We present the case of a man with a history of migraines treated with propanolol, referred with a rash, diarrhoea, vomiting and hypotension. Our case highlights how prior beta-blocker use may prolong anaphylaxis and cause refractory hypotension.

**KEYWORDS:** Beta-blockers, prolonged anaphylaxis, tryptase, refractory hypotension

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**Case presentation**

A 43-year-old male IT consultant presented to the accident and emergency department of the Royal Free Hospital with a new rash, vomiting, diarrhoea and profound postural hypotension unresponsive to fluids. He had a long history of migraines for which he was taking prophylactic propranolol; on the day prior to admission, he had received a repeat prescription of propranolol from a new manufacturer, which contained cellulose, and eaten a meal containing cooked salmon.

On review by the medical team, he reported some facial and finger swelling and dizziness on sitting. Examination revealed lip and finger swelling and a widespread urticarial rash over the trunk and limbs (Fig 1). Measurement of lying and sitting blood pressures revealed a postural drop in systolic blood pressure of greater than 50 mmHg. The remainder of the examination was unremarkable. His blood tests were normal apart from a neutrophilia (white blood cell count 12.69×10^9/L, neutrophils 10.89×10^9/L) and elevated C-reactive protein (19 mg/L rising to 81 mg/L within 8 hours).

**Differential diagnosis**

This patient had been referred with refractory hypotension, diarrhoea and vomiting and a new rash, thought to be associated with a recent change in his beta-blocker manufacturer. His symptoms initially were thought to be due to viral gastroenteritis but this did not explain the new urticarial rash. With this in mind, it was thought that he showed a delayed anaphylactic response to cellulose or scombroid poisoning from salmon ingestion the day before. During the course of his illness, he developed a fever and bacterial sepsis was considered as another differential diagnosis for his refractory hypotension.

To confirm the diagnosis, we proceeded to measure the mast cell tryptase response and sent blood and stool for culture and viral polymerase chain reaction (PCR).

**Case progression**

Initially, the patient was treated with hydrocortisone, chlorpheniramine and intramuscular adrenaline (500 mcg of 1:1000 concentration). At first, he showed a good response with a reduction in facial swelling, fading of the rash and improvement in blood pressure. However, the response was limited and he subsequently experienced two further episodes of facial swelling and hypotension both requiring further doses of intramuscular adrenaline.

During the admission he developed a fever and intravenous ceftriaxone was commenced to treat potential bacterial sepsis, although subsequent blood cultures were negative. Further blood tests showed an initial rise in mast cell tryptase (Fig 2) supporting a diagnosis of anaphylaxis rather than scombroid poisoning. Additionally, PCR of stool was positive for norovirus.
administration of adrenaline and initiation of aggressive fluid
by norovirus infection. His management consisted of the
standing history of beta-blocker use and gastroenteritis caused
slow to treat and resuscitate, plausibly because of a long-
new cellulose-containing beta-blocker preparation. He was
protracted and difficult to treat anaphylaxis. 3 In our case, it
administration of epinephrine leading to a more severe,
tryptase and complete resolution of symptoms within 36 hours.

Discussion
In this case report, we describe the delayed presentation and
protracted reversal of an anaphylactic reaction in a patient
treated with beta-blockers. We show how mast cell tryptase
measurement can be useful in the follow-up of suspected
anaphylactic reactions, although clinicians must be mindful
that collection should not delay resuscitation. 1 It is likely in
this case that the symptoms were exacerbated both by prior
use of beta-blockers and a concomitant norovirus infection.
Scombroid poisoning was considered as a differential diagnosis
as it can lead to ‘allergic-like’ symptoms, including an urticarial
rash, vomiting, diarrhoea and hypotension. This is a complex
syndrome caused by biogenic amines – mainly histamine –
contained in seafood. However, it was felt that this was not
the cause because it typically results in no significant rise in
mast cell tryptase 2 and would usually affect all of the people
who ingested the fish. We also considered whether this was a
biphasic anaphylactic reaction but this was thought unlikely
because of the failure to fully respond before requiring more
treatment, the absence of a persistent or second rise in mast cell
tryptase and complete resolution of symptoms within 36 hours.

Beta-blockers inhibit both the endogenous and exogenous
administration of epinephrine leading to a more severe,
protracted and difficult to treat anaphylaxis. 7 In our case, it
appears that the patient experienced an allergic reaction to a
new cellulose-containing beta-blocker preparation. He was
slow to treat and resuscitate, plausibly because of a long-
standing history of beta-blocker use and gastroenteritis caused
by norovirus infection. His management consisted of the
administration of adrenaline and initiation of aggressive fluid
resuscitation, 4 which in this case was successful. If adrenaline
and fluids fail to restore the blood pressure, other agents like
glucagon could be considered. 5,6 Patients who have suffered a
suspected anaphylaxis should be observed closely and referred
to an appropriate allergy service for follow-up. Adverse drug
reactions should be reported to the Medicines and Healthcare
products Regulatory Agency (www.mhra.gov.uk). Clinicians
should also be aware of biphasic reactions (incidence ranges
from 1–20%), a reoccurrence of symptoms within 72 hours
following apparent complete recovery of anaphylaxis: management is the same as for the first episode. It has been
suggested that patients should be observed for 24 hours after
recovery in view of this possibility. 7–9

Key learning points
Consider a delay in presentation of anaphylaxis and response
to intramuscular adrenaline in patients who have been
taking beta-blockers.
Allergies to medicines may occur simply because of a change
in manufacturer.
Mast cell tryptase levels may be used to diagnose acute
anaphylaxis and exclude other differentials, like scombroid
poisoning, but measurement should not delay treatment.
Consider other causes of refractory hypotension, including
sepsis.
Patients may require observation for up to 24 hours to
exclude a biphasic reaction.

Conflicts of interest
The authors declare no conflicts of interest.

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the clinical details and images in this article.

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Fig 2. Response seen by the mast cell tryptase during the course of the
illness.

Mast cell tryptase (µg/L)