Case Reports and Reviews

Case Report

Clinical Ischemic Heart Scombroid Syndrome: A Presumed Case of Kounis Syndrome

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Abstract

Scombroid poisoning is a type of food poisoning that results from the consumption of fish with high levels of histamine due to improper storage. The implementation of proper food handling and storage practices in the fishing industry, distribution, and retail sectors plays a crucial role in preventing scombroid poisoning. It is generally not considered life-threatening, but its symptoms can be uncomfortable and, in some cases, severe. Ischemic heart Scombroid Syndrome is a rare, usually transient, complication of scombroid poisoning, caused by coronary vasospasm in response to a nitroxide-mediated histamine-induced tissue hypoperfusion. We present the case of a 21 – years old female with no history of coronary artery disease (CAD) or atopy, who entered the Emergency Department after eating cooked tuna. She was immediately treated with intravenous antihistamine and cortisone. However, she suffered chest pain and severe hypotension, needing admission in the Intensive Care Unit and blood pressure support with vasopressors. Patient's final diagnosis was vasospastic angina due to presumed scombroid fish poisoning (SFP), a rare form of acute myocardial damage with nonobstructive coronary arteries secondary to coronary vasospasm, also known as "Ischemic heart Scombroid Syndrome" (ISS), causing a Kounis Syndrome type 1. Prompt recognition and management of both the allergic reaction and cardiovascular symptoms are crucial in the treatment of Ischemic heart Scombroid Syndrome.

Keywords

scombroid syndrome; ischemic heart scombroid syndrome; vasospastic angina; scombroid fish poisoning

Introduction

Scombroid poisoning is a type of food poisoning that results from the consumption of fish with high levels of histamine due to improper storage [1,2], or endogenous histidine present in the flesh of the fish that is converted by some bacteria, such as *Morganella morganii*, *E. coli*, and *Klebsiella pneumoniae*, commonly found on the surface of the fish. These bacteria use the enzyme histidine decarboxylase to transform histidine into histamine: it happens if fish are not properly stored at cold temperatures. The term "scombroid" refers to the Scombridae family, that includes tuna, mackerel, and bonito, among others. Scombroid poisoning can occur globally, and its prevalence is not limited to a specific region. However, the types of fish commonly implicated may vary based on regional dietary habits. Incidence may also show seasonal variation. The implementation of proper food handling and storage practices in the fishing industry, distribution, and retail sectors plays a crucial role in preventing scombroid poisoning [3, 4]. Fish should be stored at the recommended temperatures (0°C – 3°C), and if it is not going to be consumed immediately, it should be properly refrigerated or frozen. Cooking does not destroy the histamine once it has been produced. Symptoms of histamine fish poisoning usually begin within a few minutes to a couple of hours after consuming the contaminated fish and may include skin flushing, headache, nausea and vomiting, abdominal cramps, and diarrhea. In severe cases, symptoms may include difficulty in breathing and a drop in blood pressure. While histamine fish poisoning is generally not life-threatening, severe cases may require medical attention, and antihistamines may be administered to alleviate symptoms.

Case report

We present the case of a 21 – years old woman who entered the Emergency Department for sudden skin flushing of the whole body, headache, and gastrointestinal symptoms. She reported that she ate cooked tuna for dinner: tuna was bought fresh by her mother and stored frozen months before, until they decided to cook it. Immediately after the consumption, the patient and her sister (the only people who ate tuna) showed

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Table 1. *Blood Gas Analysis 01.30 a.m.*

pH	7.42
pCO_2	35 mmHg
pO_2	96 mmHg
Na^+	137 mmol/L
K^+	3.4 mmol/L
Glu	122 mg/dL
Lact	1.2 mmol/L
Hb	11.7 g/dL
sO_2	99 %

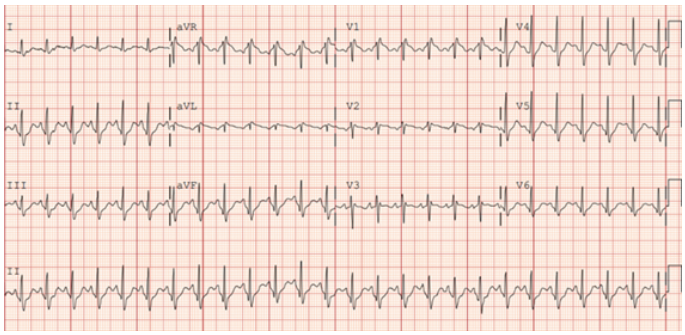

Figure 1. *Initial electrocardiogram: sinus tachycardia, no significant anomalies of ventricular repolarization*

Table 2. *Blood Gas Analysis 02.00 a.m.*

pH	7.36
pCO_2	34 mmHg
pO_2	204 mmHg
Na^+	139 mmol/L
K^+	3.3 mmol/L
Glu	127 mg/dL
Lact	4.3 mmol/L
Hb	9.6 g/dL
sO_2	99 %

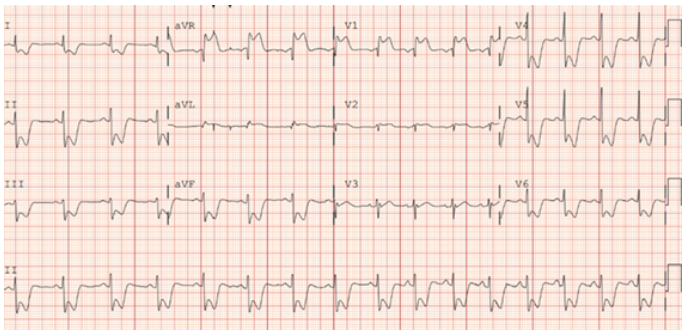

Figure 2. *Second electrocardiogram: elevation of the ST segment in the leads V1 and aVR, and ST segment depression in precordial leads (V3 – V4 – V5 – V6) and limb leads (D2, D3 and aVF)*

Table 3. *Blood Gas Analysis 04.00 a.m.*

pH	7.44
pCO_2	28 mmHg
pO_2	60 mmHg
Na^+	138 mmol/L
K^+	4 mmol/L
Glu	85 mg/dL
Lact	0.9 mmol/L
Hb	10.9 g/dL
sO_2	91.4 %

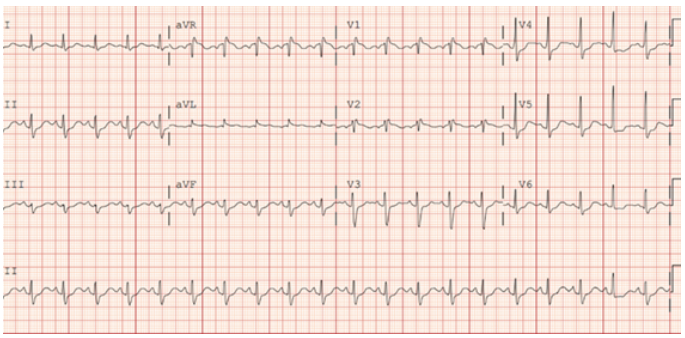

Figure 3. *Third electrocardiogram: after two hours, less evident anomalies of ventricular repolarization*

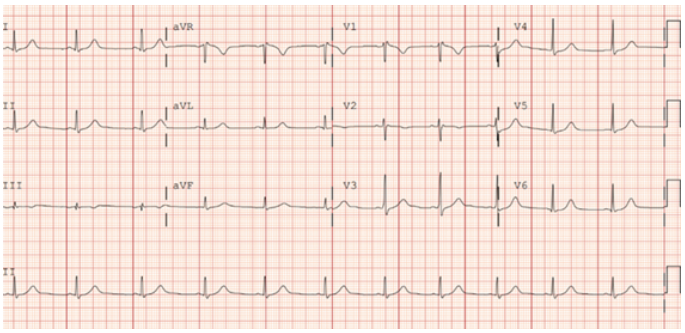

Figure 4. *Electrocardiogram at 24 hours: normalized*

skin flushing and gastrointestinal symptoms. The patient arrived alert, with stable vital signs: oxygen saturation of 98%, sinus tachycardia (160 bpm) and normal blood pressure (110/70 mmHg). Blood tests and blood gas analysis (Table 1.0) were performed showing normal values and, immediately, intravenous antihistamine (chlorphenamine 10 mg) and cortisone methylprednisolone 40 mg) were administered, suspecting an allergic reaction. Intravenous fluid therapy was also provided (crystalloids, infusion rate of 100 ml/h). The patient's initial electrocardiogram (Figure. 1) showed sinus tachycardia with a frequency of 160 bpm and no significant anomalies of ventricular repolarization. Ultrasensitive Troponin value was normal (< 1,5 ng/L). The patient's sister showed the same clinical condition and was admitted to the paediatric ward (she was 16 -years old). After an hour from

Table 4. *Variants of Kounis Syndrome*

Type I (Allergic Angina)	Type II (Allergic Myocardial Infarction)	Type III (Coronary Stent Thrombosis)
It involves coronary artery spasm without the presence of atherosclerotic lesions. It typically occurs in individuals without a history of heart disease	It is associated with the rupture of atheromatous plaques in the coronary arteries, leading to myocardial infarction. It may affect individuals with pre-existing coronary artery disease	It is related to allergic reactions following the implantation of coronary stents. It can result in the formation of blood clots within the stent, leading to acute coronary events.

the arrival at the hospital, the patient had sudden hypotensive shock, with a very low pressure (BP 60/40 mmHg), refractory to fluid resuscitation (2000 ml of crystalloids administered) and to hydrocortisone (1 gr). At the same time, she suffered chest pain. Another electrocardiogram was performed (Figure 2). It showed an elevation of the ST segment in the leads V1 and aVR, and ST segment depression in precordial leads (V3 – V4 – V5 – V6) and limb leads (D2, D3 and aVF). The echocardiogram performed showed hypokinesia of the interventricular septum with a preserved systolic function (EF 65%) and no significant valvular disease or pericardial effusion. Another blood gas analysis was performed (Table 2.0), showing significant increase in lactates. The cardiologist on duty did not give indications for a coronary angiography study given the negative history of cardiovascular pathologies, suspecting coronary vasospasm during anaphylactic shock. The patient was admitted to Intensive Care Unit. Upon admission, the patient appeared hypotensive (80/ 50 mmHg) and tachycardic (125 bpm), with decreased urinary output (20 ml/h). Invasive blood pressure monitoring was started, together with continuous norepinephrine infusion (starting with an infusion rate of 0.10 mcg/kg/min, up to a maximum of 0.20 mcg/kg/min). The patient did not require ventilatory support. She continued fluid resuscitation with crystalloids (infusion rate of 80 ml/h). The ECG was repeated after 2 hours: the anomalies of ventricular repolarization were less evident (Figure. 3). The HS Troponin value reached 101 ng/L. In the following hour, there was a progressive improvement in clinical symptoms: chest pain disappeared, with resumption of diuresis (80 ml/h) and improvement of vital parameters (invasive blood pressure 115/80 mm Hg, HR 98 bpm) and blood gas values (Table 3.0). After 24 hours, continuous infusion of norepinephrine was discontinued. A blood gas analysis performed showed normal value of lactate (0.9 mmol/L). The ECG had completely normalized (Figure 4), the patient was asymptomatic and the segmental kinetic anomalies on cardiac ultrasound had disappeared. HS Troponin reached the peak value of 1983 ng/L. After 72 hours the young patient was discharged from ICU. She made a complete recovery and returned home after seven days from admission.

Discussion

Patient's final diagnosis was vasospastic angina due to presumed scombroid fish poisoning (SFP), a rare form of acute myocardial damage with nonobstructive coronary arteries secondary to coronary vasospasm, also known as "Ischemic heart Scombroid Syndrome" (ISS) [5]. We cannot differentiate between ISS and Kounis syndrome because we could not analyse the fish eaten and we did not perform lab tests to measure tryptase and histamine serum levels. Ischemic heart Scombroid Syndrome and Kounis syndrome type 1 have a similar clinical presentation, and it is quite difficult to distinguish between them, except for the history of atopy in Kounis syndrome type 1, if we do not have specific allergic lab tests. Ischemic heart Scombroid Syndrome is due to a hypersensitivity reaction. It is not an IgE-mediated process, and its causative agent is histamine [6]. Histamine, which is present in large quantities in inadequately preserved fish, such as tuna, can induce cardiac toxicity in patients without pre-existing coronary artery disease. Coronary artery vasospasm seems to be the most likely pathophysiological mechanism of the transient ischemia. There are four types of histamine receptors in our body: H1, H2, H3 and H4. H1 - receptors mediate contraction of coronary vascular smooth muscle inducing vasoconstriction, and H2 – receptors mediate a positive inotropic and positive chronotropic response increasing sinus rate and ventricular automaticity [7]. These two receptors appear to be the two mainly involved in cardiac damage in the ISS [7, 8]. In Ischemic heart Scombroid Syndrome, prior sensitization is not required: the contaminated fish (like tuna) is rich in toxins, the "scombrotoxins", a mixture of histamine and other amines produced by decomposition of amino acids. These toxins induce an anaphylactoid reaction in the body. Otherwise, in Kounis Syndrome, also known as allergic angina or allergic myocardial infarction, histamine is released from human cells and prior sensitization is required. These two conditions share the histaminergic storm as an effector of coronary vasospasm, and it can explain the difficult to differentiate between ISS and Kounis Syndrome type 1. Kounis syndrome was first described by Dr. Nicholas G. Kounis in 1991, and it is triggered by an allergic reaction [9]. The syndrome involves the activation of inflammatory mediators, particularly mast cells and platelets, during an allergic reaction. These mediators, such as histamine, tryptase, and various cytokines, can lead to coronary artery spasm or inflammation, resulting in reduced blood flow to the heart. Kounis Syndrome can occur in individuals with or without pre-existing coronary artery disease. There are three main types or variants of Kounis Syndrome (Table 4.0). Symptoms of Kounis Syndrome can vary and may include chest pain or discomfort, shortness of breath, and other signs of a heart attack. The triggering factors for Kounis syndrome can range from insect stings, food allergies, and medication reactions to environmental exposures [10]. Management of Kounis syndrome and Ischemic heart Scombroid Syndrome involves treating the underlying allergic reaction and providing appropriate cardiovascular care. This may include administering antihistamines, corticosteroids, and medications to relieve coronary artery spasm. In severe cases, interventions such as angioplasty or stent placement may be necessary. It is important for individuals with known allergies or a history of allergic reactions to be aware of the potential cardiovascular complications associated with severe allergic responses.

Conclusion

Scombroid poisoning can occur globally, and its prevalence is not limited to a specific region. One of the worst complications

of scombroid syndrome is the induced myocardial ischemia. It is important to know about this syndrome so that the underlying cause can be identified early, and appropriate therapy can be initiated quickly. It is of particular importance as it can often affect young patients without a history of pre-existing heart disease or story of atopy. Prompt recognition and management of both the allergic reaction and cardiovascular symptoms are crucial in the treatment of Ischemic heart Scombroid Syndrome. Furthermore, it is important to know about this syndrome and its characteristics to better differentiate it from other possible diagnoses, such as Takotsubo Syndrome (a syndrome with similar electrocardiographic characteristics that generally affects middle-aged female patients). Myocardial infarction without coronary artery obstruction represents another possible differential diagnosis. In general, patients with ISS are relatively younger and the anamnestic data of recent ingestion of oriental fish towards the correct diagnosis. Ferrazzo et al. [11] suggested a flowchart for a simplified management of the patient who arrives at the emergency department with suspected myocardial ischemic and suspected scombroid syndrome. The authors suggest a therapy consisting in antihistamine drugs, fluids and circulatory support, symptomatic drugs, and steroids if needed. Furthermore, they always suggest, in case of chest pain or high suspect of myocardial infarction, to perform a cardiologic evaluation with echocardiogram, that can help in the diagnosis of exclusion of an acute coronary syndrome (ACS). Coronary angiography is recommended if the symptoms persist despite treatment or in case of clinical history of CAD.

Conflict of interest

The authors report no conflict of interest.

References

1. Feng C, Teuber S, Gershwin ME. Histamine (Scombroid) Fish Poisoning: A Comprehensive Review. Clin Rev Allergy Immunol. 2016;50(1):64-9. doi: 10.1007/s12016-015-8467-x.
2. Hungerford JM. Scombroid poisoning: a review. Toxicon. 2010;15;56(2):231-43. doi: 10.1016/j.toxicon.2010.02.006.
3. Lehane L, Olley J. Histamine fish poisoning revisited. Int J Food Microbiol. 2000;58(1-2):1-37. doi: 10.1016/s0168-1605(00)00296-8.
4. Sánchez-Guerrero IM, Vidal JB, Escudero AI. Scombroid fish poisoning: a potentially life-threatening allergic-like reaction. J Allergy Clin Immunol. 1997;100(3):433-4. doi: 10.1016/s0091-6749(97)70263-x.
5. Bassoni MS, Biancardi M, Magnani V, Alini D, Martinotti RG. Myocardic extended ischemia after scombroid syndrome. Emergency Care Journal. 2006;2(4):14–19. doi: 10.4081/ecj.2006.4.14
6. Taylor SL, Stratton JE, Nordlee JA. Histamine poisoning (scombroid fish poisoning): an allergy-like intoxication. J Toxicol Clin Toxicol. 1989;27(4-5):225-40. doi: 10.3109/15563658908994420.
7. Kounis NG, Zavras GM. Histamine-induced coronary artery spasm: the concept of allergic angina. Br J Clin Pract. 1991;45(2):121-8.
8. Traylor J, Mathew D. Histamine Toxicity. 2023 Jun 26. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
9. Kounis NG, Patsouras N, Grapsas N, Hahalis G. Histamine induced coronary artery spasm, fish consumption and Kounis syndrome. Int J Cardiol. 2015;193:39-41. doi: 10.1016/j.ijcard.2015.05.038.
10. Kounis NG, Kounis GN, Kouni SN, Soufras GD. The heart, the brain, and the Kounis syndrome. Eur Heart J. 2006 Mar;27(6):757; author reply 757-8. doi: 10.1093/eurheartj/ehi776.
11. Ferrazzo G, Perfetti S, Koniari I, Di Bella G, Kounis NG, de Gregorio C. Ischemic heart scombroid syndrome: how to recognize what you know. G Ital Cardiol (Rome). 2023;24(8):653-660. Italian. doi: 10.1714/4068.40534.