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Haff disease associated with the ingestion of the freshwater fish *Mylossoma duriventre* (*pacu-manteiga*)

Doença de Haff associada ao consumo de carne de Mylossoma duriventre (pacu-manteiga)

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ABSTRACT

Haff disease associated rhabdomyolysis is correlated with the ingestion of certain freshwater fish and shellfish and is caused by an unidentified toxin. We report the case of a patient who experienced rhabdomyolysis approximately 2 hours after ingestion of the freshwater fish *Mylossoma duriventre* (*pacu-manteiga*) approximately 3 years after an outbreak had been reported in Manaus, Brazilian Amazon.

Keywords: Rhabdomyolysis/diagnosis; Foodborne diseases; Fishes; Diagnosis, differential; Case reports

INTRODUCTION

In the summer of 1924, physicians near the Königsberg Haff shores along the Baltic coast first recognized an outbreak of an illness characterized by sudden, severe muscular stiffness that was often accompanied by dark-colored urine.[1] No neurologic abnormalities, fever, splenomegaly, or hepatomegaly were observed.[1] The clinical spectrum of the disease varied, while most patients recovered quickly, a few patients died.

In the following 9 years, similar outbreaks affecting an estimated 1,000 individuals occurred seasonally in the summer and fall along the coast of the Königsberg lagoon. The ingestion of fish, usually cooked, was common among those who became ill, and the species of fish associated with the sickness included burbot (*Lota lota*), eel (*Anguilla anguilla*), and pike (*Esox* sp.). There were also reports of seabirds and cats dying after eating fish in the wild.

Due to the absence of fever and because of the fairly rapid onset of symptoms after eating cooked fish, a toxin is believed to be the cause of Haff disease.[2] Several toxic etiologies have been proposed for the disease,[3] but none have been confirmed. They include arsenic poisoning,[3] which is still cited in modern medical dictionaries as the cause of Haff disease. The toxin does not have an unusual smell or taste, and it might be thermostable because it is not destroyed upon cooking.[4]

From 1934 to 1984, other outbreaks similar to Haff disease were described in Sweden[5] and the former Soviet Union.[6,7] The first two cases reported in the United States occurred in Texas in June 1984. From 1984 to 1996, only four other cases were reported in the United States, two in Los Angeles and two in San Francisco (both cities in California). In 1997 five cases of Haff disease were

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reported in the United States (in California and Missouri) during a 5-month period (March to August), all of the cases were associated with the ingestion of buffalo fish (*Ictiobus* sp.).[8] In 2001, more cases were reported in the United States that involved the ingestion of freshwater crayfish (*Cambaridae* family)[9] in Missouri and salmon in North Carolina.[2] In September 2010, some cases of Haff disease that were associated with the consumption of freshwater crayfish (*Parastacidae* family) were reported in China.[10]

In October 2008, an outbreak of 27 cases of Haff disease that were associated with the consumption of *Mylossoma duriventre* (*pacu-manteiga*), *Colossoma macropomum* (*tambaqui*) and *Piaractus brachypomus* (*pirapitinga*) fish from the Brazilian north Amazon region was reported.[11] Haff disease is considered an emerging disease, whose importance will increase as population growth leads to increasing consumption of freshwater fish, particularly in the Brazilian Amazon region.

CASE REPORT

A 48-year-old male patient who was taking finasteride for androgenic alopecia presented to the emergency room. He was returning from a 15-day trip to the city of *Belém* (PA) in the Northern region of Brazil. He reported that approximately 2 hours after ingesting a meal containing the fish *Mylossoma duriventre*, he experienced sudden, progressive, diffuse and lancing abdominal pain, accompanied by two episodes of vomiting, progressive polymyalgia (predominantly in the lower limbs), asthenia and progressively disabling muscular weakness. The patient was completely lucid; he reported drinking a small amount of coffee a few seconds before the onset of symptoms, he denied experiencing fever, diarrhea, ingestion of alcohol or other medications and/or use of illicit drugs.

His vital signs were within the normal range, except for his heart rate, which was elevated (at approximately 120 bpm). On physical examination, there was diffuse abdominal pain on palpation, and none of the following symptoms: pain localization, guarding, visceromegaly, palpable masses or peritoneal irritation signs.

The patient received intravenous analgesics and antispasmodic drugs, while diagnostic investigation was started. His initial laboratory tests revealed leukocytosis with neutrophilia and no elevation of C-reactive protein. Abdominal computed tomography showed no significant abnormality. His abdominal pain was refractory to intravenous analgesia, including opioids, a fact that stood out to the physicians on duty.

Due to persistence of the patient's symptoms and the reported cases of Hoff disease after ingestion of the fish *Mylossoma duriventre* in the Brazilian Northern region, his total CPK and myoglobin were measured. They were both extremely elevated (total CPK: 4,456U/L and myoglobin 37,868.5ng/mL). A diagnosis of rhabdomyolysis was made as the ratio of total CPK/CPK-MB was greater than 5 (Table 1). The patient was hospitalized, intravenous hydration was initiated, and the analgesic treatment was intensified.

Table 1 - Results of the ancillary tests on hospital admission

Tests	Results
Abdominal and pelvic CT	Within the normal range
Chest X-ray	Within the normal range
Electrocardiogram	Sinus rhythm + incomplete left bundle-branch block
Hemoglobin (/mm^3)	14.6 milion
Hematocrit (%)	41.6
Leukocytes (/mm^3)	12.6 thousand
Eosinophils (%)	1
Band neutrophils (%)	7
Segmented neutrophils (%)	73
Lymphocytes (%)	16
Platelets (/mm^3)	218.000
Glucose (mg/dL)	133
C-reactive protein (mg/dL)	0.15
Urea (mg/dL)	43
Creatine (mg/dL)	0.9
Sodium (mEq/l)	138
Potassium (mEq/l)	3.5
Total CPK (U/L)	4.456
Myoglobin (ng/mL)	37,868.5
Troponin (ng/mL)	0.01

CT - computed tomography; CPK - creatine phosphokinase.

After his admission to the intensive care unit (ICU), intravenous bicarbonate was administered to promote urine alkalization and renal protection. The patient's myoglobin (acute phase muscle injury marker) level reduced gradually, there was a sudden and transient elevation in the total CPK level followed by a gradual decrease in the level, as expected in cases of rhabdomyolysis with a benign course (Table 2).

The patient maintained good hourly diuresis and his nitrogen waste was within the normal range. He was discharged from the ICU on the 5th day after admission, at which time he did not require further urine alkalization

Table 2 - Muscle injury markers and major laboratory parameters during hospitalization

Tests	Results						
	Admission	Day 1 ICU	Day 2 ICU	Day 3 ICU	Day 4 ICU	Day 5 ICU	Day 8 at hospital
Total leukocytes (/mm^3)	12.600	19.900	18.300		10.300	8.900	6.600
Band neutrophils (%)	7	9	8		6	3	3
Total CPK (U/L)	4.456	61.730	47.764	16.170	7.127		319
CPK MB (U/L)		2.921					
Troponin (ng/mL)	0.01	0.01					
Myoglobin (ng/mL)	37.868.5	32.663	1.241	137.9	94.3		44
Lactic acid (mg/dL)		22.0	19		18	17	
C-reactive protein (mg/dL)	0.15	0.29					
Urea (mg/dL)	43	44	21	16	14	16	22
Creatinine (mg/dL)	0.9	0.8	0.6	0.7	0.7	0.6	0.7
pH		7.381	7.559	7.419	7.45	7.42	
Sodium (mEq/l)	138	139	145	142	143	142	140
Potassium (mEq/l)	3.5	3.7	3.9	3.7	3.8	4.2	4.2
Ionic calcium (mg/dl)	4.0		3.9		4.4	4.6	

ICU - intensive care unit; CPK - creatine phosphokinase.

and the muscle injury markers continued to decrease. No fluid and electrolyte imbalance was observed during this period.

The patient was discharged from the hospital on the 8th day after admission. He was asymptomatic, and his muscle injury markers were within the normal range.

DISCUSSION

Haff disease is an emerging disease that was first described less than one century ago. It is characterized by symptoms of rhabdomyolysis associated with ingestion of fresh water fish.[1] A toxin is believed to be inducing the rhabdomyolysis and causing this disease,[2] but no toxin has been identified.

Some fresh water fish species,[1-8,11] and even crawfish species,[9,10] seem to be implicated in the development of Haff disease, and the disease seems to occur in outbreaks.

The first report of an outbreak of Haff disease in Brazil was in 2009, and one of the species associated with this 2008 outbreak was *Mylossoma duriventre*.[11] Further studies are necessary to identify the toxin involved and what induces its expression because the species of fresh water fish and crawfish in all the reports are eaten daily by many people in all the countries where outbreaks were described, without developing the disease.

In the case report, we describe an unusual presentation of Haff disease, the patient who presented to the emergency room with an acute abdomen, suggesting that rhabdomyolysis should be considered a differential diagnosis for the acute abdomen when an epidemiologic history and other potential explanations for the abdominal pain have been excluded.

The diagnosis of Haff disease is based on clinical suspicion, epidemiologic history (ingestion of freshwater fish in the 24 hours preceding the event), and the levels of muscle necrosis markers, particularly myoglobin and creatine kinase. It is worth emphasizing the importance of notifying the cases and obtaining samples of the meal ingested for toxin identification. Differential diagnosis should include other toxidromes in which rhabdomyolysis is present (e.g., arsenic, mercury, organophosphate poisoning).

Haff disease and all cases rhabdomyolysis should be treated aggressively to prevent severe metabolic and renal effects, which can lead to acute renal failure and other causes of morbidity and mortality.

CONCLUSION

Haff disease must be considered a cause of rhabdomyolysis in every patient with a history of ingestion of fresh water fish in the 24 hours preceding the onset of symptoms, or in those with changes in the laboratory values of muscle necrosis markers. Haff disease must be considered in the differential diagnosis of acute abdomen

if there is an epidemiologic history (ingestion of fresh water fish or crawfish 24 hours preceding the symptoms in the case of Haff disease) and when other explanations for the causes of the acute abdomen have been excluded. The toxin and all fish species associated with the development of Haff disease are still to be identified, but it seems that *Mylossoma duriventre* is one of the species associated with Haff disease in Brazil and this is the second report linking its ingestion with Haff disease.

RESUMO

A rabdomiólise associada à doença de Haff é correlacionada com a ingestão de certos peixes e crustáceos de água doce, sendo causada por uma toxina não identificada. Relatamos o caso de um paciente que apresentou rabdomiólise cerca de 2 horas após ingerir o peixe de água doce *Mylossoma duriventre* (*pacu-manteiga*) cerca de 3 anos após o relato de um surto de doença de Haff em Manaus.

Descritores: Rabdomiólise/diagnóstico; Doenças transmitidas por alimentos; Peixes; Diagnóstico diferencial; Relatos de casos

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