



Clinical Communications: Adult

ELEVATED LIVER ENZYMES AS A MANIFESTATION OF HAFF DISEASE

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Abstract—Background: Haff disease is a rare syndrome of rhabdomyolysis thought to be caused by a heat-stable toxin associated with the consumption of seafood from fresh or brackish water. **Case Report:** We present the case of a patient with Haff disease who presented to the emergency department with nausea/vomiting, diarrhea, and myalgias after a seafood buffet. Initially, he was treated with i.v. fluids and antiemetics for presumed gastroenteritis, but his symptoms did not improve. He was found to have elevated aspartate aminotransferase and alanine aminotransferase, normal point-of-care ultrasound, urinalysis with large blood and no red blood cells, and an elevated creatine phosphokinase (CPK). He was admitted to the hospital to receive ongoing fluid resuscitation for rhabdomyolysis presumed to be from fish. Liver enzymes and CPK downtrended, and patient was discharged on hospital day 3. **Why Should an Emergency Physician Be Aware of This?:** Undiagnosed Haff disease has important clinical implications, including multi-organ failure and death. Always maintain a high level of suspicion for Haff disease in patients with symptoms suggestive of gastroenteritis, but complicated by minor liver function test elevations and dipstick positivity for heme, without significant numbers of red blood cells per high-power field, in the setting of recent seafood ingestion. © 2019 Elsevier Inc. All rights reserved.

Keywords—Haff disease; rhabdomyolysis; LFT; AST; ALT; liver enzymes; gastroenteritis; myalgias; seafood; buffalo fish; CK; CPK; urinalysis

INTRODUCTION

Haff disease is a rare syndrome of rhabdomyolysis thought to be caused by a heat-stable toxin associated

with the consumption of seafood from fresh or brackish water. We report a case of Haff disease, presenting with signs and symptoms typical of gastroenteritis, where minor elevations of liver function tests (LFTs), plus the presence of urine that was “dipstick-positive” for heme, without significant hematuria, led us to the correct diagnosis.

CASE REPORTS

A 29-year-old black male presented to the emergency department with nausea and vomiting, diarrhea, and myalgias, after a seafood buffet. Vital signs 179/110 mm Hg, pulse rate 131 beats/min, respiratory rate 18 breaths/min, and temperature 100.5°F. Physical examination revealed a non-toxic-appearing, dehydrated male with 5/5 strength in bilateral upper and lower extremities, normal gait, and otherwise unremarkable physical examination.

Initially, he was treated for presumed gastroenteritis with i.v. fluids (1 L normal saline) over 1 h and a “GI cocktail” consisting of 4 mg i.v. piggyback [IVPB] Zofran, 20 mg IVPB Pepcid, and 30 mL Maalox by mouth. After 2 h of observation, his symptoms did not abate and laboratory tests were ordered.

Laboratory evaluation revealed hemoglobin 14.4 g/dL (normal range 14–18 g/dL), WBC $22.0 \times 10^3/\mu\text{L}$ (normal range $4.5\text{--}10.9 \times 10^3/\mu\text{L}$), platelet count $219 \times 10^3/\mu\text{L}$ (normal range $130\text{--}400 \times 10^3/\mu\text{L}$), sodium 126 mmol/L (normal range 136–146 mmol/L), potassium 3.4 mmol/L (normal



Figure 1. Buffalo fish.

range 3.5–5.0 mmol/L), chloride 82 mmol/L (normal range 98–106 mmol/L), bicarbonate 21 mmol/L (normal range 24–31 mmol/L), blood urea nitrogen 15 mg/dL (normal range 6–20 mg/dL), creatinine 1.71 mg/dL (normal range 0.70–1.20 mg/dL), and glucose 121 mg/dL (normal range 70–99 mg/dL). LFTs included aspartate aminotransferase (AST) 174 U/L (normal range 10–50 U/L), alanine aminotransferase (ALT) 63 U/L (normal range 0–41 U/L) with total bilirubin 0.50 mg/dL (normal range 0.0–1.2 mg/dL), and alkaline phosphatase 78 U/L (normal range 35–145 U/L). Point-of-care ultrasound in the emergency department (ED) revealed normal gallbladder wall thickness, without pericholecystic fluid, gallbladder sludge, or stones. Urinalysis (UA) revealed large blood by dipstick with 0–5 red blood cells (RBCs), small ketones, and negative results for nitrite, leukocyte esterase, and bacteria.

The urinalysis results and elevated LFTs expanded the differential to include rhabdomyolysis. The creatine phosphokinase (CPK) level was therefore ordered, and was revealed to be 7518 IU/L (normal range 24–170 IU/L). The patient was admitted to the hospital for ongoing i.v. fluid hydration with the diagnosis of rhabdomyolysis presumed to be from fish, that is, Haff disease.

Hospital Course

The patient was resuscitated with a total of 4 L i.v. normal saline. On day 2, his CPK downtrended along with LFTs. The patient was discharged on hospital day 3 with resolution of myalgias and tolerating a normal diet.

DISCUSSION

We present this case to show that even minor elevations in LFTs, usually overlooked in the ED and often attributed to medications or minor genetic variations, may lead to expanded differentials. Our patient's elevated LFTs were the first diagnostic clue that led us to consider other etiologies beyond gastroenteritis, such as hepatitis (ie, alcoholic, autoimmune, viral, toxic), extrahepatic liver

disease, such as celiac, thyroid, hemochromatosis, Wilson's disease, metastatic disease, and sepsis, as well as extrahepatic extra-liver diseases, such as rhabdomyolysis, polymyositis, and dermatomyositis.

In our patient, his elevated LFTs, a normal point-of-care sonogram, and a UA with large blood on dipstick but no RBCs, made us suspect rhabdomyolysis, later confirmed by an elevated CPK. The diagnosis of Haff disease was inferred by his recent seafood ingestion.

Haff disease is the development of rhabdomyolysis within 24 h of ingesting fish. The name is derived from the German word *Konigsberg Haff*, with *Haff* meaning shallow lagoon (1). Our patient presented with similar complaints to other Haff patients in the review of 1000 cases of Haff disease by Diaz in 2015 (2). The most common symptoms identified were chest pain, nausea or vomiting, myalgias, shortness of breath, profuse sweating, pain to light touch, muscle stiffness, and back pain (2–4).

In the United States, the most common implicated fish are buffalo fish (Figure 1), grass carp, salmon, crayfish, burbot, eel, and pike (5–7). All cases involved cooked fish, consistent with a heat-stable toxin, which has yet to be identified.

Presentation occurs acutely, within 24 h of ingestion, with symptom onset over approximately 30 min. Typically, elevated ASTs/ALTs and CPKs consistent with rhabdomyolysis are found on day 1. On days 2 to 3, CPK and LFTs may increase then rapidly return to normal levels on day 4 or 5.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

Undiagnosed Haff disease has important clinical implications, including multi-organ failure and death (3). Most causes of death from Haff disease have been a result of misdiagnosis and treatment delay. Expeditious i.v. fluid and urine alkalization with bicarbonate is the key to preventing myoglobinuric renal failure (6).

Rhabdomyolysis from Haff disease is a common presentation of a rare disease. Always maintain a high level of suspicion for Haff disease in patients with gastroenteritis with minor LFT elevations after recent seafood ingestion.

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