Severe scombroid poisoning and life-threatening hypotension

Shalika Basnayake Katugaha ,[1] Andrea Christine Carter,[1] Shashank Desai,[1] Pelayia Soto[2]

[1]Inova Fairfax Medical Campus, Falls Church, Virginia, USA
[2]National Capital Poison Center, Washington, DC, USA

Correspondence to
Dr Shalika Basnayake Katugaha; skb1078@gmail.com

Accepted 9 April 2021

SUMMARY

Scombroid fish poisoning (SFP), the most common fish-related illness worldwide, is a histamine response caused by the heat stable toxin histamine. A healthy 48-year-old woman and co-author of this paper developed palpitations, tachycardia and hypotension 10 min after a tuna steak dinner. She subsequently developed numbness of her face, flushing, conjunctival erythema, abdominal pain, nausea, vomiting, diarrhoea, headache and chest pain. Her ECG revealed tachycardia with ST depression. Her hypotension did not respond to fluid resuscitation, and she required phenylephrine. Based on exposure history, clinical syndrome, exclusion of other diseases and consultation with poison control, a diagnosis of scombroid poisoning was established. The state health department was notified. The patient was weaned off vasopressors, dosed famotidine and discharged 43 hours after fish ingestion with no symptoms and normal ECG. SFP is an often misdiagnosed and underreported illness with the potential to cause life-threatening hypotension.

BACKGROUND

Scombroid or histamine food poisoning (scombrotoxism, scombroid ichthyotoxicosis) is a foodborne illness resulting from ingestion of *Scombroidea* fish (tuna, mackerel, albacore, bonito) or non-scombroid fish (mahi-mahi, amberjack, bluefish, herring, anchovies, sardines) undergoing bacterial decomposition and cheeses that contain unusually high levels of histamine.[1 2] Scombroid fish poisoning (SFP) is a histamine response caused by the ingestion of histamine, a heat stable toxin. Bacteria (*Proteus*, *Klebsiella*, *Enterobacter*, *Serratia*, *Citrobacter*, *Vibrio*, *Acinetobacter*, *Aerobacter*, *Escherichia coli*, *Morganella morganii*, *Pseudomonas aeruginosa*, *Clostridium* and salmonellae) are normal constituents of the fish gills and gastrointestinal tract. The bacteria contain an enzyme, histidine decarboxylase, which breaks down the amino acid histidine into histamine when the temperature of the flesh reaches above 40°F.[3] The histidine decarboxylase can continue to function even when the bacteria are no longer viable.[4] Many fish proteins contain histidine, but fish that are darker in colour tend to contain more. Each excursion above 40°F allows histamine to be produced, and the final amount of histamine is compounded.[5] Neither cooking, freezing nor canning will destroy the heat stable histamine.[6]

The US Food and Drug Administration (FDA) has mandated regulations for rapid cooling of captured fish.[6] Fish are cooled by refrigerated sea water, sea water-crushed ice slurries, quick gutting of fish and packing with ice. Larger fish and warmer waters carry the greatest risk of delayed cooling times. Starting at the fishing boat, data logs must document information such as the earliest possible time of death, air and water temperatures and fish cooling method hourly. These logs are to be passed along and scrutinised continuously until the final destination is reached: the grocery store, restaurant or other food location.[5]

Freshly caught fish have less than 1 mg of histamine/100 g of flesh. A histamine concentration of 20 mg/100 g is considered to be the threshold of clinical poisoning, and levels over 100 mg/100 g are related to severe poisonings.[1] The FDA maximum allowable histamine level is 5 mg/100 g fish.[1] SFP most often occurs after the ingestion of fresh rather than canned fish, which have more regulatory scrutiny.[7] The fish sometimes contain a 'peppery' taste.

CASE PRESENTATION

A 48-year-old woman and co-author of this paper presented to the emergency department (ED) with palpitations, face numbness, head flushing, redness in her eyes and recorded heart rate (HR) in the 120 s and systolic blood pressure (BP) 82 mm Hg despite attempts to hydrate. Symptoms started 1 hour and 15 min earlier after a normal tasting meal of fully cooked tuna steak (figure 1).

The patient was a physically active woman, non-smoking and with a medical history of coronary vasospasm worked up over 10 years prior (with normal coronary CT angiography (CTA) and stress echocardiogram) that occasionally causes chest pain with exertion. She did not take any medications and had no known drug allergies. She denied similar reactions to food or other substances in the past. Her family history included chronic obstructive pulmonary disease (COPD), diabetes, pernicious anaemia and thyroid disorder.

Prior to the tuna meal, the patient had no symptoms. On arrival to the ED, she developed abdominal pain, nausea and vomiting, and explosive diarrhoea. She endorsed a headache and felt pre-syncopal. Despite abnormal vital signs at home, she had normal temperature and vital signs on initial ED check. She was well-developed and uncomfortable appearing.

To cite: Katugaha SB, Carter AC, Desai S, *et al*. *BMJ Case Rep* 2021;**14**:e241507. doi:10.1136/bcr-2020-241507

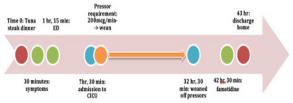

Figure 1 Timeline of events.

She had conjunctival injection. Her neck, cardiac, pulmonary, abdominal, extremity, neurological and dermatological examinations revealed no abnormalities. She had no bronchospasm, rash, urticaria, angioedema or other signs of allergy. Her ECG was normal.

On re-evaluation 2 hours later, the patient's HR was in the 120 s and BP 79/42 mm Hg. Coinciding with hypotension, the patient experienced acute-onset chest pain that radiated to her jaw and bilateral upper extremities, left greater than right. She received 3 L of normal saline (NS) without improvement in her pressures or symptoms. Because of the hypotension and chest pain, a follow-up ECG was done which showed tachycardia with ST depression in leads II, III, augmented Vector Foot (aVF) and V3–V6 (figure 2). The interventional cardiologist noted sinus tachycardia with no evidence of ST elevation myocardial infarction and recommended supportive care and heparin pending further work-up to rule out pulmonary embolus (PE). For ongoing hypotension despite fluid resuscitation, she was started on phenylephrine, which increased her systolic BP to the 100 s. She was admitted to the Cardiac Intensive Care Unit (CICU) on hospital day (HD) 1.

INVESTIGATIONS

Please see table 1 for pertinent elevated laboratory values: lactic acid, white cell count and glucose.

Normal/negative laboratory values included: troponin, haemoglobin, platelet count, sodium, potassium, creatinine, calcium, protein, liver function tests, albumin and urinary pregnancy test. Her urinalysis was notable only for ketonuria and proteinuria. She had negative blood cultures, influenza testing and stool studies for *Cryptosporidium parvum* and *Giardia lamblia*. She had a normal chest X-ray, chest CTA and bedside echocardiogram.

DIFFERENTIAL DIAGNOSIS

The patient's differential included cardiogenic shock related to acute coronary syndrome, but her cardiac markers were negative. Pericarditis and myocarditis were considered because of her sudden onset of tachycardia and hypotension with diffuse ST segment depressions. In light of past workup, vasospasm of anatomically small coronary arteries may also have explained chest pain in the setting of hypotension. Also in the differential was coronary microvascular dysfunction. PE was ruled out since the CTA was normal. Distributive shock was also in the differential in the setting of hypotension and lactic acidosis. We ruled out septic shock due to pneumonia, urinary tract infection and influenza. Viral or bacterial gastroenteritis may have been culprits because of the vomiting and diarrhoea. Additional considerations were allergic reaction, staphylococcal enterotoxin-induced food poisoning and other types of marine foodborne poisoning.

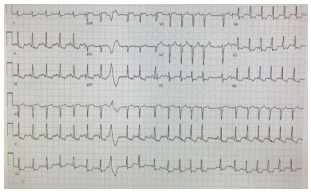

Figure 2 ECG reveals tachycardia, diffuse ST depressions with ST elevation on augmented Vector Right (aVR).

Table 1 Pertinent elevated laboratory values

Lactic acid	White cell count	Glucose
2.9 mmol/L	13.5×10^9/L (82% neutrophils, 12% lymphocytes)	244 mg/dL

TREATMENT

Given exclusion of cardiac, infectious and metabolic etiologies and the sudden and rapidly resolving course, we considered the patient's exposures further. The infectious diseases (ID) physician consulted with poison control and a working diagnosis of SFP was established. No one else had consumed the tuna, and the tuna was not available for testing. The state health department was notified, interviewed the patient and notified the local grocery store. Though there is no definitive connection to our case, the FDA investigated and identified 47 cases of SFP related to yellowfin tuna that occurred within the 2-month period surrounding the patient's admission.[8] There was a yellowfin tuna supplier recall in the USA for production in 2019 affecting eight companies.[9]

OUTCOME AND FOLLOW-UP

After the CTA, heparin infusion was discontinued. The patient was initiated on broad spectrum antimicrobials. She required phenylephrine, up to 200 mcg/min, which was weaned by HD2. On HD2, she received a dose of famotidine, was asymptomatic and was discharged 43 hours after fish ingestion. As an outpatient, she had a normal ECG follow-up and coronary CTA showing 20%–50% stenosis in the left anterior descending artery.

DISCUSSION

The onset of symptoms in SFP usually occurs within a few minutes after ingestion of implicated food and are maximal about 2 hours after ingestion.[10] The effects of poisoning can last for up to 48 hours.[1] The severity of symptoms depends on the quantity of histamine ingested, rate of histamine deactivation and individual sensitivity.[6] The illness typically runs a mild, self-limiting course with most patients reporting flushing, rash, pruritus, sweating, palpitations, headache, nausea, vomiting, abdominal pain and diarrhoea.[6] Our patient did report a majority of these symptoms including palpitations, headache, nausea, vomiting, abdominal pain and diarrhoea. Major or severe poisoning includes localised swelling around the mouth and tongue, bronchospasm, wheezing, respiratory distress, hypotension or hypertension, acute pulmonary oedema, dysrhythmias, myocardial dysfunction, ischemia or infarction.[1] There are few isolated reports of adverse effects of scombroid poisoning such as hypotension, bronchospasm, anaphylactic shock, arrhythmias and visual loss.[1] Reviewing the last 10 years of National Poison Data System information from the American Association of Poison Control Centers, the majority of case exposures related to SFP with known outcomes resulted in minor effects (50.79%). Moderate effects were reported in 36.72% of the cases, major effects in 1.71% and no effects in 10.78%.[11]

Table 2 Table of all reported cases of scombroid fish poisoning and life-threatening hypotension

	Country	Age/ gender	Medical history	Fish ingested	Fish taste	Ingestion to start of symptoms	Associated symptoms /PE	Blood pressure	ECG	Therapy	Resolution of symptoms
Resuscitation 2007	UK	80F	Hypertension	Mackerel		'After finishing meal'	Dizziness, nausea, vomiting, collapse, loss of consciousness; erythematous rash on anterior aspect of neck	60/40 mm Hg	'Unremarkable'	Intravenous fluids, intravenous cyclizine, oral chlorpheniramine	Discharged after 24 hours[12]
Central European Journal of Medicine 2010	Romania	20F	'Neg for cardiac, respiratory or allergic diseases'	Fried mackerel	'Peppery'	10 min	Flushing, headache, nausea, vomiting, anxiety, palpitations; erythema, injected conjunctivae, tachycardia	70–85/ 40–55 mm Hg	Sinus tachycardia with ST segment depression in anterior and inferior leads, and ST segment elevation in leads aVR, aVL, V1	Intravenous fluids (crystalloid solutions 2000 mL in 1 hour followed by 80 mL/hour infusion for the next 6 hours) and subcutaneous epinephrine (0.5 mg sol. 1:1000, repeated after 15 min), intravenous diphenhydramine (50 mg, repeated after 4 hours) and cimetidine (300 mg, repeated after 6 hours)	Discharged from ED after 24 hours of observation, being asymptomatic and having normal ECGs[1]
Central European Journal of Medicine 2010	Romania	26F	'Neg for cardiac, respiratory or allergic diseases'	Fried mackerel	'Peppery'	10 min	Flushing, headache, nausea, vomiting, anxiety, palpitations; erythema, injected conjunctivae, tachycardia	70–85/40–55 mm Hg	Sinus tachycardia with ST segment depression in antero-lateral and inferior leads, and ST segment elevation 1–3 mm in leads aVR, V1	Intravenous fluids (crystalloid solutions 2000 mL in 1 hour followed by 80 mL/hour infusion for the next 6 hours) and subcutaneous epinephrine (0.5 mg sol. 1:1000, repeated after 15 min), intravenous diphenhydramine (50 mg, repeated after 4 hours) and cimetidine (300 mg, repeated after 6 hours)	Discharged from ED after 24 hours of observation, being asymptomatic and having normal ECGs[1]
Central European Journal of Medicine 2010	Romania	44F	'Neg for cardiac, respiratory or allergic diseases'	Fried mackerel	'Peppery'	10 min	Flushing, headache, nausea, vomiting, anxiety, palpitations; erythema, injected conjunctivae, tachycardia	70–85/40–55 mm Hg	Accelerated idioventricular rhythm with ST-T changes in inferior leads	Intravenous fluids (crystalloid solutions 2000 mL in 1 hour followed by 80 mL/hour infusion for the next 6 hours) and subcutaneous epinephrine (0,5 mg sol. 1:1000, repeated after 15 min), intravenous diphenhydramine (50 mg, repeated after 4 hours) and cimetidine (300 mg, repeated after 6 hours)	Discharged from ED after 24 hours of observation, being asymptomatic and having normal ECGs[1]

Continued

Table 2 Continued

	Country	Age/ gender	Medical history	Fish ingested	Fish taste	Ingestion to start of symptoms	Associated symptoms /PE	Blood pressure	ECG	Therapy	Resolution of symptoms
Cardiovasc Toxicol 2011	Italy	16F	'Without previous history of cardiac or pulmonary abnormalities, allergies, or other relevant diseases'	Grilled tuna		'Within a short time'	Flushing, palpitations, tachycardia, diffuse skin erythematous rash, nausea, abdominal pain, acute pulmonary oedema	90/60 mm Hg	First ECG: sinus tachycardia; After few minutes, a supraventricular tachycardia occurred with diffuse severe ST segment depression	Steroid, chlorpheniramine intravenous infusion, norepinephrine, epinephrine, diuretics	Rash resolution; myocardial ischemia and cardiogenic shock requiring mechanical ventilator support and continuous intravenous inotropics with resolution of symptoms 'only several days later'[14]
JGIM 2012	Canada	25F	Mild intermittent asthma, allergic rhinitis, eczema and recurrent ovarian cysts	Tuna sandwich made with a can of solid white tuna in water	'Odd taste and appearance,' 'She removed portions that appeared discoloured'	'Immediately on finishing the tuna'	Burning sensation in tongue, flushing and warmth, tongue, lip, face and ear swelling, an erythematous pruritic rash over face, neck and torso, dyspnoea, wheezing, abdominal pain, diarrhoea, severe headache	86/53 mm Hg		Three intramuscular doses of 0.3 mg 1:1000 (1 mg/mL) epinephrine, normal saline, intravenous methylprednisolone, ranitidine, diphenhydramine, and nebulised salbutamol	Discharged within 24 hours; Readmitted within 3 hours due to an asthma exacerbation; Four recurrent admissions for asthma exacerbations within 2 months[9]
AMJ 2015	Australia	30M	'Fit and well'	Cooked mackerel fish caught on a fishing trip; fish not refrigerated and exposed to sunlight for a prolonged period		2 hours	Widespread erythema, dizziness, profuse sweating and chest tightness; coronary artery vasospasm		Sinus tachycardia with marked widespread ST segment depression and ST elevation in aVR	Intravenous fluid rehydration, antihistamines and glyceral trinitrate	'Prompt resolution of chest pain and profound ischaemic ECG changes with glyceryl trinitrate'[15]
JACC 2019	USA	53M	Hypertension, alcohol use disorder, obstructive sleep apnoea	Home-cooked tuna steaks		1 hour	Chest pain with radiation to the back, dyspnoea, facial flushing, subjective warmth, acute-onset profuse diarrhoea; facial erythema, rash of upper torso, abdomen soft but distended with diffuse tenderness to palpation	88/48 mm Hg	Diffuse ST-segment depressions	Intravenous fluid resuscitation, famotidine and intravenous steroids and 0.3 mg of intramuscular epinephrine for assumed allergic reaction	Final diagnosis: vasospastic angina secondary to SFP, type two myocardial infarction; all symptoms resolved within 18 hours of presentation[6]
Case presentation	USA	48F	Coronary vasospasm	Fully cooked tuna steak from local grocery store	Normal appearance and taste	10 min	Palpitations, tachycardia, numbness of face, flushing, redness in eyes, abdominal pain, nausea, vomiting, diarrhoea, chest pain	79/42 mm Hg	Tachycardia with ST depression in leads II, III, aVF and V3–V6	CICU: Intravenous fluids, phenylephrine, famotidine	Asymptomatic and discharged in 43 hours ; no sequalae

ED, emergency department; PE, pulmonary embolus; SFP, scombroid fish poisoning.

Histamine causes vasodilatory effects: decreases total peripheral resistance, decreases BP and increases capillary permeability. Vasodilation and reduced peripheral resistance may contribute to a significant fall in BP.[12] Histamine causes direct effects on the heart: increases contraction of both atrial and ventricular muscle by promotion of influx of calcium, increases HR by increasing diastolic depolarisation in the sinoatrial node, increases automaticity and triggered activity of atrial, Purkinje and ventricular fibres and slows atrioventricular conduction.[13] Histamine can cause, directly or indirectly, coronary spasm.[1] In this patient with left anterior descending artery narrowing, the histamine-induced hypotension, increased contraction and coronary spasm may have caused transient obstruction resulting in chest pain and ECG abnormalities. Histamine is also a chemical mediator of inflammation, airway smooth muscle contraction, gastric acid secretion and induction of pain and itching through sensory nerve stimulation.[1]

Diagnosis of SFP is clinical and requires appropriate history and index of suspicion. The gold standard of diagnosis is histamine quantification in the suspected fish. Although not routinely performed, blood sampling within 4 hours of ingestion may reveal a high plasma histamine concentration.[11]

Management of mild scombroid toxicity focuses on supportive care. For moderate symptoms, histamine antagonists are the mainstay.[6] Both H1 and H2 receptor blockers are recommended. H1 blockers are diphenhydramine, chlorpheniramine and promethazine. H1 antihistamines are effective in decreasing symptoms of scombroid.[1] H2 antihistamines, such as ranitidine, cimetidine or famotidine, may shorten the course of illness.[1] Supportive care with systemic steroids is not thought to provide benefit to scombroid treatment except in cases of bronchospasm.[1] Severe hypotension may require intravenous fluids and pressor support. No recommendations exist for the management of severe SFP.[6] The health department should be contacted for possible fish testing and further investigations. Scombroid poisoning is not an allergic reaction, and fish consumption does not have to be withheld.[1]

Our case is unique because of the haemodynamic consequence and duration of symptoms. In an extensive literature search on patients with SFP and life-threating hypotension, we found nine cases including this case from 2007 to 2019 (table 2). Ages were variable from 16 to 80. Two patients were male and seven female. The ingested fish were mackerel and tuna. Seven of the nine patients had ECG changes. All patients received antihistamines. Our case is also unique in the high pressor requirement. Every patient had complete resolution of symptoms. With the exception of the 16-year-old girl with myocardial ischemia and cardiogenic shock, symptoms resolved immediately after therapy to 24 hours after presentation, and our patient had had the longest duration of symptoms reported. Of note, our patient did not receive histamine antagonists early in her course, and possible earlier use may have curtailed symptoms. Though SFP has the potential to cause life-threatening hypotension, there has never been a death due to SFP reported in the USA and only one death reported worldwide.[1]

Patient's perspective

I have been working in a hospital for 31 years. I am very fortunate that I have no chronic health conditions or do not take any medication on a regular basis. I cannot express in this small space what it was like to diagnose myself with shock. I was too weak to express to the new emergency room (ER) attending that despite my lack of medical history, I was having a medical emergency. I couldn't express completely that I needed intravenous pressor support after my second litre of intravenous fluid because I could not speak in complete sentences. I didn't know that I was writhing on the stretcher because I couldn't feel my arms or legs. Later after I was on 150 mg of neosynephrine I had to sleep suddenly and my breathing changed. I knew in my mind I must have a metabolic acidosis and was trying to correct my CO_2 with my respiratory drive. I was thinking all these things, taking in all the data and diagnosing myself but I did not have the ability to communicate it. It was a surreal experience to say the least. In the intensive care unit, I have always assumed my patients could hear me, now I know they can.

Learning points

- Scombroid poisoning is often misdiagnosed and therefore underreported.[1]
- History of recent fish consumption, especially tuna or mackerel, should raise suspicion of scombroid poisoning.
- Hypotension is a rare but serious presentation of scombroid poisoning.[1]
- Severe scombroid poising can be mistaken for acute coronary syndrome, cardiogenic or distributive shock.
- Prompt reporting will assist in preventing additional cases and outbreaks.

Contributors All authors contributed greatly to this work. SBK and PS drafted the initial manuscript. SBK is the ID consultant involved in the case and PS the toxicologist at Poison Control. It was edited thoroughly by the patient and SD. SD, the cardiologist in the case, specifically edited the cardiology/intensive care unit aspects.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests SK is currently employed by GlaxoSmithKline. She remains affiliated with Inova Fairfax Hospital, and the case is from when she was in practice at Inova Fairfax Hospital. Her work at GSK in vaccine research in no way is a competing interest as pertains to this case report about scombroid.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD
Shalika Basnayake Katugaha http://orcid.org/0000-0002-7163-0734

REFERENCES

1 Lionte C. An unusual cause of hypotension and abnormal electrocardiogram (ECG) — scombroid poisoning. *Open Med* 2010;5:292–7.
2 Taylor SL, Stratton JE, Nordlee JA. Histamine poisoning (scombroid fish poisoning): an allergy-like intoxication. *J Toxicol Clin Toxicol* 1989;27:225–40.
3 USDA. Fighting BAC! by chilling out. Available: https://www.fsis.usda.gov/wps/wcm/connect/fsis-content/internet/main/topics/food-safety-education/get-answers/food-safety-fact-sheets/safe-food-handling/fighting-bac-by-chilling-out/ct_index#:~:text=To%20survive%20and%20reproduce%2C%20bacteria,calls%20the%20%22Danger%20Zone.%22 [Accessed 4 Dec 2020].
4 Feng C, Teuber S, Gershwin ME. Histamine (scombroid) fish poisoning: a comprehensive review. *Clin Rev Allergy Immunol* 2016;50:64–9.
5 Florida Sea Grant. Preventing Scombrotoxin (histamine) poisoning on a fishing vessel. Available: https://www.youtube.com/watch?v=sHUu2zRxzwY&t=194s [Accessed 4 Dec 2020].
6 Manjur JE, Ciuffo MM, Burdowski J. Scombroid fish poisoning leading to vasospastic angina a rare etiology of chest pain. *JACC: Case Reports* 2019;1:322–6.
7 Wilson BJ, Musto RJ, Ghali WA. A case of histamine fish poisoning in a young atopic woman. *J Gen Intern Med* 2012;27:878–81.

8 Gallagher GM. *Fda investigates Scombrotoxin fish poisoning linked to yellowfin tuna. contagion live*, 2019.
9 US FDA. Outbreak investigation of Scombrotoxin fish poisoning: Yellowfin/Ahi tuna (November 2019). Available: https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwi5nNXxnrbtAhUBrFkKHSy8AU0QFjAAegQIAhAC&url=https%3A%2F%2Fwww.fda.gov%2Ffood%2Foutbreaks-foodborne-illness%2Foutbreak-investigation-scombrotoxin-fish-poisoning-yellowfinahi-tuna-november-2019&usg=AOvVaw2KshQe8RPAnoCVD6DgkZ5I [Accessed 5 Dec 2020].
10 Guly HR, Grant IC. Case of the month: Lesson of the week: don't forget scombroid. *Emerg Med J* 2006;23:955–6.
11 AAPCC. American association of poison control centers. Available: https://www.aapcc.org/ [Accessed 5 Dec 2020].
12 Borade PS, Ballary CC, Lee DKC. A fishy cause of sudden near fatal hypotension. *Resuscitation* 2007;72:158–60.
13 McInerney J, Sahgal P, Vogel M, *et al*. Scombroid poisoning. *Ann Emerg Med* 1996;28:235–8.
14 D'Aloia A, Vizzardi E, Della Pina P. A scombroid poisoning causing a life-threatening acute pulmonary edema and coronary syndrome in a young healthy patient. *Cardiovasc Toxicol* 2011;3:280–3.
15 Anastasius M, Yiannikas J. Scombroid fish poisoning illness and coronary artery vasospasm. *Australas Med J* 2015;8:96–9.