

Case Report

Scombrotxin poisoning: an important differential diagnosis for anaphylaxis

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Key Learning Points

- Scombrotxin poisoning is an acute illness characterised by histamine-release type symptoms contracted by the consumption of improperly processed fish such as tuna.
- Scombrototoxicosis may be mis-diagnosed as anaphylaxis, a diagnosis that can have a profound effect on the subsequent life of a patient
- Scombrotxin poisoning usually responds to high dose antihistamines but adrenaline, corticosteroids and bronchodilators should not be withheld in cases where there is hypotension or bronchospasm
- Mast cell tryptase should be taken at the time of presentation and serially at 3 and 24 hours from all patients with suspected anaphylaxis or scombrototoxicosis, to aid the subsequent diagnosis
- In all suspected cases, efforts must be made to obtain a sample of the fish which was consumed, to enable histamine testing.

Abstract

We report a case of scombrotxin poisoning, an acute illness that develops within minutes to hours of eating poorly processed oily fish, such as tuna or mackerel. It presents with symptoms that can mimic an anaphylactic reaction. It is presumed to arise due to ingestion of histamine that is formed by contaminating bacteria that have flourished during periods of suboptimal refrigeration, following capture. Knowledge of this underdiagnosed malady as a potential differential diagnosis for patients presenting with symptoms suggestive of histamine release is important. It is a notifiable condition. The alternative diagnosis of anaphylaxis may have significant lifestyle implications for the patient. This article reports on one such presentation and the way that the diagnosis was explored.

Keywords

Scombrotxin, scombroid, histamine, anaphylaxis

Case History

A 32-year old woman presented to a health centre following the acute onset of a rash. She described the onset of an erythematous, non-itchy rash over her trunk and limbs with associated flushing and palpitations within minutes of eating a fresh tuna steak, purchased from a supermarket fishmonger. She had eaten fresh tuna previously on many occasions with no symptoms.

She was previously fit and well, but did have a history of hypersensitivity reactions to aspirin and ibuprofen characterised by urticaria and inflamed conjunctivae. Her symptoms had always been mild, resolving either spontaneously or with antihistamines. There was no personal or family history of atopy. On this occasion, despite oral

antihistamines, her symptoms persisted and in view of this and a tachycardia of 125/minute, she was referred to hospital.

She arrived at the emergency department 3 hours after her symptoms had started with a blood pressure of 80/40 mmHg. Examination revealed a widespread erythematous rash but was otherwise unremarkable with no angioedema, urticaria or wheeze. The working diagnosis was anaphylaxis and intravenous chlorpheniramine and hydrocortisone were administered. She was given a rapid infusion of 2 litres of crystalloid followed by intramuscular adrenaline in view of persisting symptomatic hypotension. Her cardiovascular instability responded to this and she was transferred to the Medical Assessment Unit where, apart from an episode of transient abdominal pain and diarrhoea, she remained stable. Within 8 hours of presentation, the rash had completely resolved. The speed of onset and hypotension suggested histamine release, but the atypical history and absence of angioedema, urticaria or laryngeal oedema led to the consideration of alternative diagnoses.

A full blood count showed a mild neutrophilia of $8.6 \times 10^9/l$ but was otherwise normal including eosinophil and mast cell counts. Mast cell tryptase levels were performed at 11 and 24 hours after the first symptoms. These were normal at 3.9 and 4.3 ng/ml respectively (normal range 2-14 ng/ml). Total serum immunoglobulin E (IgE) at this time was normal at 90 IU/ml (normal range 0-100 IU/ml) and no specific IgE to tuna was detected.

She was observed overnight and discharged uneventfully after 24 hours on short courses of chlorpheniramine and prednisolone. Skin prick

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allergy testing with tuna was completely negative. A diagnosis of scombrototoxin poisoning was considered to be the most likely explanation for her symptoms.

Discussion

Scombrototoxin poisoning arises on consumption of fish containing high levels of histamine arising from contamination with bacteria during handling.¹ These bacteria form histamine via decarboxylation of histidine. Histidine occurs in large amounts in many fish, especially those of the scombroid family such as tuna and mackerel. Proliferation of the bacteria is promoted by inadequate refrigeration. Additional biogenic amines are also thought to play a role. Symptoms usually begin at levels > 100mg/100g (normal level: < 1mg/ml) but can present at levels as low as 20mg/100g.^{2,3} Histamine levels are not affected by subsequent cooking. The symptoms are similar to anaphylaxis, occurring within minutes of consumption and include flushing, erythema, diarrhoea and abdominal cramps. Less commonly patients develop angioedema, urticaria, bronchospasm or hypotension.

Scombrototoxicosis is often a diagnosis of exclusion with a history of rapid onset of typical symptoms following fish ingestion. The main diagnosis to exclude is an anaphylactic or allergic reaction. Tests that can be performed at presentation to help exclude these include levels of antigen-specific serum IgE and mast cell tryptase. The use of IgE is based on the assumption that a true allergy or anaphylaxis is usually driven by IgE. No tuna-specific IgE was detected in the 11hr sample thus excluding a diagnosis of a true IgE-mediated (i.e. anaphylactic/allergic) reaction.

Mast cell tryptase is a useful tool for investigating and monitoring cases of anaphylaxis. These are enzymes released in massive quantities in mast cell degranulation, which occurs in anaphylaxis. Ideally samples should be taken within 1 hour of symptom onset and serial levels

taken at 3 and 24 hours.^{4,5} Mast cell tryptase is highly specific for anaphylaxis but normal levels do not rule out anaphylaxis and are sometimes seen in cases of food-induced anaphylaxis.^{6,7,8} Elevated serum tryptase levels in anaphylaxis tend to return to normal within 6–8 hrs.^{4,5} Although mast cell tryptase levels in this case were normal, the samples were taken too late (at 11hrs and 24hrs) to allow exclusion of anaphylaxis. The absence of a response to skin-prick testing with tuna does not completely rule out an anaphylactoid reaction to a thus far unidentified contaminant in the tuna meal. Given her history consistent with salicylate sensitivity (aspirin and NSAIDs), this remains a possible differential.

A diagnosis of scombrototoxicosis can be further strengthened by testing the actual fish itself for histamine. We were unable to do this – neither the fish consumed nor the shipment it originated from were available.

Most cases of scombrototoxicosis present with mild, self-limiting symptoms which resolve within 12–36 hrs. Patients with more severe symptoms usually respond well to very high dose antihistamine therapy (up to 6 times normal hayfever dosages). A subset present with severe hypotension and/or wheeze, needing fluid resuscitation and/or bronchodilators. It is important in such cases that clinicians do not withhold potentially lifesaving steroids and/or adrenaline, as scombrototoxin poisoning and anaphylaxis are often clinically indistinguishable. Suspected cases must be reported to public health authorities for urgent investigation.

Interestingly her two children who consumed the same tuna steak remained asymptomatic. Similarly in groups of patients presenting simultaneously, there is wide variation in severity of symptoms.⁹ This observation has been attributed to dramatic variation in levels of histamine within different parts of the same fish and to a direct relationship between symptom severity and the amount of fish ingested.¹⁰

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