
Letters

FATAL GAS GANGRENE RELATED TO SELF-INJECTION TREATMENT OF ANAPHYLAXIS

We describe a patient who died as a result of self-treatment of anaphylaxis. This case reminds us that even a low-risk intervention can sometimes have severe consequences.

The patient was a 49-year-old nurse employed at a nursing home who had a complex medical history, including asthma, chronic pain, hypertension, and obesity (body mass index [calculated as weight in kilograms divided by height in meters squared], 37). She had a number of episodes that could be interpreted as anaphylaxis. No trigger was proven and no clinical signs were evident on multiple hospital presentations, but her history and symptoms supported a diagnosis of anaphylaxis, and this diagnosis appeared on her hospital discharge reports. Serum tryptase levels at baseline and shortly after these occurrences were within the normal range and did not vary.

An epinephrine autoinjector (Epipen) was prescribed with an action plan. The episodes continued, and she used her autoinjector at the onset of symptoms before onset of signs (contrary to advice) at least 6 times during 2 years.

A typical episode, consisting of pruritus, rhinorrhea, wheeze, and throat irritation, occurred at her site of work after lunch. She self-injected 300 µg of epinephrine via autoinjector into her left thigh, self-administered 50 mg of prednisone orally, and additionally self-injected 50 mg of promethazine (site unknown). The latter 2 were not part of her prescribed treatment plan. Subsequent assessment by ambulance officers and emergency department physicians did not reveal any clinical signs of an allergic reaction. She was observed in the emergency department for 4 hours, with the only notable event being pain in the left leg.

Twenty-two hours after self-injection, she presented with left leg pain and signs of sepsis, with a temperature of 39.3°C, heart rate of 132/min, blood pressure of 154/76 mm Hg, and a respiratory rate of 26/min. At 24 hours, the diagnosis of gas gangrene was made on the basis of cutaneous discoloration and tissue crepitus. Intravenous benzylpenicillin and lincomycin were administered, and she was transferred for immediate surgery. In the following hour the cutaneous discoloration spread to cover an area between her hip and calf. Incision of the fascia revealed gray purulent muscle and bubbles of gas. She underwent a high thigh amputation. Microscopic examination of tissue fluid identified gram-positive bacilli, and subsequent culture confirmed *Clostridium perfringens*.

After surgery, signs of sepsis advanced. A computed tomographic (CT) scan at 44 hours demonstrated gas within the psoas muscle, placing the patient beyond surgical salvage. Supportive management continued, but the patient died at 50 hours after the self-injection.

This event cannot be ascribed to either the epinephrine injection or the promethazine injection specifically, but one of these injections introduced clostridial spores and may have helped provide environmental conditions to allow germination and growth. The CT scan of her unaffected thigh showed that the epinephrine autoinjector should have delivered the intended injection intramuscularly rather than subcutaneously.

Infection after intramuscular injection is rare. A large study¹ of 12,134 injections found no deep tissue infections and 15 cases of superficial abscess. However, at least 31 cases of gas gangrene associated with injections have been reported since 1960. Both intramuscular and subcutaneous injections were implicated, with a range of drugs. The most common single drug associated with this complication was epinephrine (10 reports); however, most of these were epinephrine in oil used to treat asthma in the 1960s.

Clostridial infection from injections derives from spores transported from the skin surface to deep tissue, where suitable nutrient conditions cause germination and rapid reproduction. Clostridial spores originate from decaying vegetation and the intestine and can often be found on normal skin; recovery of spores is not reduced by alcohol swabbing.² Local conditions conducive to germination³ are potentially enhanced by tissue necrosis induced by intramuscular injections⁴ and local ischemia induced by the vasoconstrictive effect of epinephrine. In this patient's case, scarring from multiple previous injections (revealed by CT scan), her occupation and obesity (increasing skin contamination risk), and the coadministration of corticosteroids are other potential cofactors. One could speculate on the increased risk of the introduction of foreign matter if the injection were delivered through clothing, especially if soiled.

It is difficult to make recommendations to reduce the risk of this extremely rare outcome. Several factors, including exact placement of injections and method of injection, remain unknown in this case. Avoidance of injection through soiled skin or clothing is recommended, but skin preparation is unlikely to be effective. We suggest that if persistent pain occurs in the setting of a recent intramuscular injection, this should lead to urgent assessment and careful monitoring.

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ANAPHYLAXIS TO MOPANE WORMS (IMBRASIA BELINA)

Food allergy is common in westernized countries, affecting 6% of children and 3.7% of adults in the United States.¹ The most notable

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types of food allergy are milk, egg, peanut, tree nuts, fish, and shellfish.¹ Regional variation depends on diet, such as snail allergy in the Mediterranean.² Mopane worm (MW), the larva of the emperor moth (*Imbrasia belina*), is harvested by hand, degutted, boiled, and dried.³ Dried MW has 3 times the protein content of beef by unit weight and is easily stored.⁴ They are an important source of protein and income in the Southern African rural population and a delicacy for the wealthy.⁴ Previously, 1 adult was reported to have MW allergy.⁵ We describe an adolescent with anaphylaxis to MW.

A 15-year-old Zimbabwean boy presented for evaluation a year after a severe reaction to eating 20 MWs. Ten minutes after ingestion, he experienced headache, dyspnea, cough, wheeze, palatal pruritus, urticaria, tongue, and lip swelling. Symptoms gradually resolved after antihistamine use, but drowsiness persisted for 48 hours.

Since the age of 8 years, he had mouth and ear itching to MW ingestion. Summer seasonal rhinitis started 12 years ago. Infantile eczema resolved after the age of 2 years. He was neither asthmatic nor drug or latex allergic. His mother has allergic rhinitis, asthma, and oral allergy syndrome. Two siblings have food allergy and allergic rhinitis, respectively. No long-term medications are used.

On examination, he was alert and well nourished, with a blood pressure of 120/80mm Hg, heart rate of 80/min, and respiratory rate of 14/min. Pertinent findings included infraorbital bluish discoloration, pale inferior turbinates, and pharyngeal cobblestoning. Other systems were all normal.

Skin prick testing (SPT) was performed using lancet and allergen extracts (ALK-Abelló, Madrid, Spain), with positive and negative controls read at 15 minutes. Positive reactions were to tree pollen (oak, *Acacia*), grass pollen (Bermuda, Timothy, maize), English plantain, dust mite mix (*Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*), and cockroach (*Blattella germanica*). SPT results were negative to molds, cat, and dog. Dried MW was reconstituted with normal saline. Direct SPT with this resulted in a wheal of 7 mm and a flare of 15 mm.

Further testing at the Allergy Diagnostic and Clinical Research Unit, University of Cape Town Lung Institute, showed a total IgE level of 622 kU/L. Positive ImmunoCap radioallergen sorbent assay (RAST) results were as follows: *D pteronyssinus*, 5.07 kUA/L; *Anisakis*, 0.06 kUA/L; tree mix, 0.06 kUA/L; weed mix, 0.55 kUA/L; grass mix, 4.98 kUA/L; mealworm, 3.39 kUA/L; *Schistosoma*, 0.59 kUA/L; and *Ascaris*, 0.18 kUA/L.

Allergen microarray test results (Immuno Solid-phase Allergy Chip [ISAC]; Phadia, Uppsala, Sweden) were positive for the following: Bermuda grass (nCyn d1), 23 ISAC standardized units (ISU); Timothy grass (rPhl p1), 4.6 ISU; Japanese cedar (nCry j1), 1.7 ISU; cypress (cCup a1), 14 ISU; *D pteronyssinus* (nDer p1), 2.3 ISU; *D pteronyssinus* (nDer p2), 2.8 ISU; *D farinae* (rDer f2), 3 ISU; olive (nOle e2), 0.9 ISU; and latex (rHev b8), 0.7 ISU.

Microarray test results were negative to foods (fruits, nuts, peanut, milk, egg, soybean, wheat, shrimp, codfish, carp), pollens (plane, ragweed, mugwort, saltwort), tropomyosin in shrimp (rPen a1, nPen i1, nPen m1), *D pteronyssinus* (rDer p10), cockroach (nBla g7), and *Anisakis* (rAni s3).

Western blot (WB) was then performed with chopped, dried MW; tumbled overnight in Tris-buffered saline; then centrifuged, filtered, and stored at -80°C . Established protein content was separated by sodium dodecyl sulfate–polyacrylamide gel electrophoresis and blotted onto polyvinylidene difluoride membrane. Blots were blocked with 2% powder milk and 0.05% Tween in Tris-buffered saline. The patient's serum was diluted 1:20, applied to a blot, and incubated on a rocking platform overnight. After washing with phosphate-buffered saline and Tween buffer, rabbit anti-human IgE

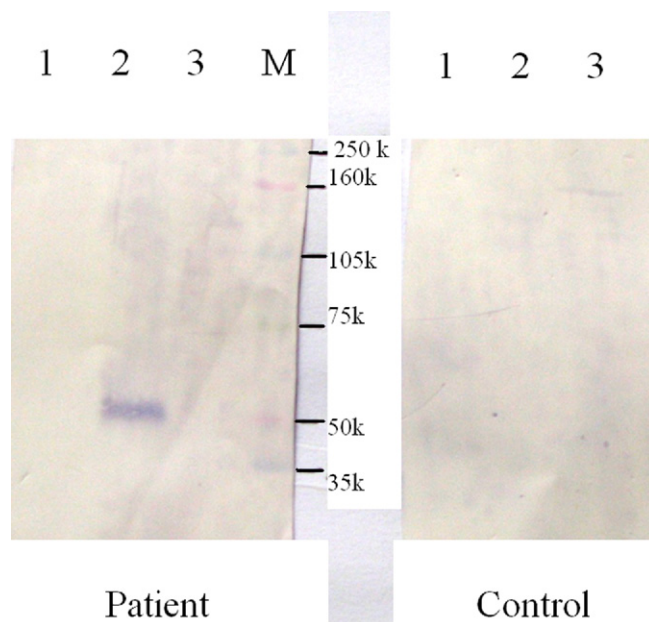


Figure. Western blot illustrating a strong 50-kD IgE binding protein recognized by the patient's serum to Mopane worms. 1, *Ascaris lumbricoides* extract; 2, Mopane worm extract; 3, *Anisakis* extract; M, molecular marker.

was applied and blot incubated for 2 hours. After extensive washing, the substrate solution was applied, and when development completed, the blots were rinsed and dried.

WB with 3 worms (*Ascaris*, *Anisakis*, and Mopane) and the patient's serum showed a clear band at 50 kD for MW and some faint bands for *Anisakis*. There were no visible bands for the control (Fig).

This atopic adolescent had anaphylaxis to ingested MW. The results of both SPT and WB to MW were positive, confirming sensitization. Sensitization to dust mites (SPT, ImmunoCap RAST, and ISAC), cockroach (SPT), *Ascaris* (ImmunoCap RAST), and *Anisakis* (ImmunoCap RAST and WB) suggest a cross-sensitization. This may result from glutathione transferases or tropomyosin, which have been implicated in cross-reactivity among *Ascaris*, dust mites, cockroach, crustaceans, and molluscs.^{6,7} Unfortunately, this was not detected by microarray testing with common recombinant animal and plant allergens, suggesting that the novel 50-kD MW allergen is not represented in the ISAC panel. Another possibility for this allergenic protein may be unrelated to MW itself but to their gut content if not properly prepared.

Further studies on the prevalence of this allergy and the immunologic and biochemical nature of the MW antigens are in progress.

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DOES THE EASI SCORE REFLECT ITCH SEVERITY?

Itch is the prerequisite symptom for a diagnosis of atopic dermatitis (AD). Chrostowska-Plak et al¹ reported a positive correlation between itching intensity and the Scoring of Atopic Dermatitis (SCORAD) index. We report our own recent findings regarding the correlation between clinical parameters of AD and the itching intensity in AD.

Our study included 83 patients who were diagnosed as having AD according to Hanifin's diagnostic criteria.² There were 53 men (64%) and 30 women (36%) (age range, 6–56 years; mean [SD] age, 20.6 [10.2] years). After assessing the Eczema Area and Severity Index (EASI) score, we evaluated the itching intensity at the time of examination (VAS_{itch}) and the degree of sleep disturbance due to itch (VAS_{sleep}) by using a 10-cm visual analog scale (VAS). All statistical analyses were performed using SPSS statistical software, version 15.0 (SPSS Inc, Chicago, Illinois). The associations among the EASI score, VAS_{itch}, and VAS_{sleep} were determined using Pearson correlation. $P < .05$ was considered statistically significant.

The EASI score ranged from 0.4 to 56.4 points (mean [SD], 10.8 [9.8] points), VAS_{itch} from 0 to 10 cm (mean [SD], 5.4 [2.8] cm), and VAS_{sleep} from 0 to 10 cm (mean [SD], 3.9 [3.3] cm). The EASI score was not correlated with VAS_{itch} ($r = 0.169$, $P = .13$, Fig A), whereas there were significant correlations between EASI score and VAS_{sleep} ($r = 0.346$, $P = .002$, Fig B) and between VAS_{itch} and VAS_{sleep} ($r = 0.512$, $P = .001$, Fig C).

Several clinical parameters are considered for assessing AD severity.³ Of these, the EASI score and the SCORAD index are widely used and validated in clinical trials.⁴ A study comparing the usefulness of the SCORAD index and the EASI score had shown that the SCORAD index is useful for detecting the development of AD, whereas the EASI score is useful for detecting the subtle differences in the severity of AD.⁵

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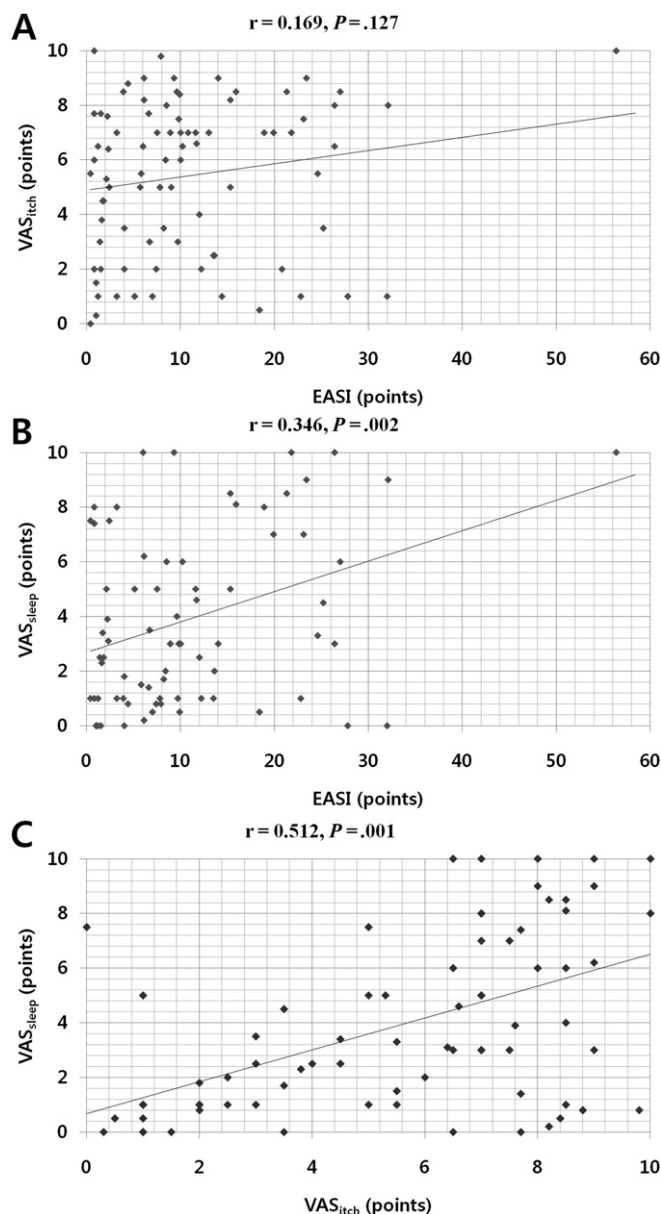


Figure. Correlation between the Eczema Area and Severity Index (EASI) score and itching intensity at the time of examination measured by visual analog scale (VAS_{itch}) (A), EASI score and degree of sleep disturbance due to itch measured by visual analog scale (VAS_{sleep}) (B), and VAS_{itch} and VAS_{sleep} (C).

Chrostowska-Plak et al¹ reported that the SCORAD index was significantly correlated with the itching intensity on the basis of the findings obtained by 2 methods: (1) validated 4-item questionnaire and (2) VAS for determining the itching intensity at the time of examination and at the time of maximal itching. However, we believe that the results of their study may not be significant because the SCORAD index involves a VAS for evaluating the itching intensity as a part of the AD assessment.¹ Therefore, in our study, EASI score was used as the clinical parameter for assessing the severity of AD to prevent the statistical bias in the interpretation of