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A Toxic Fish Dinner

Two patients ate the same fish dinner and now have life-threatening symptoms. This case highlights the risks associated with ciguatoxin and other toxins that bioaccumulate in certain fish and shellfish.

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Case

A 48-year-old woman and her 16-year-old daughter present to the ED with diarrhea and vomiting approximately 5 1/2 hours after eating dinner. They report having eaten a steamed fish that was purchased at a local fish market. Their symptoms started with diarrhea approximately 4 hours following dinner. The mother also complains of light-headedness and perioral tingling.

The mother's initial vital signs are as follows: blood pressure, 90/65 mm Hg; heart rate, 48 beats/min; respiratory rate, 16 breaths/min; and temperature, 37.3°C. Her Spo_2 level is 99% on room air. The daughter's initial vital signs include a blood pressure of 83/41 mm Hg; heart rate, 45 beats/min; respiratory rate, 17 breaths/min; and temperature, 37.5°C. Her Spo_2 level is 98% on room air. Findings on physical examination, including the neurologic examination, are normal in both patients.

The hypotension and bradycardia persist despite adequate volume resuscitation with normal saline. Both mother and daughter receive age- and weight-appropriate doses of atropine, with transient improvement in heart rate.

The other two members of the family (the father and son), who also ate the meal, are seen in urgent care with subjective tingling in their extremities and normal vital signs. Both are discharged home prior to the realization of the context of their illness. Following evaluation of the index cases, they are contacted to return to the ED but decline a return visit.

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What is the differential diagnosis of foodborne poisoning with neurologic symptoms?

Although the differential diagnosis for foodborne illness is quite vast (encompassing infectious and toxicologic etiologies), the complaint of concomitant neurologic symptoms considerably narrows the differential diagnosis. The history of the shared fish meal strongly suggests that this is the point source for their exposure. However, before assuming that the fish is primarily responsible, it is important to consider that spices, flavorings, and other ingredients may contain toxicants, such as monosodium glutamate, pesticides, or metals, that may be contributing to the clinical effects.

The combined findings of perioral paresthesia and the vital sign abnormalities suggest that the toxin alters the normal function of neuronal sodium channels. The small unmyelinated nerve fibers in and around the mouth and in the distal extremities are highly sensitive to the effects of sodium channel blockers. In the myocardium, sodium channels are responsible for normal electrical conduction through the His-Purkinje system. Both activating and inhibiting sodium channel function can produce neurotoxic and cardiotoxic effects.

Toxins that have been associated with both gastrointestinal and neurologic effects are listed in the Table.[1] Other toxins are associated with distinct forms of neurotoxicity that occur through unique mechanisms. For example, domoic acid, implicated in amnesic shellfish

poisoning, is a glutamate analog that causes excitotoxicity. Botulinum toxin leads to paralysis via blockade of presynaptic release of acetylcholine.

How are the fish-borne neurotoxic syndromes distinguished?

Since the patients became ill despite steam cooking of the food, they likely ingested a heat-stable toxin. Ciguatera toxin and tetrodotoxin are both heat stable, and the fish from which the toxin derives is usually normal in appearance, odor, and taste.

Ciguatoxin is actually a family of related toxins that are produced by dinoflagellates, specifically *Gambierdiscus toxicus*, that live within the reef in tropical areas such as the Caribbean Sea and the South Pacific and Indian oceans. The distribution of *G toxicus* is often described to be between the 35°N (border between North Carolina and Georgia) and 35°S (just south of the tip of Africa) latitudes. Ciguatoxin is lipid soluble, odorless, and tasteless. It is most concentrated in the viscera, flesh, and adipose tissue of the fish.[2] The toxin bioaccumulates in many species of large reef fish, such as barracuda, amberjack, and grouper. The majority of the cases in the United States can be traced to fish caught in the waters around Florida.

Tetrodotoxin is produced by marine bacteria (particularly *Vibrio* species) and bioaccumulates in fish from the order Tetraodontiformes, which are found worldwide. In the United States, California and Florida are common origins of implicated fish, though cases have occurred elsewhere, including New Jersey. Most commonly associated with puffer fish, this toxin is also present in various unrelated species such as the blue-ringed octopus and newts of the genus *Taricha* found in the Pacific Northwest. The toxin concentrates in the fish skin, ovaries, and liver, although smaller amounts may be found in muscle. Puffer fish sashimi, known as *fugu*, is occasionally associated with morbidity in Japan. In fact, the emperor of Japan has been forbidden to eat this delicacy. This form of sushi is legal in the United States but requires special testing and preparation.

Tetrodotoxin-induced effects typically begin within minutes of ingestion and may evolve rapidly. Ciguatoxin-induced symptoms commonly appear between 2 and 6 hours following ingestion.

Case Continuation

The case patients state that they ate meat from a large barracuda that was caught off the coast of Florida and

Table. Syndromes Associated With Consumption of Fish and Shellfish

Toxin (syndrome)	Toxin source	Mechanism	Onset
Fish consumption syndromes			
Ciguatoxin (ciguatera fish poisoning)	*Gambierdiscus toxicus* (dinoflagellate found in predatory reef fish [eg, barracuda, grouper])[a]	Increases sodium channel permeability	2 to 30 h
Tetrodotoxin	*Vibrio* spp bacteria found in fish of the order Tetraodontiformes (eg, puffer fish)	Decreases sodium channel permeability	Minutes to hours
Shellfish consumption syndromes			
Brevetoxin (neurotoxic shellfish poisoning)	*Karenia brevis*[b] (a dinoflagellate found in mussels, clams, scallops, oysters)	Increases sodium channel permeability	15 min to 18 h
Saxitoxin (paralytic shellfish poisoning)	*Alexandrium catenella*, *Alexandrium tamarense* (dinoflagellates found in mussels, clams, scallops, oysters)	Decreases sodium channel permeability	30 min

[a]*G toxicus* bioaccumulates upward in the food chain, ultimately affecting large reef fish.
[b]Formerly known as *Ptychodiscus brevis*.
Adapted from Tunik.[1]

then transported to New York. This additional history points to ciguatoxin as the most likely etiology of their signs and symptoms.

What are the clinical signs of ciguatera toxicity?

Gastrointestinal findings predominate early and include diarrhea, abdominal pain, nausea, and vomiting.[2] The classic neurologic finding is dysesthesia, or uncomfortable tingling, typically in the extremities. Affected persons may report the reversal of hot and cold discrimination. In addition, they may describe the sensation of loose or painful teeth. Other possible neurologic symptoms include paresthesias, itching, vertigo, headache, and metallic taste. Myalgias, especially in the lower extremities, arthralgias, ataxia, and visual disturbances have also been described.[2]

Common cardiovascular manifestations include bradycardia and orthostatic hypotension.[3] Although the mechanism of these cardiovascular disturbances has not been fully elucidated, proposed explanations include inhibitory effect of the ciguatoxin on the outflow of norepinephrine from the autonomic ganglia and direct effects on the cardiac conduction.

Although gastrointestinal effects commonly resolve within 24 to 48 hours, the cardiovascular manifestations may persist for days, and the neurologic issues for years.

How should ciguatera poisoning be managed?

The diagnosis can be confirmed by laboratory analysis of an affected patient's serum using either an enzymatic assay or HPLC (high-performance liquid chromatography). The remaining uneaten fish may be analyzed as well in special laboratories.

The management of acute ciguatera toxicity is largely supportive. IV isotonic saline should be administered to patients with volume loss from emesis or diarrhea.

Symptomatic bradycardia may be managed with atropine. Hypotension is primarily orthostatic and responsive to saline, but an α_1-adrenergic agonist, such as phenylephrine, may be required.

Mannitol is commonly cited as a means to alleviate the dysesthesias, although the evidence supporting this therapy is largely anecdotal. One randomized trial failed to show a benefit.[4] Its use is based on the finding that ciguatoxin leads to increased swelling around the nodes of Ranvier, or unmyelinated portions, of frog axon.[5] By reducing axonal swelling, mannitol improves the rate of saltatory conduction. Mannitol should be administered only to patients who have had adequate volume resuscitation, since it may induce osmotic diuresis. Anecdotal experience suggests 1 g/kg IV as an effective dose.

Chronic paresthesias or neuropathic pain following ciguatera poisoning may be managed with cyclic antidepressants or anticonvulsants such as gabapentin. It is unclear why agents of either class are effective, although it may be due to their ability to block neuronal sodium channels.

Ciguatera poisoning cases should be reported to the local poison control center and the health department to allow for a public health investigation of the place of purchase. Reported cases are often collated and collectively may highlight a public health concern.

Case Conclusion

Both patients were admitted to the ICU, primarily due to the abnormalities in their vital signs. They received adequate volume expansion with normal saline. Bradycardia was managed with IV atropine at weight-appropriate doses. The mother, who continued to experience perioral paresthesias, received 1 g/kg of IV mannitol, with improvement. She remained in the ICU for 6 days; the daughter had a 5-day stay in the ICU, mostly due to continued asymptomatic bradycardia.

The case was reported to the local department of health. A representative interviewed the family, obtained a sample of the fish for testing, and investigated at the place of fish purchase. **EM**

References

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