

### Fatal anaphylaxis due to transcutaneous allergen exposure: An exceptional case



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#### Clinical Implications

- We describe an unprecedented case of food-induced fatal anaphylaxis, with severe cutaneous exposure through excoriated skin but no obvious ingestion. This highlights the importance of treating symptoms of anaphylaxis promptly in someone with known food allergies, even where exposure is unclear.

#### TO THE EDITOR:

We describe a case of fatal anaphylaxis in a 13-year-old British boy of North Indian descent, in the absence of obvious oral ingestion but under circumstances of extreme cutaneous allergen exposure through excoriated skin.

The patient was diagnosed in early childhood with severe atopic eczema and multiple IgE-mediated food allergies (cow's milk, egg, wheat, legumes, peanut, tree nuts), with at least 3 episodes of anaphylaxis occurring following diagnosis, none thought to be due to milk but 1 definitely caused by wheat that responded to intramuscular epinephrine. His last documented skin prick tests in 2016 were positive to cow's milk extract (4 mm), egg (4 mm), wheat (7 mm), peanut (7 mm), and cashew (10 mm). He was diagnosed with asthma at 5 years and prescribed daily inhaled beclomethasone, and perennial allergic rhinitis with seasonal exacerbation. Despite regular reviews, his asthma control remained suboptimal with frequent breakthrough symptoms most days. Last recorded lung function testing, approximately 7 months before the fatal event, demonstrated a reversibility of 34% in FEV<sub>1</sub>. A further follow-up appointment was cancelled by the hospital because of staffing issues and not rebooked. His eczema remained active despite daily treatment with 0.1% mometasone furoate and emollients.

The fatal event occurred at school in 2017; the circumstances were subject to a criminal investigation, and the chronology of events is based on sworn witness statements. Another child threw a 2 × 2 cm piece of cheese from a sandwich (containing wheat) at the patient, which dropped down the back of his shirt collar. The patient complained of localized pruritus and became increasingly agitated, scratching furiously at his neck and back. He was given oral chlorphenamine within 5 minutes by school staff, but the reaction rapidly progressed. He pulled off his shirt, and was noted to have blood on his back due to the excoriation. He was visibly distressed with labored breathing, and self-administered salbutamol via his inhaler 9 minutes after exposure. The school called for an emergency ambulance, but his breathing further deteriorated and a staff member administered an Epipen 0.3 mg at 13 minutes after exposure (into the anterolateral thigh). He lost consciousness 2 minutes later with no detectable signs of life, and resuscitation was

commenced. The Epipen device used had been prescribed to the patient for use in school, and was 11 months past its expiry date.

No further doses of epinephrine were administered until advanced resuscitation by the attending paramedics, who arrived 24 minutes after initial exposure. At this stage, the patient was pale, exhibited agonal breathing, and had no recordable pulse or blood pressure; cardiac monitoring demonstrated pulseless electrical activity. He was intubated and advanced life support initiated (including intraosseous epinephrine at 35, 38, and 41 minutes and intramuscular epinephrine at 43, 48, and 53 minutes after exposure). Ventilation was difficult, with bilateral expiratory wheeze and a "sharks-fin" appearance to the end-tidal capnography waveform, consistent with intrathoracic airway obstruction. Spontaneous circulation was restored 47 minutes after initial exposure. He was transferred to the intensive care unit but never regained consciousness. Testing was consistent with hypoxic brain injury secondary to cardiac arrest, and life support was withdrawn 12 days later. Postmortem findings were nonspecific for anaphylaxis, which is unsurprising given the time between anaphylaxis and death. A sample taken for mast cell tryptase during initial resuscitation in hospital was unfortunately unsuitable for analysis; a convalescent sample taken 24 hours later was 4.7 µg/L (normal). The chronology of symptoms strongly supports food-induced anaphylaxis as the most likely explanation.

The coronial and criminal investigations both concluded there was no evidence to suggest an oral route of exposure: there are multiple sworn witness statements from both adult staff and students regarding the trajectory of the cheese, removal of the shirt by the patient, and the fact he was experiencing severe pruritus causing excoriation—all of which make it highly unlikely for oral exposure to have occurred, at least before self-administration of the inhaler by which time he was already experiencing significant anaphylaxis.

We believe this is the first documented case of fatal anaphylaxis potentially due to cutaneous exposure to a food allergen, in the absence of oral exposure. Reactions from skin contact to allergens are well described,<sup>1,2</sup> but those resulting in anaphylaxis are limited to a few case reports<sup>3,4</sup>; none resulted in fatality. These include a 12-month-old infant with cow's milk allergy who developed dyspnea and cyanosis 10 minutes after application of a casein-based cream onto severe diaper dermatitis<sup>3</sup> and a teenager who developed anaphylaxis (witnessed by an allergologist) following cutaneous cheese exposure.<sup>4</sup> Both reactions were treated successfully with epinephrine.

There are a number of recognized risk factors for severe anaphylaxis in this particular case: a teenage boy of Asian descent, with severe eczema and asthma as well as rhinitis<sup>5,6</sup>; the reaction occurred on a day when the pollen count was high. Although epinephrine was administered 13 minutes after exposure, administration was delayed because of uncertainty over appropriate use (despite earlier administration of salbutamol) and its potency may have been reduced because of expiration. No further epinephrine was administered until intraosseous access was secured by paramedics. This may have been a contributing factor, although the success of subsequent epinephrine would have been dependent on adequate circulation, either spontaneous or through cardiopulmonary resuscitation.

This case is noteworthy in that exposure to the allergen was not accidental, resulting in a criminal manslaughter investigation. The coroner considered this to be “a childish and thoughtless act, but was not calculated to cause serious harm” and recommended against criminal proceedings. Food allergy—related bullying is increasingly recognized, and health care professionals and school staff alike need to take steps to tackle this and improve safety, including asking food-allergic individuals about potential bullying at clinical review.<sup>7</sup>

We consider this case to be unique and unprecedented. It does not challenge standard advice that cutaneous exposure through nondenuded skin is extremely unlikely to cause severe reactions. Food anaphylaxis is *not* uncommon, but fatal anaphylaxis due to oral exposure is a rare but unpredictable event.<sup>6</sup> The literature reports contact reactions to food allergens, but anaphylaxis as a consequence is very rare. There are several factors in this case that might have uniquely contributed to the severe outcome. This case tragically highlights the risks associated with food allergy and the need for whole-school education — including tackling allergy-related bullying — to avoid what the inquest called a “missed opportunity” to educate pupils about the potential seriousness of food allergies.

Finally, this case reinforces the need for any symptoms consistent with anaphylaxis, in a person with known food allergies, to be treated promptly with intramuscular epinephrine, even where the circumstances of exposure are unclear.

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