

Scombroid pancreatitis from mahi-mahi consumption

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SUMMARY

A 61-year-old woman with no significant previous medical history presented to an urgent care facility with generalised rash, flushing and abdominal pain after eating mahi-mahi. She was diagnosed with an allergic reaction and discharged home. Later she experienced severe acute abdominal pain and multiple episodes of vomiting, which prompted her to go to the hospital. On admission, the patient had an elevated white count, lipase, amylase and C reactive protein with normal liver enzymes and bilirubin. Imaging showed acute pancreatitis that was suspected to be secondary to scombroid poisoning. This was confirmed by elevated immunoglobulin E and histamine levels. The acute pancreatitis was treated with pain management and supportive treatment. Scombroid poisoning is a well-recognised disease, however, acute pancreatitis secondary to this is rare as only two cases have been reported in the literature, one with codfish and the second an unknown type of fish.

BACKGROUND

Scombroid poisoning can develop after the consumption of fish with elevated histamine levels. This is a well-documented disease that causes nonspecific histamine-induced symptoms, such as diffuse flushing, edema, urticaria and abdominal reports.^{1,2} However, it is rare for scombroid poisoning to produce acute pancreatitis. This association is highly suspected in the absence of other inciting factors. Also, histamine is a known potent vasodilator that is thought to play an important role in acute pancreatitis by causing increased vascular permeability leading to pancreatic inflammation.³ This is the first reported case of acute pancreatitis developing following the consumption of mahi-mahi and subsequent scombroid poisoning.

CASE PRESENTATION

A 61-year-old woman with no significant medical history presented to an urgent care facility for a generalised rash in the hips and shoulders, flushing and mild abdominal pain that started 20 min after consuming fully cooked mahi-mahi at a restaurant. She was the only person who ate this fish, out of a group of seven people, and the only one developing symptoms thereafter. The abdominal pain was nonspecific, diffuse and had a severity of 6/10. Other symptoms included itching, lip swelling and mild shortness of breath. The urgent care treated this as an allergic reaction with methylprednisolone

and discharged her home with ondansetron, diphenhydramine and famotidine. Shortly after the patient arrived home, the abdominal pain acutely returned, now 10/10 in severity, and was localised to the epigastrium. Additionally, she began to experience multiple episodes of nonbloody emesis, thus, she sought further medical attention at the emergency department (ED). On further questioning, the patient denied a history of allergies, gallstones, pancreatitis or hypertriglyceridemia. She did not take any daily medications at home. The patient admitted to social alcohol use, usually 1–2 glasses of wine per week. She did have half a glass at the restaurant before this episode but denied any other alcohol for the past week. Additionally, she denied smoking, recreational drug use, frequent fish consumption or past allergic reactions of this nature.

In the ED, the patient was afebrile, haemodynamically stable and in no acute distress. An initial physical examination showed an obese patient (body mass index of 29.4) with epigastric tenderness but without rebound, guarding or other peritoneal signs. Initial laboratory workup showed an elevated white cell count of $16.9 \times 10^9/L$, lipase of 4513 U/L and amylase of 547 U/L; however, liver enzymes and bilirubin were within normal limits (table 1). CT of the abdomen and pelvis with contrast showed findings consistent with acute pancreatitis and no gallstones (figure 1). Therefore, the patient was made nil per os and given intravenous fluids, pain medications, ondansetron and diphenhydramine. Additional workup was also ordered to determine the aetiology of the acute pancreatitis, with the pertinent positives being elevated IgE of 66.4 kU/L and histamine of 10.34 ng/mL (table 2). Gastroenterology was consulted and ordered a magnetic resonance cholangiopancreatography (MRCP), which was performed 26 hours after presentation and showed acute pancreatitis and cholelithiasis; however, there was no evidence of biliary obstruction, ductal dilation, choledocholithiasis (figure 2). Surgery was consulted as well in view of the cholelithiasis but recommended no surgical management as there was no evidence indicating that gallstones caused this episode. Poison control was contacted who agreed with the diagnosis of scombroid poisoning and the current treatment regimen. The patient improved symptomatically and was discharged home 6 days after initial presentation with instructions to ensure that all meats and seafood are well cooked and



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Case report

Table 1 Initial laboratory investigations

	Initial values	Institution ranges
White cell count ($10^9/L$)	16.9	4–12
Aspartate transaminase (U/L)	18	10–40
Alanine aminotransferase (U/L)	15	3–45
Total bilirubin (mg/dL)	0.4	0.2–1.2
Lipase (U/L)	4513	7–60
Amylase (U/L)	547	20–100
C reactive protein (mg/dL)	21.7	0–1

refrigerated before eating and to follow-up with her primary care physician as scheduled.

INVESTIGATIONS

CT abdomen and pelvis with contrast (figure 1):

Diffuse peripancreatic inflammatory fat stranding in an organised fluid, compatible with acute pancreatitis. No definite evidence of organised pseudocyst or abscess. No gross component of haemorrhage or necrosis. No gallstone or ductal dilatation.

MRCP (figure 2):

1. Marked amount of oedema seen throughout the pancreas and peripancreatic fascial planes compatible with acute pancreatitis. No abnormal ductal dilation of the pancreas.
2. Five visible stones within the gallbladder, with largest measuring 17×15 mm. No abnormal biliary ductal dilation with common bile duct measuring up to 4 mm. No evidence for choledocholithiasis, stricture or obstruction. No intrahepatic ductal dilation.

DIFFERENTIAL DIAGNOSIS

When delineating the aetiology of acute pancreatitis, gallstone and alcoholism are the two most common with incidences of 40% and 35%, respectively. Other common causes are hypertriglyceridemia (2% of cases), postendoscopic retrograde cholangiopancreatography (2%), drug-induced (2%), autoimmune, hereditary, abdominal trauma, postoperative, ischemia, infections, hypercalcemia, posterior penetrating duodenal ulcer and scorpion venom.⁴ The patient's



Figure 1 CT scan of the abdomen with contrast on admission.

symptoms, history and laboratory findings did not indicate the presence of any of these causes. Due to the temporal onset of symptoms following fish consumption along with elevated IgE and histamine levels, the patient was diagnosed with scombroid poisoning, which most likely triggered acute pancreatitis.

OUTCOME AND FOLLOW-UP

The patient improved with appropriate medical management, including antihistamines, intravenous hydration and pain control. Abdominal pain resolved by day 5 of hospital stay and she was discharged the following day with complete resolution of her symptoms and tolerating oral diet. The patient went home with instructions to follow-up with her primary care physician, and due to her concern for recurrence of pancreatitis in the future, with the known presence of gallstones, she was advised to follow-up with general surgery for outpatient evaluation for elective cholecystectomy.

DISCUSSION

Scombroid poisoning, the most common seafood-borne illness in the USA, presents following consumption of inadequately stored fish containing high levels of histamine.⁵ The most commonly implicated fish are tuna, mackerel and mahi-mahi, adding up to over 80% of the cases. When fish is inadequately refrigerated or stored at room temperature after cooking, bacterial overgrowth occurs producing the enzyme histidine decarboxylase that reacts with histidine (naturally present in fish) leading to the formation of histamine, which can accumulate to toxic levels within 2–3 hours. The frequently implicated bacteria include *Proteus*, *Enterobacter*, *Serratia*, *Citrobacter*, *Escherichia coli*, *Klebsiella*, *Clostridium*, *Vibrio*, *Acinetobacter*, *Pseudomonas*, *Morganella* and *Photobacterium* sp. These bacteria may produce histamine at a wide range of temperatures, however, this occurs more rapidly over temperatures of 70°F or higher.

Table 2 Confirmatory laboratory investigations

	Initial values	Institution ranges
Immunoglobulin E (kU/L)	66.4	2.9–48.2
Histamine (ng/mL)	10.34	0–1
Cholesterol (mg/dL)	131	<200
Triglyceride (mg/dL)	48	<150
High density lipoprotein (mg/dL)	49	>39
Low density lipoprotein (mg/dL)	72	<130
Hepatitis A immunoglobulin M	Non-reactive	N/A
Hepatitis B surface antigen	Non-reactive	N/A
Hepatitis B core immunoglobulin M	Non-reactive	N/A
Hepatitis C antibody	Reactive	N/A
Hepatitis C RNA antibody viral load	Not detected	N/A
Tryptase (ng/mL)	2	<11.5
Anti-gliadin immunoglobulin G (U/mL)	0.3	0–10
Anti-gliadin immunoglobulin G (U/mL)	0.4	0–10
Tissue transglutaminase immunoglobulin A (U/mL)	0.3	<7
Tissue transglutaminase immunoglobulin G (U/mL)	0.6	<7
Endomysial immunoglobulin A	Negative	N/A
Antinuclear antibody	Negative	N/A
HIV antigen–antibody combo	Negative	N/A
C1 esterase inhibitor	30	19–37
C4 complement	29	16–38

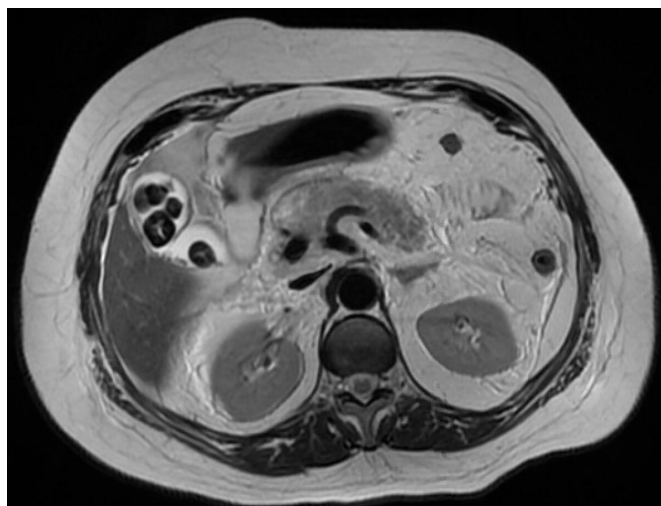


Figure 2 Magnetic resonance cholangiopancreatography performed 26 hours after initial presentation.

Once histamine decarboxylase is present in the fish, it can stay active even when refrigerated and remains stable when frozen.⁶ While both the bacteria and enzyme can be inactivated by cooking, the accumulated histamine is heat stable and cannot be eliminated by subsequent cooking, freezing, canning or smoking.¹⁷

Histamine, also named scombrotoxin in cases like this, induces a set of nonspecific symptoms that include diffuse flushing, oedema, urticaria, sweating, headache, dizziness, oral paresthesia, burning sensation, tachycardia, palpitations, abdominal pain, nausea, vomiting and diarrhoea. Rarely, the patient has respiratory complaints, but wheezing, bronchospasm, angioedema, respiratory distress and vasodilatory shock have been described. After eating the inciting fish, symptoms begin within 10–90 min, resolve within 3–8 hours with fatigue typically lasting 36 hours. Treatment usually consists of antihistamines, supportive management and education on proper ways to storage fish.^{17–9} This disease is classified as a poisoning, not an allergic or anaphylactic reaction, because it develops after the ingestion of histamine from a secondary source, which may affect large groups of people, many with no previously known allergies.^{7 10}

Acute pancreatitis is a relatively common disease that typically presents with upper abdominal pain of acute onset, moderate to severe intensity and commonly associated with nausea and vomiting.⁴ Diagnosis is made based on the symptoms described accompanied by elevation of amylase or lipase at least three times the upper limit of normal. Abdominal CT may be useful to confirm the diagnosis if biochemical testing and clinical picture are not conclusive. Of the multiple known aetiologies, the most common causes of acute pancreatitis are gallstones and alcohol misuse, with both of them adding up to 75% of total cases.¹¹ It is important to note that, in patients with asymptomatic gallstones, the risk for developing biliary pancreatitis is very low.¹²

Food-induced allergy has been linked as an aetiology of acute pancreatitis. The literature reports that these patients develop elevated histamine, bradykinin, cytokines and IgE that produce intestinal wall oedema, and duodenal and pancreatic inflammation.^{13–15} As the pathogenesis of allergic reactions and scombroid poisoning are both through histamine, a similar effect on the pancreas can be suspected.

Furthermore, the periacinar space, pancreatic interstitium and mesentery have a large population of mast cells, which degranulate and release histamine during the early phase of acute pancreatitis.³ Although scombroid poisoning has gastrointestinal symptoms, only two cases have reported its association with pancreatitis. An 8-year-old boy and a 38-year-old man who ate codfish and unknown types of fish, respectively, developed histamine-induced symptoms along with acute pancreatitis.^{16–18} Therefore, we present the first case of scombroid pancreatitis from the consumption of mahi-mahi.

Our patient initially presented with the typical findings of scombroid poisoning, as seen by the temporal onset within 20 min of fish ingestions, symptoms of generalised rash, flushing, abdominal pain and improvement with an antihistamine. However, her subsequent presentation with severe epigastric pain, vomiting and elevated values of lipase, amylase, IgE and histamine was rare and atypical. Despite the presence of calculi in the gallbladder, this was not considered to be the inciting aetiology of the acute pancreatitis due to no other signs or symptoms of choledocholithiasis, normal liver function tests and no evidence of biliary ductal dilation on MRCP. In addition to this, the timeline of events with symptoms points towards scombroid poisoning as the triggering event of pancreatitis. Furthermore, the other common causes of acute pancreatitis were ruled out by the patient's history and laboratory findings.

Learning points

- The most commonly implicated fish of scombroid poisoning are tuna, mackerel and mahi-mahi as they compromise over 80% of the cases.
- When the fish is inadequately refrigerated or stored at room temperature after cooking, toxic levels of histamine can accumulate within 2–3 hours and cannot be eliminated by subsequent cooking or freezing.
- Scombroid toxicity, though developed through accumulated histamine, is not an allergic or anaphylactic reaction but is considered poisoning.
- The periacinar space, pancreatic interstitium and mesentery have a large population of mast cells that degranulate early in acute pancreatitis.

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