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To cite this article: Cesare de Gregorio, Giuseppe Ferrazzo, Ioanna Koniari & Nicholas G. Kounis (2021): Acute coronary syndrome from scombroid poisoning: a narrative review of case reports, Clinical Toxicology, DOI: [10.1080/15563650.2021.1959605](https://doi.org/10.1080/15563650.2021.1959605)

To link to this article: <https://doi.org/10.1080/15563650.2021.1959605>



Published online: 16 Aug 2021.



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REVIEW



Acute coronary syndrome from scombroid poisoning: a narrative review of case reports

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ABSTRACT

Background: Scombroid syndrome constitutes a toxic illness caused by ingestion of improperly stored fish, usually contaminated by Gram-negative bacteria producing histamine and other toxins. Scombroid currently accounts for approximately 5% of food toxicities in the United States. Though cardiovascular complications are infrequent, some patients experienced acute coronary syndrome (ACS) on admission to hospital. This article focuses on the main pathophysiology, clinical features, therapy, and outcomes in scombroid-related ACS.

Methods: Starting from the consolidated knowledge on histaminergic syndromes, we performed a literature search for studies describing patient series and single cases presenting at emergency department with scombroid toxicity complicated by myocardial ischemia.

Results: After a pathophysiological overview on histaminergic syndromes, we carefully analyzed a dataset of 19 patients from 13 studies, published from 1997 to December 2020. Electrocardiographic, echocardiographic, angiographic features, clinical course, hospital complications, and therapeutic approach were described. Shared and differential aspects of scombroid ACS with typical atherosclerotic ischemia, Kounis, MINOCA and Takotsubo syndromes are also discussed.

Conclusion: An ischemic heart scombroid syndrome may occur in some patients after the eating of improperly stored fish food. Currently available studies indicate this as a benign condition, except for patients with history of coronary artery disease, previous ACS, or anaphylaxis. Of clinical concern, there is a potential of hemodynamic failure in the acute stage, even in apparently healthy people.

ARTICLE HISTORY

Received 2 February 2021

Revised 10 July 2021

Accepted 16 July 2021

KEYWORDS

Acute coronary syndrome; fish food; histamine; poisoning; toxic disease

Introduction

Scombroid fish poisoning syndrome (hereinafter, *scombroid*) constitutes a toxic disease usually caused by improperly stored fish-food ingestion, contaminated by Gram-negative bacteria. Although poisoning from the eating of fish was known since biblical times, it was clearly described in 1799 in Britain, and then again after the 1950 commercial outbreaks of improperly stored tuna fish products in the USA (1968), Japan (1970), and Britain (1976) [1–5].

In 1973, the US Food and Drug Administration (FDA) officials accredited this syndrome as a gastrointestinal illness, at times associated with allergic-like symptoms, in people living in north-central States. Most microorganisms have been identified to cause scombroid, and other studies confirmed its histaminergic nature [4–6]. Scombroid currently accounts for approximately 5% of all reported food toxicities in the United States [5,6]. Clinical picture usually consists of nausea, vomiting, abdominal spasm, diarrhea, peppery or metallic taste, and/or oral numbness. Flushing, cutaneous rash, headache, dizziness, respiratory fatigue, have also been reported, resembling an allergic disease [3,7–11].

Although cardiovascular complications rarely occur in scombroid patients, acute coronary syndrome (ACS), whether associated with severe circulatory failure, has been reported in some cases. This article focuses on the main pathophysiology, clinical features, and prognostic implications of scombroid-related myocardial ischemia.

Pathophysiology

Histamine is a common effector of allergic and inflammatory disorders. High levels of circulating histamine from both an endogenous and exogenous origin cause analogous systemic disorders [12–14]. Scombroid usually results from ingestion of *scombrototoxin*, a mixture of histamine and other potentiating diamines like putrescine and cadaverine. Diamines stem from decomposition of the amino acids within the fish muscle, as the consequence of improperly stored (also termed as mistreated) food products [7–11].

Histamine comes from decarboxylation of histidine, whereas cadaverine and putrescine come from lysine and ornithine, respectively. These amines are quickly formed by post-mortem breakdown of the native amino acids, after

exposure of the fish to warm ambient temperature that promotes proliferation of Gram-negative bacteria like *Acinetobacter*, *Citrobacter*, *Clostridium*, *Enterobacter*, *Escherichia coli*, *Klebsiella*, *Morganella morganii*, *Proteus*, *Pseudomonas*, *Salmonella*, *Serratia*, etc. Cold storage and handling inhibit the breakdown and conversion of histidine into histamine. However, once diamines are formed, they are thermo-resistant to cooking, smoking, or late freezing [10–13].

Fish species belonging to the family of *Scombridae*, such as tuna, mackerel, mahi-mahi (dolphin fish), sea urchins, herring, sardines, bluefish, and others, are more likely to get infected by bacteria [3–7,11]. Tuna and mahi-mahi were the most frequent culprit fish species in the review of Feng et al. [12], making up more than 80% of reported scombroid cases in the USA from 1998 to 2012. More recently, Colombo et al. confirmed tuna fish as the most common source of food-borne histaminergic intoxications [13]. Analysis by the European Food Safety Authority identified seafood as the leading class of foods causing illness from histamine ingestion and ranked it far ahead of cheeses, sauerkraut, and other foods formed with fermentation [14].

Two enzymes inactivate ingested histamine [14]. First, diamine oxidase (DAO) in the intestinal epithelium acts on ingested histamine prior to entering the portal circulation. In the liver, histamine-N-methyltransferase (HNMT) also inactivates histamine by ring methylation. Intoxication occurs after saturating these counteractive mechanisms [8–14].

Fresh fish should contain a minimum amount of histamine, less than 0.01 mg/100 g of fish muscle. Intoxication can occur at concentrations that are orders of magnitude higher. At least 50 mg/100 g are necessary to determine scombroid [8–14]. To ensure a wide margin of error, the European food regulations require the histamine tissue concentration to range from 10 to 20 mg/100 g in fresh foods, or to 40 mg/100 g in fishery products which have undergone enzyme maturation treatment in brine and manufactured from fish species associated with a high amount of histidine [15]. More recently, FDA regulatory commitment established a more stringent cutoff of 50 ppm (5 mg/100 g) in fresh fish [16].

Histamine and myocardial ischemia

Myocardial function and coronary circulation can impair during histaminergic reactions [17,18]. Histamine transported into or produced within isolated cardiomyocytes elicits a rise in reactive oxygen species levels mediated by the monoamine oxidase activity, through G-protein coupled H1 receptor (H1r). Histamine enters the heart through the organic cation transporters, especially the isoform 3, that is expressed in the myocardium [18–21]. However, it is unclear whether H2 and H3 receptors also participate as modulators or boosters to histaminergic disorders of the heart [22].

Myocardial injuries from histaminergic disorders have been acknowledged primarily by the Kounis syndrome (KS), a rare ACS affecting atopic individuals after prior exposure to allergens like foods, drugs, excipients, chemical agents, and other substances. In those patients, type-1 allergic reaction

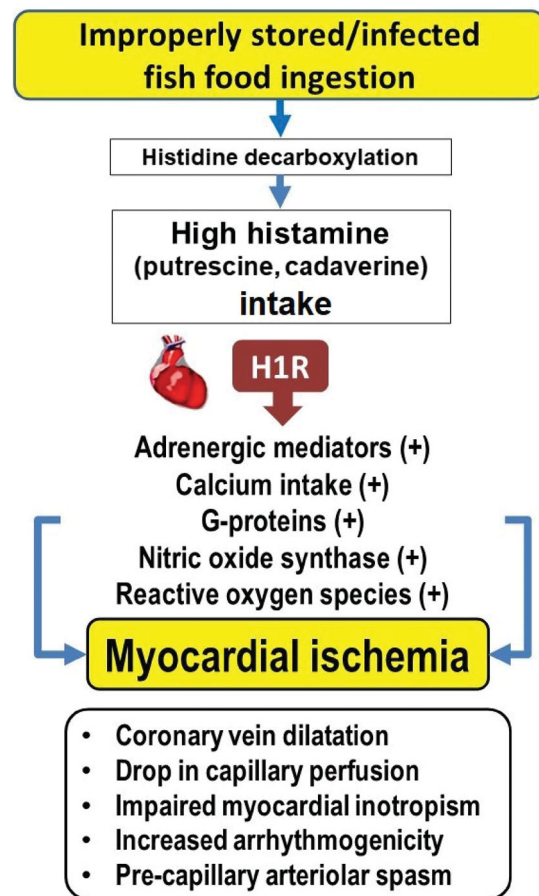


Figure 1. Pathophysiology underlying myocardial ischemia during scombroid syndrome. H1R: histamine receptor 1.

induces mast cell degranulation, macrophages and T-lymphocytes activation, and cytokine release. These are responsible for inflammation, platelet activation, thrombotic complications, and finally myocardial ischemia [17,18,23]. KS is also due to abundance of mast cells and macrophages in the myocardium, preferentially located at the sites of coronary plaques [23,24], which contributes to boosting systemic anaphylaxis [25].

Focusing on exogenous histamine, the present article underlines a similar pathomechanism for myocardial ischemia in scombroid patients. Even if scombroid is not an allergic disease, ingestion of histamine results in anaphylactoid reactions resembling an allergy [10,26]. Based on early reports on this syndrome [27–29], myocardial ischemia may be less dramatic in scombroid than in KS patients, because it tends to be a self-limiting disease, due to individual counteractive methylation [12,14,19,20,26]. In case of eating large quantity of infected fish or with high histamine concentration, distinguishing scombroid from anaphylaxis based upon the clinical presentation can be problematic. Nevertheless, severe hypotension with hemodynamic impairment has occurred even in apparently healthy people at emergency department [27–29].

Main effects of (exogenous) histamine on the heart appear in Figure 1. Pre-capillary arteriolar vasospasm results from activation of G-protein coupled receptors, release of reactive oxygen species, and catecholamine formation. Ensuing precapillary arteriolar constriction arises in response

Table 1. Main characteristics of the patient population showing myocardial ischemia on admission to hospital for scombroid.

Author	Sex, years	Allergy	Clinical presentation (time from meal)	BP	ECG changes	Arrhythmic; systemic complications	Cardiac ultrasound on admission	Coronary angiography	Hospital stay
Ascione et al, [27] Palermo, Italy 1997	M, 75 Case 1	No	Abdominal pain, asthenia, hypotension, vomiting (2 h)	65/40	Widespread ST-dep (ST-el aVR)	Atrial fibrillation	NA	NA (previous AMI)	17 days (discharged)
	F, 22 Case 2	No	Asthenia, chest pain, cutaneous rash, palpitations, vomiting (2 h)	<60/?		APE and severe hypotension requiring OTV	Global LV hyperkinesis	NA	4 days (discharged)
Grinda et al, [28] Clamart, France 2004	F, 36 Case 3	No	Laryngeal dyspnea, lip edema, bright red rash, nausea, headache, burning in the mouth, tachycardia, tachypnea (20 min)	80/50	NA	SV tachycardia; biventricular pump failure, requiring extracorporeal mechanical support	Global severe LV dysfunction	NA	17 days (discharged)
Lionte, [29] IASI, Romania 2010	F, 24 Case 4	No	flushing, headache, nausea, vomiting, anxiety and palpitations (10 min)	<90/60	Widespread ST-dep (ST-el aVR)	—	NA	NA	24 h (discharged)
	F, 26 Case 5	No	flushing, headache, nausea, vomiting, anxiety and palpitations (10 min)		Widespread ST-dep (ST-el aVR)	—	NA	NA	
	F, 44 Case 6	No	flushing, headache, nausea, vomiting, anxiety and palpitations (10 min)		Abnormal QRS	Accelerated idioventricular Rhythm	NA	NA	
D'Aloia et al, [33] Brescia, Italy 2011	F, 16 Case 7	No	Abdominal pain, cutaneous rash, palpitations, vomiting (short time)	90/60	Widespread ST-dep (ST-el aVR)	Supraventricular tachycardia; circulatory shock, mechanical ventilation	Global LV hypokinesis (EF 30%), severe mitral regurgitation	No stenosis	7 days (discharged)
Coppola et al, [34] Palermo, Italy 2012	M, 56 Case 8	NA	Facial rash, retrosternal pain, dyspnea, headache, sweating, tachycardia (NA)	80/-	ST-el inf leads, then widespread ST-dep (ST-el aVR)	Premature ventricular beats; transient AV block; marked hypotension	Hypokinetic LV anterior wall (EF 55%)	LAD artery critical stenosis (PCI)	6 days (discharged)
Sarullo et al, [35] Palermo, Italy 2013	F, 56 Case 9	No	Flushing, headache, nausea, dyspnea, vomiting, abdominal pain (10 min)	85/60	ST-el inf leads (spasm) + ST-dep (anterior leads)	Transient AV block	Akinetic LV apex + inferior wall (EF 40%)	NA	5 days (discharged)
Tortorella et al, [36] Catanzaro, Italy 2014	F, 32 Case 10 M, 35 Case 11	No	palpitations, headache, heat all over their body, rash, eyelid edema, chest pain (short time)	85/50 70/35	Widespread ST-dep (ST-el aVR) Widespread ST-dep (ST-el aVR)	— Ventricular fibrillation; severe hypotension requiring OTV	LV apical-septal hypokinesis NA	NA No stenosis	36 h (discharged) 3 days (discharged)
Anastasius et al, [37] Concord, Australia 2015	M, 30 Case 12	No	Widespread erythema, chest tightness, dizziness, hypotension, profuse sweating (2 h)		Widespread ST-dep (ST-el aVR)	—	Normal LV (pre-discharge)	Negative exercise test	Short time (discharged)
Cucunato et al, [38] Messina, Italy 2015	F, 28 Case 13	NA	Nausea, vomiting, profuse sweating weakness, hypotension (1 h)	NA	Widespread mild ST-dep	—	NA	No stenosis	After 3 days (discharged)
Jermini-Gianinazzi et al, [39] Bellinzona Switzerland, 2018	F, 59 Case 14	No	Chest pain, dyspnea, facial flushing, hypotension, weakness (20 min)	77/49	Widespread mild ST-dep (ST-el aVR)	—	Normal LV function	No stenosis	NA (discharged)
Marissiaux et al, [40] Liege, Belgium 2018	F, 50 Case 15	No (*)	Facial flushing, palpitations, headache, dizziness, chest oppression (10 min)	85/40	ST-dep inf leads (ST-el aVR)	Supraventricular tachycardia	Global LV hyperkinesis	NA	6 h (discharged)
Ferrazzo et al, [32]	M, 56 Case 16	No	Flushing, chest pain, dyspnea (1 h)	115/60	Widespread ST-dep (ST-el aVR)	—	Global LV hypokinesis (EF 45%)	No stenosis	3 days (discharged)

(continued)

Table 1. Continued.

Author	Sex, years	Allergy	Clinical presentation (time from meal)	BP	ECG changes	Arrhythmic; systemic complications	Cardiac ultrasound on admission	Coronary angiography	Hospital stay
Messina, Italy 2019	M, 58 Case 17	No	Abdominal cramps, chest pain, dyspnea flushing, vomiting (2 h)	70/30	Widespread ST-dep (ST-el aVR)	Severe hypotension	NA	No stenosis	3 days (discharged)
	F, 48 Case 18	No	Abdominal cramps, chest stress, dyspnea, flushing, palpitations (3 h)	90/60	Widespread ST-dep (ST-el aVR)	—	NA	NA	7 h (discharged)
Manjuri et al. [41] New York City New York, 2019	M, 53 Case 19	No (**)	Chest pain, dyspnea, facial flushing, profuse watery diarrhea, subjective warmth, tachypnea (1 h)	88/48	Widespread ST-dep (ST-el aVR)	—	Normal LV (pre-discharge)	No stenosis	NA (discharged)

NA: not available or not performed; aVR: amplified right arm lead on ECG; BP: blood pressure; EF: ejection fraction from the LV; LV: left ventricle/ventricular; OTV: orotracheal tube ventilation; ST-dep, ST segment depression on ECG; ST-el: ST segment elevation on ECG. *History of hypertension; **History of alcohol assumption, and obstructive sleep apnea syndrome.

to nitric oxide-mediated post-capillary venous dilatation, and/or as direct histamine-mediated vasoconstriction. Falling venous resistance causes a drop in capillary pressure perfusion with ensuing generalized precapillary vasoconstriction, that leads to subendocardial ischemia [30,31].

Scombroid complicated by coronary syndrome: case studies

We performed a literature search through MEDLINE, life science journals, SCOPUS database, and books, using the following MESH terms: ACS, cardiac pump failure, fish food toxicity, heart failure, ischemic heart disease, scombroid poisoning, scombroid syndrome, and tuna-fish toxicity, for articles published till December 2020. From a total of 238 articles, we excluded general studies, systematic reviews, non-cardiac reports, duplicates, incomplete, misdiagnosed, or doubtful reports. Our final analysis included thirteen articles describing 19 patients with documented myocardial ischemia (by ECG, echocardiography, exercise ECG, and/or coronary angiography) [27,28,32–41]. Further patients were found with symptoms suggestive of cardiac involvement, but they were excluded because of partial findings or suspected to be on allergic basis [42–47].

Demographic and clinical characteristics of patient population appear in Table 1. Other than gastrointestinal symptoms, patients also complained with weakness, sweating,

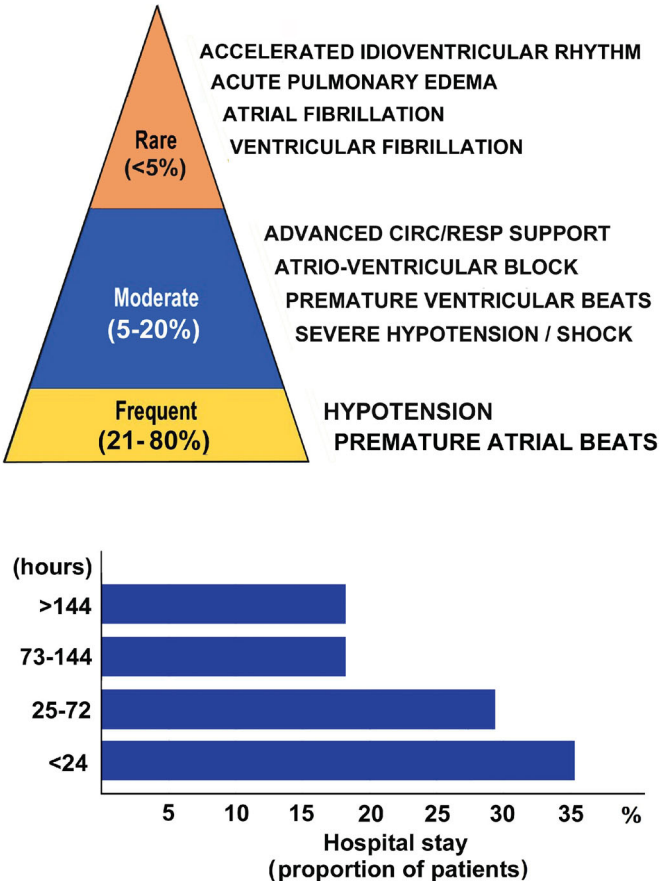


Figure 2. Cardiac and respiratory complications from 19 patients with ACS during scombroid (top diagram), and in-hospital length of stay (percent of patients, bottom bar graphs).

flushing and dyspnea. Hypotension was the most common and problematic issue on admission to hospital, and four cases with hemodynamic impairment required intensive care, endotracheal intubation, or mechanical life support [27,28,33,36]. Cardiac symptoms such as chest heaviness, chest pain or dyspnea initiated usually with gastrointestinal illness shortly after the eating of fish (range: 10 mins – 3 h). Hence, patients underwent 12-lead ECG recording, echocardiography and/or coronary angiography to confirm or rule out an ACS. Laboratory investigations showed mildly increased troponin concentrations, at times with elevated natriuretic peptides.

Clinical complications on admission and the length of hospital stay appear in Figure 2. Although some patients required critical care, none died. Full clinical recovery needed less than 24 h in 6/17 patients (missed information from 2 reports). Five patients who underwent coronary angiography were discharged 3–4 days later. Three patients had a prolonged stay, with the need for intensive care unit in cases 3 and 7. The index patient in 1997 required 17-day hospitalization due to an established CAD and subsequent myocardial damage [27]. All patients had uneventful follow-up after recovery and hospital discharge.

Electrocardiogram

All patients, except for one [28], had an ECG performed upon admission. Fifteen patients (83%) showed widespread ST-segment depression (limited to the inferior leads in one), apart from the lead aVR where the ST might be elevated (Figure 3). This pattern resembled that one described by Gorgels et al. [48] in patients with three-vessel disease or left main coronary artery stenosis.

Widened QRS occurred in a 44-year-old woman (case 6) who had accelerated idioventricular rhythm masquerading repolarization anomalies. In 2 patients (cases 8 and 9) there was transient ST elevation on the inferior leads, but case 8 was known to be an ischemic patient [34].

Arrhythmic disorders occurred in 8 patients (42%). Supraventricular tachycardia was the most frequent arrhythmic disorder likely due to catecholaminergic response to acute histaminergic reaction. Atrial fibrillation occurred in a single patient (case 1), as well as ventricular fibrillation in a 35-year-old male (case 11) who developed critical hemodynamic failure, requiring intubation and advanced medical support [36]. Transient atrio-ventricular block was observed in a 56-year-old woman (case 9) [35], whose clinical presentation and echocardiographic findings were suggestive of *takotsubo*-like syndrome [49].

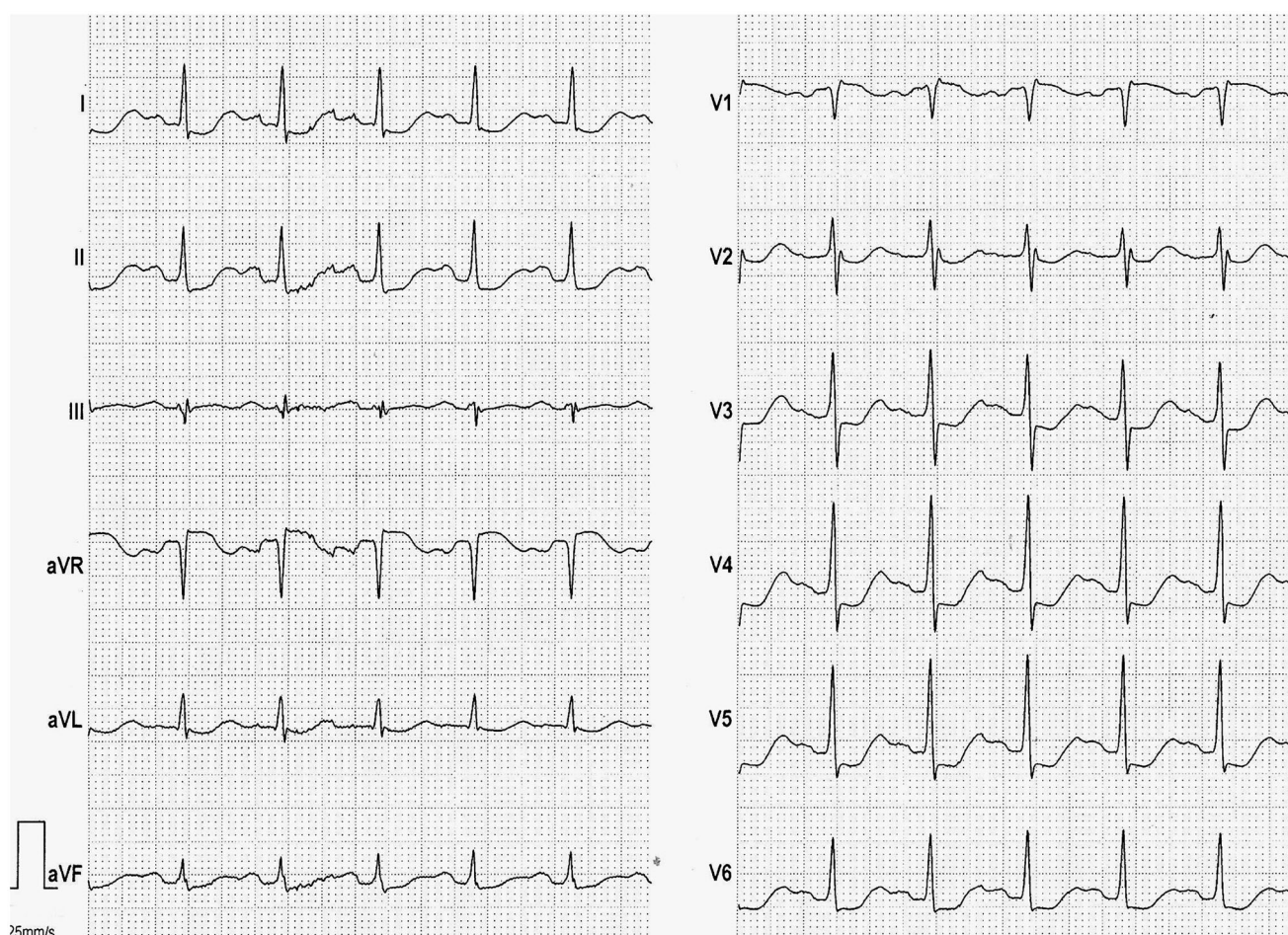


Figure 3. Admission ECG in a patient with IHS (case 16) showing widespread ST-segment depression (except for lead aVR).

Echocardiogram

Eleven patients had cardiac ultrasound performed. Three occurred just before hospital discharge. In general, there were consistent left ventricular dysfunctional pictures, with findings ranging from mild hyperkinesis (cases 2 and 9) to generalized hypokinesis (cases 3, 7, and 16). Though patients 3 and 7 showed severely impaired systolic function, there was no clear relationship between ECG presentation and left ventricular dysfunction, likely encouraging further study on such discrepancy. Of clinical interest, everyone (except for CAD patients 1 and 8) were discharged with recovered ventricular function.

Coronary angiography

Coronary angiography occurred in 8/19 patients, particularly after 2011. Angiographic findings were unavailable from the first four reports. Seven patients (cases 7, 11, 13, 14, 16, 17, and 19) had no coronary stenoses. A single male patient (case 8) with previously known CAD required the left descending coronary artery stenting [34].

In one case, emergency physicians aware of a batch of contaminated tuna-fish in their geographic area prevented a 48-year-old-woman (case 18) from coronary angiography. She quickly recovered with antihistamine and steroid treatment [32].

Another young male patient (case 12) underwent an exercise stress test before leaving the hospital with no demonstration of exercise-induced myocardial ischemia [37].

Laboratory testing

In general, mild-to-moderate increase in troponin and creatine-kinase serum concentrations occurred in most patients on admission to hospital. However, their enzymatic trend was on a smaller scale and quicker than usually seen in typical ACS. This finding likely confirmed a transient and trivial ischemic damage in such patients [50]. There was no clear relationship between severity of intoxication and the enzymatic curve.

In patients experiencing foodborne histaminergic reactions, differential diagnosis between toxic and allergic diseases is important also in term of prevention. Nonallergic etiology allows the patient to eat same fish in the future, which is not possible in allergic diseases. High serum concentrations of tryptase, which is mainly released from activated mast cells, likely confirms an allergic etiology. A peak >11 mg/L can occur 60–90 mins after the onset of anaphylaxis, with a gradual decrease 5–6 h later. Therefore, the optimal timing for testing tryptase is 1–6 h after the onset of symptoms [51].

Fish muscle specimens

Microbiological integrity of the fish (or meat) foodstuffs cannot be simply recognized by appearance and odor. Abnormal histamine content may be determined through food remnant analysis in scombroid patients. High tissue concentration of histamine or its precursors is a confirmatory

finding [11,12,14], but it is unlikely that a patient will bring uneaten fish to emergency department.

In the meta-analysis by Colombo et al. [13], the observed concentration varied from 1.8 to 811 mg/100 g, with a combined estimate of 110 mg/100 g of fish muscle. In the present case series, D'Aloia et al. reported an extremely high concentration (>1000 mg/100 g) in the food remnants eaten by a severely symptomatic 16-year-old girl. She had hypotension (90/60 mmHg), supraventricular tachycardia (160 beats/min), ST segment depression, diffuse left ventricular hypokinesis on echocardiogram, and a peak troponin concentration of 45 ng/mL [33]. Authority investigation demonstrated 300–900 mg/100 g from different fish muscle specimens in the case from Jermini-Gianinazzi et al. [39].

Differential diagnosis

Kounis syndrome

Kounis syndrome is an anaphylactic illness related to IgE-antigen immune complexes that activate mast-cells, basophils, macrophages, and cytokine system after the ingestion of an allergen [23,31]. Cases of KS have occurred after honey-bee and Hymenoptera stings, ingestion of drugs, fish-foods, blue-crabs, and after the exposure to chemical or contrast agents during coronary angiography [23,44–47,52]. There are three variants of KS. Type I is an ACS characterized by coronary vasospasm, not necessarily resulting in myocardial infarction, in patients with normal or nearly normal coronary arteries. Type II involves ACS patients with pre-existing CAD, often complicated by coronary vasospasm, plaque disruption and thrombosis, resulting in myocardial infarction. Type III consists of thrombotic/stenotic inflammation of pre-existing coronary artery stents. Most cases of scombroid in this series were like Type I, with the sole exception of a non-allergic causality. Unless antihistamines promptly resolve cardiac symptoms and any ECG changes, coronary angiography is mandatory in KS patients [17,18,23,25].

Anisakiasis

Anisakiasis simplex is a rare fish parasitosis caused by one or more nematode-secreted allergic substances. Somatic allergens are secreted by the parasite body, such as cuticular proteins, aimed at protecting the nematode from digestive juices when the larva penetrates the gastric or gut mucosa. In some cases, the larva migrates into the peritoneal or pleural cavity, mesentery, and the liver, pancreas and/or ovaries as well [53]. Anisakiasis infestation has been encountered among the triggers of KS, because it can determine type 1 allergy, at times involving the heart [54]. High serum IgE, positive prick-test and RAST test usually allow differential diagnosis [53].

MINOCA syndrome

Myocardial infarction with non-obstructed coronary arteries (MINOCA) refers to the 5–10% of all cases with an acute

myocardial infarction with minimal or no discernable coronary artery stenoses [55]. Although two-thirds of such patients present with ST-elevation on ECG, another third may show ST-segment depression as in scombroid cases. Therefore, differential diagnosis among MINOCA or atypical ACS and scombroid is difficult at emergency department. In general, MINOCA patients are old women with a substantial burden of atherosclerotic risk factors such as diabetes mellitus, hypertension, hyperlipidemia, and history of allergy in someone [56]. Conversely, scombroid patients with ACS usually were younger than 60 years, with the distinctive feature of the recent eating of fish foods.

Takotsubo syndrome

Takotsubo syndrome is a stress-related catecholaminergic cardiomyopathy characterized by transient left ventricular dysfunction (involving the apical region in the classic variant) [49], somehow resembling the cardiac impairment in brain-injured patients [57,58]. Electrocardiographic features consist of ST-segment elevation or depression, negative T-waves, QT-interval prolongation. This syndrome primarily affects post-menopausal women experiencing stressful occasion(s) or acute diseases. Furthermore, single case descriptions have been reported soon after histaminergic reactions [59], as we suspected in the 56-year-old woman (case 9) reported by Sarullo et al. [35]

Treatment

Basic treatment of the 19 scombroid patients complicated by ACS was not different from other histaminergic illnesses. Therefore, almost all patients received antihistamines (e.g., *diphenhydramine* 1–2 mg/kg) and isotonic crystalloid fluids. In severe cases, patients received both anti-H1 (diphenhydramine every 6 h as needed, 25–100 mg in adults) and anti-H2

(cimetidine, ranitidine, or famotidine) intravenously, especially for relieving gastrointestinal symptoms.

In addition, most patients received antithrombotic or anticoagulant drugs for ACS or in preparation for coronary angiography [32–36,41]. Patients with edema in the respiratory tract or bronchospasm received steroids and β_1 -receptor agonists. Severe hypotension or acute cardiac pump failure required vasopressor amines (dopamine, dobutamine or norepinephrine) [27–29,32–41].

Due to frequently reported supraventricular tachycardia, in the absence of bronchoconstriction, β -blockers might be used for rate control and anti-arrhythmic effect. Four young patients (cases 2, 3, 7, 11) required advanced cardiorespiratory support and orotracheal tube. All patients were discharged in good clinical condition within one to four days (except for patient 3, who required prolonged hospitalization).

Unlike the striking cases with adrenergic coronary vasospasm [60], there is little evidence that nitrates and non-dihydropyridine calcium-channel blockers like verapamil are useful in patients with histaminergic syndromes.

Based on the present case analysis, coronary angiography remains mandatory in patients with history of CAD or previous ACS, as well as allergy, due to the risk for coronary complications. In contrast, uncomplicated scombroid patients do not need urgent coronary angiography [23,54,58], unless cardiac symptoms persist. Accordingly, they should not be given anti-thrombotic agents, heparin, and aspirin, which are indicated in typical ACS [61] and KS [23]. Figure 4 illustrates a proposed flow-chart for a quick assessment and treatment of scombroid patients at emergency department.

Discussion

Myocardial ischemia is a rare complication of scombroid. Our case series included 19 patients from all over the world till December 2020. Scombroid was more frequent in warm countries, where higher ambient temperatures may favor

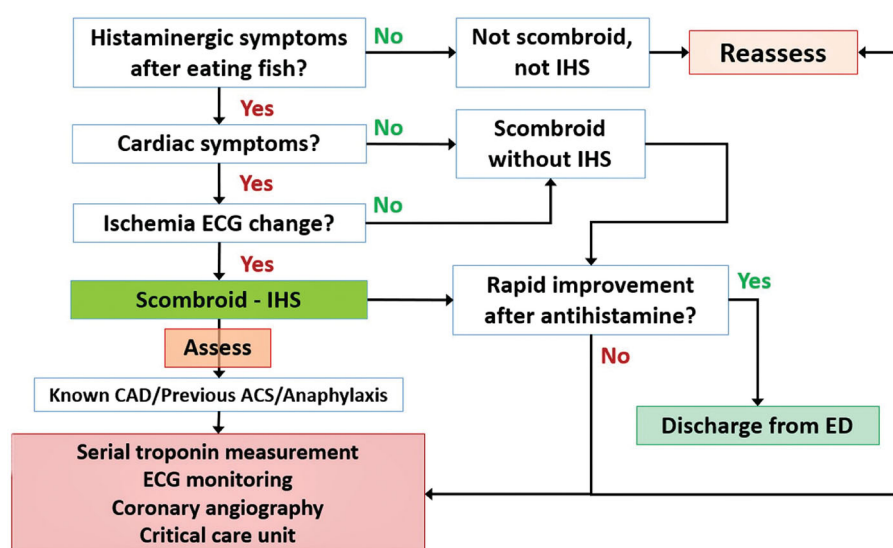


Figure 4. Proposal of diagnostic flow-chart in scombroid patients presenting to emergency department with signs/symptoms suggestive of myocardial ischemia. Caution is needed in patients with CAD, history of prior ACS, and/or allergic diathesis because they are at risk of coronary plaque destabilization and should be admitted to coronary care unit and cardiac catheterization laboratory. ACS: acute coronary syndrome; CAD: coronary artery disease; IHS: ischemic heart syndrome.

bacterial growth. Time course relative to meal was 10 mins to 3 h. Although the low number of ACS patients during scombroid illness, it is likely that further patients might be underdiagnosed or missed due to unfamiliarity with that complication. As recently suggested [62], we propose "Ischemic Heart Scombroid" (IHS) as unifying definition for scombroid patients presenting at emergency department with cardiac symptoms. Severe hypotension, chest oppression and/or arrhythmias require 12-lead ECG recording and cardiac ultrasound, when possible, to make or rule out diagnosis. A clear relationship between severity of clinical picture and histamine concentration in fish food remnants cannot be established based on main findings from the present case series. As in typical ACS, most IHS patients showed ST-segment depression in the anterior/inferior leads, likely subtended by a histaminergic (and transient) coronary spasm, usually recovered by appropriate therapy. Occasionally, severely affected patients may present with life-threatening hemodynamic failure or ventricular arrhythmias.

Currently available studies suggest coronary angiography not to be necessary, except for patients at risk for coronary thrombosis, like those with known CAD, previous ACS, or history of anaphylaxis.

Conclusions

Acute myocardial ischemia may occur in some scombroid patients. Although prevention by appropriate treatment and storage of fish-food products unquestionably remains the best solution to the problem, important findings from the present study indicate the IHS as a benign condition, even if with a potential of hemodynamic failure in the acute stage. Our hypothesis-generating study encourages further work aimed at better understanding the pathophysiology of this syndrome, as well as predisposing and protective conditions.

Acknowledgements

The authors are sincerely grateful to Prof. Michael Mullins for his insightful editorial guidance in refining the manuscript. This study was not supported by any agency or third parts. Authors received no grants, equipment(s), drug(s), or a combination of these, no funding for this work from the National Institute of Health or other Societies.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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