improperly stored fish, vasopressin has no role.

Our patient was given epinephrine and an H_1-blocker because of the severity of his symptoms. The hypotension, abdominal pain, and flushing began to resolve following administration and appropriate fluid resuscitation. Our patient was ultimately discharged 1 day later with complete resolution of symptoms.

4. Which *one* of the following is the *best* means of preventing this illness in the future?

a. Fish should be cooked at a minimum temperature of 100°C
b. Fish should be stored at a temperature below 4°C immediately following preparation
c. Fish should be stored at a temperature below 4°C immediately after catch
d. Avoid raw seafood
e. Take antihistamines along with meals

Histamine, the causative substance of scombroid poisoning, is a heat-stable molecule and is not denatured by cooking. It will also retain its properties when stored at low temperatures once present, which generally occurs shortly after the fish is caught. Therefore, storing fish at low temperatures following preparation is likely too late. Storing fish at temperatures below 4°C immediately after being caught will prevent bacterial overgrowth and concomitant histamine formation.

Scombroid poisoning can be transmitted via raw or cooked meat. Therefore, avoiding raw fish will have no effect on disease transmission. Administration of prophylactic antihistamines before seafood consumption is not necessary. If fish are stored appropriately, the probability of the development of scombroid poisoning is exceedingly low. Furthermore, empiric antihistamine can have adverse effects such as urinary retention, dry mucous membranes, drowsiness, and impaired coordination.

5. Which *one* of the following statements is *true* regarding this patient's illness?

a. This disease should be reported to local authorities
b. Histamine levels are needed to make the diagnosis
c. Recovery usually occurs in days
d. A course of antihistamine should be initiated before the patient is discharged and continued for at least 1 week
e. This illness is related to other food allergies

Scombroid poisoning should be reported to the local authorities in order to confirm the diagnosis and prevent the consumption of contaminated fish. Histamine levels can be evaluated, but this test is not readily available and not routinely performed. With early recognition of disease and appropriate treatment, disease recovery is usually achieved within 30 minutes of presentation. An extended course of antihistamine is not needed because recurrence is unlikely without a second exposure. Scombroid poisoning is not a food allergy and has no known correlation with hypersensitivity reactions or food allergies.

DISCUSSION

One of the most common seafood-associated diseases, scombroid poisoning is believed to cause up to 40% of all seafood-borne illnesses.[1-3] Scombroid poisoning is a clinical syndrome that results from the consumption of foods that contain unusually high levels of histamine.[2-5] Certain fish in the Scombridae family, including tuna, mackerel, bonito, and skipjack, contain a high content of histidine in muscle tissue.[1-5] When improperly stored, generally in temperatures greater than 4°C, the bacteria within the fish convert histidine to histamine via a decarboxylase reaction, resulting in the production of large amounts of histamine within the fish before it is consumed.[3,4] Other fish, including mahi-mahi, swordfish, marlin, salmon, trout, and herring, as well as certain

cheeses are known to cause scombroid poisoning. Histamine is not broken down by freezing or cooking, which makes it difficult to prevent this illness after the initial histamine production. To the same extent, the taste of the contaminated fish is generally unchanged, making it difficult to alert the patient to its contamination.[3-5] Scombroid toxicity is not a seafood allergy, and patients should be told that they can still consume properly handled fish.

Clinical manifestations, as seen in our patient, are consistent with the consumption of large amounts of histamine. Symptoms can vary, yet generally include flushing, urticaria, headache, abdominal cramps, diarrhea, and dizziness. Hypotension can also develop as a result of distributive shock from the substantial histamine release. Bronchospasm and cardiac arrhythmias have also been reported but are not as common. Symptoms of scombroid poisoning manifest within minutes to hours after consumption of the contaminated fish.[2-5] Symptoms usually resolve within 24 hours of onset. However, depending on the severity of symptoms, a higher level of supportive care may be indicated.[5] The duration and severity of the poisoning depend on the amount of the contaminated food consumed.[2,3]

Diagnosis of scombroid poisoning is clinical. No particular testing modality can be used to confirm its diagnosis. It is important to consider other possible etiologies of a patient's symptoms, leaving scombroid as a diagnosis of exclusion.[2-5] Fish can be examined for histamine content, but this is very rarely performed. Plasma histamine levels of patients with suspected scombroid poisoning can be examined, but this also is not routinely performed.[3,5]

The treatment and management of patients with scombroid poisoning is primarily supportive. Patients should be given antihistamines and can generally be discharged home if symptoms are mild. In patients with more severe symptomatology, admission to the hospital may be warranted.[2-5] Intravenous fluid administration and, if needed, pressor support should be used to help manage hypotension.[5] Epinephrine should be reserved for patients presenting with bronchospasm.[4]

It is important to recognize scombroid poisoning in patients presenting with a variety of symptoms, as described in this case. Studies have found that scombroid poisoning is underrecognized and underdiagnosed.[2,3] Although most cases are self-limiting, prompt diagnosis can help to alleviate the burden of symptoms and prevent further sequelae in patients with hemodynamic compromise.

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CORRECT ANSWERS: 1. b. 2. c. 3. d. 4. c. 5. a

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