

Haff Disease after Eating Crayfish in East China

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Abstract

Haff disease, first identified in Europe, is unexplained rhabdomyolysis in a person who ingested fish within the 24 hours before onset of illness. Cases of Haff disease after the consumption of fresh water fish have never been reported in China but have been frequently reported from the Baltic region. We first describe five cases of muscle weakness and rhabdomyolysis that occurred after eating crayfish in China and discuss the different epidemiologic and etiologic aspects of this disease.

Key words: crayfish, Haff disease, rhabdomyolysis

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Introduction

Haff disease, first reported in the Baltic region in 1924, is defined as illness in a person with unexplained rhabdomyolysis who ingested fish within the 24 hours before onset of the disease (1). No neurological abnormalities, fever, splenomegaly or hepatomegaly are observed. All of the patients had recently consumed cooked freshwater fish (burbot, eel and pike). Most patients survived without sequelae but a few died quickly. Outbreaks resembling Haff disease were reported in Sweden and Soviet Union from 1934 to 1984 (2). To date only 23 cases have been reported in U.S. literature (2, 3). Cases in the U.S. have been associated with consumption of Buffalo fish, crawfish or salmon (3). Recently, outbreaks of Haff disease were reported in Brazil between June and September, 2008 (4). Haff disease has never been reported in China or even in Asia. We first described five cases associated with the ingestion of crayfish in August 2010 in the first affiliated hospital of Nanjing medical University, Nanjing, China.

Case Report

Case 1. A 26-year-old woman ate cooked crayfish that she purchased at a local seafood market for dinner. After 5 hours, she developed symptoms of diffuse myalgia, chest pain, shortness of breath, numbness of the whole body and muscular stiffness. She denied nausea, vomiting, diarrhea

and bellyache. She went to the local hospital emergency room and was hospitalized. The physical examination was normal. Her deep tendon reflexes and sensory examination were unremarkable. Laboratory evaluation included a normal complete blood count, normal electrolytes, blood urea nitrogen and creatinine. Her aspartate aminotransferase (AST) was elevated at 371.3 U/L (0-45 U/L), lactate dehydrogenase (LDH) was 866 U/L (110-250 U/L), creatine phosphokinase (CPK) was 8,487.1 U/L (25-190 U/L), CKMB was 81 U/L (0-25 U/L) and myoglobin was more than 1,000 µg/L (0-46 µg/L). Urinalysis showed 1+ for protein but was negative for leukocytes, glucose, blood or nitrite. A urine culture proved negative. On the following day, repeated urinalysis was normal. After 5 days the patient felt better and was discharged and her CPK was 344 U/L.

Case 2. A 31-year-old man was admitted to the hospital with chest pain, shoulder and back pain, numbness of the whole body. He had a history of consuming crayfish 5 hours before. His physical examination was normal. Laboratory evaluation included a normal complete blood count, normal electrolytes, blood urea nitrogen and creatinine. His AST was 124.7 U/L, LDH was 434 U/L, CPK was 2,515.4 U/L, CKMB was 134 U/L and myoglobin was more than 1,000 U/L. After 6 days he was discharged and CPK was 220.1 U/L.

Case 3 & Case 4. These two patients were mother and daughter, ages 44 years old and 20 years old, respectively. They ate cooked crayfish at a restaurant at 3 : 00 AM together. By 7 : 00 AM they felt weak and their muscles

Table 1. Symptoms of Haff Disease Cases, China, 2010

Symptom (n=5)	Number of reports
Myalgia	5
Musular stiffness	1
Pain to light touch	5
Painful breathing	1
Chest pain	5
Back pain	5
Shortness of breath	1
Numbness of the whole body	2
Nausea or vomiting	0
Diarrhea	0
Brown urine / hematuria	0

ached, with chest and back pain. They were admitted to the local hospital. Physical examination was normal. Laboratory evaluation included a normal complete blood count, normal electrolytes, blood urea nitrogen and creatinine. Urinalysis of mother showed 1+ for protein, 3+ for blood, but was negative for leukocytes, glucose or nitrite. Urinalysis of daughter showed trace for protein, 3+ for blood, but was negative for leukocytes, glucose or nitrite. Mother and daughter's AST were 146.2 U/L, 115.8 U/L, respectively; LDH were 340 U/L, 366 U/L, respectively; CPK were 4,998.3 U/L, 3,584.3 U/L, respectively; CKMB were 29 U/L, 12 U/L, respectively and myoglobin levels were both more than 1,000 U/L. After 5 days they were discharged and CPK levels were 586 U/L, 219 U/L, respectively.

Case 5. A 43-year-old woman was admitted to the hospital with chest pain, shoulder and back pain, and weakness and diffuse myalgia. She had a history of consuming crayfish 6 hours before. Physical examination was normal. Laboratory evaluation included a normal complete blood count, normal electrolytes, urinalysis, blood urea nitrogen and creatinine. Her AST was 146.2 U/L, LDH was 584 U/L, CPK was 3,486.4 U/L, CKMB was 104 U/L and myoglobin was more than 1,000 U/L. This patient was not hospitalized. After 7 days, CPK was reduced to 286 U/L.

Serology for leptospirosis and hepatitis A and B were negative in all of the patients. Troponin T values were also within the normal range. All of the patients denied a history of hypertension or diabetes. The brownish urine was not observed in our series. Patients were treated with intravenous fluid hydration and bicarbonate infusion. No deaths occurred. All of the patients had no recurrence of symptoms during the three months of follow-up.

Discussion

This is the first report about an outbreak of Haff disease in China. Cases were identified through county and state epidemiologists, as well as State Food and Drug Administration (SFDA) laboratory and Centers for Disease Control and Prevention (CDC) in Beijing, China. In our series, all patients were hospitalized with myalgia of sudden onset, mostly localized at the beginning of symptoms and followed

by generalized spreading within a few hours in August 2010. All of the patients reported prominent chest pain, among other symptoms (Table 1). No fever was observed. Gastrointestinal and neurologic manifestations were absent in our series. Three patients showed abnormal urinalysis on admission, but repeated urinalysis was normal on the following day. Predominant laboratory abnormalities were elevated CK serum activity and myoglobin. None of the cases reported had CK-MB levels >5%. Serum activities of transaminases and lactate dehydrogenase were also elevated. The diagnosis of Haff disease was made based on the fact that none of the cases could be explained by classic causes of rhabdomyolysis; all of the patients reported consumption of crayfish within 24 hours before the onset of symptoms. The median incubation period from onset of symptoms after crayfish ingestion was 5 hours (4-6 h).

Historically, Haff disease has been identified during seasonal outbreaks in Europe, it may also occur sporadically or in small clusters (5). The present patients had the same or similar clinical and laboratory characteristics with the cases reported in the Europe and U.S. Most reported cases of Haff disease have been associated with freshwater fish, unlike most other seafood-related illnesses (4-6). Crayfish, as well as Buffalo fish, are bottom-feeder freshwater animals. There are more than 540 species of crayfish in the world. Crayfish are widely natively distributed in the world except for Africa and Antarctica. Ecological conditions of the areas from the middle and lower reaches of the Yangtze River are favorable for the growth and reproduction of crayfish in China. In recent years, more and more people prefer to eat crayfish, especially in June to September every year. In Nanjing, the central city in the middle and lower reaches of the Yangtze River, people consumed 60t to 80t crayfish per day from June to September every year. The widespread increase of various pollutants and poisonous or toxic substances in the river has had obvious local impacts on the food chain of crayfish. To date, the toxin that may be responsible for the illness has not yet been identified.

Only in August, 5 cases of Haff disease were reported in Nanjing. No new cases were reported over the next six months. This possible association between crayfish eating and rhabdomyolysis in the Yangtze River may have an important impact, as crayfish is a major food consumed in this area from June to September.

State and local environmental management staff visited restaurants and markets where crayfish was bought to trace the implicated crayfish lots. The origin of the crayfish eaten by the patients was traced to one market. Samples of suspected food were sent to the SFDA and China CDC laboratory. Tests of the crayfish for toxins were either negative or below toxicity thresholds, such as saxitoxins, brevetoxins, ciguatoxins, palytoxins. A toxin is believed to be the cause of Haff disease due to the fairly rapid onset of symptoms after eating thoroughly cooked crayfish, and the absence of fever, which makes an infectious agent unlikely. The fact that the eaten crayfish was thoroughly cooked suggests that the

presumed toxin is heat-stable. Unusual smell or taste does not help identify toxic crayfish, and normal cooking methods cannot detoxify a crayfish capable of causing Haff disease.

In conclusion, when a case or cluster of patients present with severe myalgia or weakness of unknown etiology, they should be asked about ingestion of crayfish within the previous 24 hours. Identification of the toxin is a long and complicated process.

The authors state that they have no Conflict of Interest (COI).

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