

Haff Disease: Rhabdomyolysis After Eating Buffalo Fish

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Haff disease, rhabdomyolysis after ingesting certain types of fish, was first reported in 1924 in Europe. There have been a limited number of cases reported in the United States. We present the case of a patient who presents with symptoms of rhabdomyolysis after eating cooked buffalo fish purchased at a suburban grocery market. [West J Emerg Med. 2014;15(6):664-666]

INTRODUCTION

Fish consumption is considered part of a healthy diet. Fish is lower in total calories, saturated fat and total fat than a comparable amount of red meat. However, like all food products, there are potential illnesses associated with the consumption of fish. Common illnesses known to be associated with fish consumption in the United States include Scombroid and Ciguatera poisoning and are well known to emergency medicine (EM) physicians, but Haff disease is unfamiliar to most. A rare consideration, it is important to recognize the symptoms that occur with Haff disease because the treatment of the rhabdomyolysis requires specific interventions, primarily larger amounts of intravenous fluid than those used to replace the fluid loss from the vomiting and diarrhea associated with more common fish poisonings.

Chest pain accompanying the presentation of Haff disease may be confused with aortic dissection or cardiac ischemia. This may result in extensive, invasive and expensive testing for conditions that the patient does not have. We present the case of a patient who developed rhabdomyolysis after ingestion of cooked buffalo fish. The patient's initial presentation included back and chest pain prompting concern for a possible aortic dissection. Despite the sporadic nature of the presentation of this etiology for rhabdomyolysis, Haff disease must be considered in the differential diagnosis so that appropriate treatment can be initiated.

CASE REPORT

An otherwise healthy 34-year-old white female presented to the emergency department (ED) with one-hour history of back pain. The pain began gradually in the center of her thoracic spine at the level of T7-T8 and progressively became

worse. She described the pain as a severe dull pain, constant, radiating through to the chest, up the back into the neck and down the back into both buttocks. She attempted to relieve the pain by soaking in warm water; when that was unsuccessful her family member brought her to the ED. She denied history of back pain, trauma, fever, abdominal pain, paresis, paralysis, urinary retention, or paresthesias.

On initial examination, the patient was uncomfortable and moaning. Vital signs were blood pressure 155/90 mm Hg, pulse rate 82 beats/min, respiratory rate 20 breaths/min, and temperature 36.2 degrees C (97.1 F). She was mildly tender over the mid thoracic spine. Heart sounds were regular, pulses were equal in both extremities and bilaterally in the groin, and no other abnormalities of the physical exam were found.

Electrocardiogram performed upon arrival was interpreted as normal sinus bradycardia, rate of 58 bpm, with nonspecific ST segment and T-wave changes. Laboratory evaluation revealed hemoglobin 13.6 g/dL (12.0 to 15.3 g/dL), WBC $11.0 \times 10^3/\mu\text{L}$ (4.0 to 11.0), platelet count $286 \times 10^3/\mu\text{L}$ (150 to $450 \times 10^3/\mu\text{L}$), sodium 141 mmol/L (135-145 mmol/L), potassium 3.3 mmol/L (3.5-5.1 mmol/L), chloride 106 mmol/L (98 - 109 mmol/L), bicarbonate 29 mmol/L (23 to 31 mmol/L), blood urea nitrogen 13 mg/dL (6 to 26 mg/dL), creatinine 0.83 mg/dL (0.5 to 1.20 mg/dL), and glucose 120 mg/dL (70 - 99 mg/dL). Troponin level was <0.01 ng/mL (<0.01 ng/mL = Expected range for 99% population), myoglobin was 7534 ng/mL (28 - 72 mg/mL) and creatine kinase 2336 IU/L (24 -170 IU/L). Urinalysis revealed large blood by dipstick with 31 to 50 RBCs (patient was menstruating), negative results for nitrite and leukocyte esterase. Urine toxicology was negative for illicit drugs, and

Table. Symptoms of Haff Disease cases, United States, 1997, 2001, 2013, 2014.

Symptom (n=20)	Number of reports
Myalgia	10
Muscles stiffness	5
Pain to light touch	6
Dry mouth	3
Painful breathing	2
Shortness of breath	9
Chest pain	14
Profuse sweating	8
Nausea or vomiting	13
Numbness of thighs	1
Numbness of whole body	1
Brown urine/hematuria	3
Back pain	4
Stomach cramps	1
Diarrhea	1

the urine pregnancy test was negative. Chest radiograph was negative for any lung pathology, mediastinum was normal width and no pathology was seen on the thoracic vertebrae. Computed tomography angiogram of the chest was normal; no aortic dissection was found.

An intravenous catheter was inserted when blood was drawn for laboratory evaluation. Hydromorphone 0.5 mg and diazepam 2.5 mg was intravenously given for pain relief and normal saline was begun at 150 ml/hour. Approximately one hour after arrival the patient complained of aching all over and then began to vomit, undigested food with no blood. She mentioned to the staff that a friend with whom she had had dinner had called her and told her that she was also ill. The patient explained that they had eaten fish that her friend had purchased at a local market and cooked for dinner. It was buffalo fish (*Ictiobus*).

After reviewing the laboratory values, the rate of intravenous normal saline was increased to 300 ml/hour. The patient was further questioned for an etiology of the rhabdomyolysis and an ingestion of a toxin was considered. An Internet search was performed looking at buffalo fish and rhabdomyolysis, and information on Haff disease was identified. The Illinois Poison Control Center was notified. The Illinois Poison Control Center subsequently contacted the Cook County Board of Health and all buffalo fish were removed from the local market.

The patient was admitted to the hospital for continued hydration. On day two the creatine kinase peaked at 30,549 IU/L, approximately 19 hours after arrival. Blood urea nitrogen and creatinine remained normal. Creatine kinase levels began to decline, and the patient was discharged on day three.

DISCUSSION

Back pain is a common complaint of patients who present to the ED, and the most common etiology is musculoskeletal. The differential for back pain is extensive and etiologies range from benign to life-threatening. Our patient had several “red flags” in her history; sudden onset, associated symptoms of nausea and vomiting, and radiation to the chest. Rarely do musculoskeletal causes of back pain occur with a pinpoint time of onset without a precipitating event. Radiation to the chest is concerning for an aortic dissection even without other physical findings. The accompanying nausea and vomiting were considered as possible symptoms of either a cardiac or gastrointestinal etiology.

Rhabdomyolysis is caused by the breakdown of skeletal muscle with the subsequent release of cell contents into the blood. Myoglobin, a muscle cell protein, circulates to the kidneys where it is filtered. Myoglobin can precipitate in the renal tubules, causing obstruction and acute renal failure. The symptoms of rhabdomyolysis are nonspecific; muscle weakness, pain, and light to dark brown urine. The etiology of rhabdomyolysis is also diverse: congenital metabolic myopathies, prolonged immobilization, trauma, exertion, high-voltage electrical injury or lightning injury, heat and cold injury, drugs and toxins, infections, electrolyte abnormalities, connective tissue disorders, rheumatologic disorders, endocrine disease, tissue hypoxia and ischemia as well as various miscellaneous causes.¹

An outbreak of an unknown illness was first reported in 1924, in which the victims had unexplained severe muscular rigidity. It was named Haff disease because the cluster of victims occurred near the shores of Königsberg Haff (Haff means shallow lagoon) in East Prussia.²⁻⁴ Recent ingestion of fish was identified as a common characteristic in all individuals that had become ill, although the species of fish differed - burbot, eel, and pike. Outbreaks resembling Haff disease have been reported in Sweden, Russia, China, and Brazil.^{2,6,7} Haff disease was first reported in the U.S. in Texas in 1984 with only 23 cases reported in the U.S. between 1984 and 2001.^{3,5} All victims had eaten buffalo fish except for two who had ingested salmon in North Carolina and nine who had ingested crayfish in Louisiana. Two more cases were reported in New York in 2013 in which there was one death reported.⁸ Again, buffalo fish was implicated as the source of the illness of the New York patients.

Haff disease is defined as illness in a person with unexplained rhabdomyolysis who has eaten fish within 24 hours before symptom onset.³ Complaints of muscular pain and stiffness are the major symptoms of the clinical presentation. Approximately 50% of patients complain of chest pain.⁵ Other predominant symptoms are nausea or vomiting, shortness of breath, profuse sweating, and pain to light touch. Dry mouth, dyspnea, numbness of thighs or whole body, brown urine, back pain, and stomach cramps are seen less frequently.

Levels of creatine kinase (CK) and myoglobin are elevated. The median time to onset is approximately eight hours. CK levels reaching five times normal are considered diagnostic for rhabdomyolysis. Myoglobinuria is typically present. Acute renal failure and disseminated intravascular coagulation are known complications of the disease, but the mortality rate is approximately 1%. The fatal New York patient's case was complicated by hypertension and intracerebral hemorrhage.⁸

It is believed that a toxin contained in the fish, although one has not been isolated at this time, causes Haff disease. It is theorized that the toxin is similar to palytoxin. Palytoxin is a potent vasoconstrictor, which has been found in several marine species such as sea anemones and soft coral. It is known to cause rhabdomyolysis, as well as excessive sweating, abdominal pain, nausea, diarrhea, cardiac arrhythmias, renal failure, paresthesias, dyesthesias, muscle tremors, and spasms.⁵ However palytoxin is found in marine fish, not freshwater fish. Haff disease has only been reported in the U.S. in patients who have ingested freshwater fish or shellfish. An infectious etiology is considered less likely because all fish involved in the reported cases were cooked. That also suggests that the toxin is heat stable and cooking does not eliminate it. Patients with Haff disease have demonstrated moderate leukocytosis, although they remain afebrile.¹

The treatment for rhabdomyolysis caused by Haff disease is supportive. The patient should remain adequately hydrated to prevent acute renal failure. Intravenous rates of normal saline should be approximately 200 – 300 ml/hour with further increases of rate depending on urine output and clinical condition. Hyperkalemia, hypo or hypercalcemia, hyperphosphatemia, and hyperuricemia are known complications of rhabdomyolysis. Serum electrolytes and renal function should be measured serially and treatment should proceed accordingly. Urine alkalization is recommended as treatment for rhabdomyolysis, although definite conclusion of its benefit has not been proven. Mannitol has sometimes been employed but also remains controversial at this time.² The Illinois Poison Control Center did not recommend the administration of bicarbonate for urinary alkalization in our patient; her creatinine remained normal throughout her hospitalization with adequate hydration.

With the use of the Internet, the diagnosis of Haff disease was determined to be the most likely etiology of our patient's rhabdomyolysis. Haff disease should be added to the differential of rhabdomyolysis, although the exact toxin causing rhabdomyolysis is not known at this time. Cases of Haff Disease should be reported to the local poison control center or board of health so that the suspected source, freshwater fish, can be removed and tested, thus preventing further cases.

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