CASE REPORT

THE PATIENT
61-year-old woman

SIGNS & SYMPTOMS
– Nausea
– Paresthesia
– Cold allodynia

Michael E. Mullins, MD; David B. Liss, MD; Evan S. Schwarz, MD; Anna Arroyo-Plasencia, MD
Division of Medical Toxicology, Department of Emergency Medicine, Washington University School of Medicine, St. Louis, MO (Drs. Mullins, Liss, Schwarz, and Arroyo-Plasencia); Department of Psychiatry, University of Michigan School of Medicine, Ann Arbor (Dr. Arroyo-Plasencia)

mullinsm@wustl.edu

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THE CASE
An active 61-year-old woman (140 lbs) in good health became ill during a sailing holiday in the Virgin Islands. During the trip, she ate various fish in local restaurants; after one lunch, she developed nausea, diarrhea, dizziness, headache, and light-headedness. In the following days, she suffered "intense itching" in the ears, dizziness, malaise, a "fluttering feeling" throughout her body, genitourinary sensitivity, and a "rhythmic buzzing sensation near the rectum."

She said that cold objects and beverages felt uncomfortably hot (cold allodynia). She noted heightened senses of smell and taste, as well as paresthesia down her spine, and described feeling "moody." She reduced her workload, took many days off from work, and ceased consuming meat and alcohol because these items seemed to aggravate her symptoms.

The paresthesia persisted, and she consulted her family physician one month later. Laboratory tests—including a complete blood count, hematocrit, thyroid-stimulating hormone, antinuclear antibodies, and titers for *Ehrlichia chaffeensis*, Lyme disease, and *Anaplasma phagocytophila*—all yielded normal results. Her symptoms continued for 3 more months before referral to Medical Toxicology.

THE DIAGNOSIS
The patient's symptoms and history were consistent with ciguatera poisoning. Features supporting this diagnosis included an acute gastrointestinal illness after eating fish caught in tropical waters and subsequent persistent paresthesia, including cold allodynia.[1] Laboratory testing excluded acute infection, anemia, thyroid dysfunction, vitamin B12 deficiency, lupus, rheumatoid arthritis, Lyme disease, ehrlichiosis, and anaplasmosis.

DISCUSSION
Ciguatera results from ciguatoxin, a class of heat-stable polycyclic toxins produced in warm tropical waters by microscopic dinoflagellates (most often *Gambierdiscus toxicus*).[2,3] Small variations exist in the Caribbean, Pacific, and Indian Ocean forms. Ciguatoxin bio-accumulates in the food chain, and humans most often ingest it by eating larger fish (typically barracuda, snapper, grouper, or amberjack).[4] Because ciguatoxin confers no characteristic taste or smell to the fish, people who prepare or eat contaminated seafood have no reliable means to detect and avoid it.

Ciguatoxin opens neuronal voltage-gated sodium channels and blocks delayed-rectifier potassium channels.[5] These cause repetitive, spontaneous action potentials that explain the paresthesia. Sodium influx triggers an increase in intracellular calcium concentrations. Increased intracellular sodium and calcium concentrations draw water into the intracellular space and cause neuronal edema.

Death is rarely associated with ciguatera (< 0.1% in the largest observational study).[1] Even without treatment (discussed shortly), symptoms of ciguatera will gradually resolve over several weeks to several months in most cases.[1,4,5] However, after recovery, patients often briefly experience milder symptoms after consuming fish, alcohol, or nuts.[6]

Treatment of ciguatera may include intravenous (IV) mannitol infusion. Other treatments, such as amitriptyline, gabapentin, pregabalin, and tocainide, have been used, but there is limited supporting evidence and they appear variably effective.[7]

Mannitol reverses the effects of ciguatoxin, with suppression of spontaneous action potentials and reversal of neuronal edema.[8,9] It is reasonable to offer mannitol for acute or persistent symptoms of ciguatera fish poisoning even after a delay of several weeks.

A recent systematic review found that mannitol has the largest body of evidence supporting its use, although that evidence is generally of low quality (case reports and large case series).[7] While these reports[10-13] describe beneficial effects of mannitol, a single randomized trial suggested that mannitol is no more effective than normal saline.[14] However, this study was underpowered and had inadequate treatment concealment; twice as many saline control patients as mannitol-treated patients requested a rescue dose of mannitol.[14]

Mannitol may be most effective when given early in the course of ciguatera but has shown some success when given later.[5,12,13] In 1 large case series, the longest interval from symptom onset to successful treatment was 70 days, although most patients with satisfactory results received mannitol in the first few days.[5]

Our patient was administered an IV infusion of 100 g of 20% mannitol over 1 hour. She received the infusion 140 days after the onset of her symptoms and experienced rapid symptom relief.

At a follow-up visit 2 weeks later, she described increased energy and further improvement in her paresthesia. She returned to a full work schedule and resumed all of her daily activities. However, she continued to avoid alcohol and proteins, as she had experienced a mild recurrence that she temporally related to eating meat and drinking alcohol.

At the 2-month follow-up, the patient reported continued improvement in her paresthesia but continued to experience occasional gastrointestinal symptoms and fatigue associated with meat and alcohol consumption.

THE TAKEAWAY

Ciguatera fish poisoning is largely a clinical diagnosis. It is based on early gastrointestinal symptoms followed by persistent paresthesia and cold allodynia after consumption of fish caught in tropical waters. Family physicians may see ciguatera in returning travelers or people who have consumed certain fish imported from endemic areas. Untreated symptoms may last for many weeks or months. IV mannitol may relieve symptoms of ciguatera poisoning even when administered several months after symptom onset. JFP

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We are grateful to our patient, who allowed us to share her story in the hope of helping other travelers.

CORRESPONDENCE
Michael E. Mullins, MD, Division of Medical Toxicology, Department of Emergency Medicine, Washington University School of Medicine, Campus Box 8072, 660 South Euclid Avenue, Saint Louis, MO 63110; mullinsm@wustl.edu

Ciguatoxin confers no characteristic taste or smell to the fish. Thus, people who prepare or eat contaminated seafood have no reliable means to detect and avoid it.

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PHOTO ROUNDS

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removing the larvae or forcing them out of the lesion. Wounds can be covered with a substance, such as petrolatum, nail polish, beeswax, paraffin, or mineral oil, to block respiration.[3] Occlusion may be needed for 24 hours to create adequate localized hypoxia to force the larvae to migrate from the wound and allow for easier manual extraction. Surgical removal of the larvae is also effective. A cruciate incision can be made adjacent to the central pore to avoid damaging the organism.[3] A topical, broad-based antiparasitic, such as a 10% ivermectin solution, has also been successfully used to treat furuncular myiasis. This approach works by either inducing larval migration outward or simply killing the larvae.[3]

Our patient recovered well after we performed a punch biopsy to make a larger wound opening and remove the intact larvae. JFP

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