Anaphylactic Shock Following Spray of “Gulliver” (Azimsulfuron), A Herbicide Belong To Sulfonylurea Group; A Case Report

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Case Report

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Abstract

Background

Anaphylactic shock is a life threatening emergency encountered frequently with rising incidence worldwide. It is an extreme end of a spectrum of allergic reactions commonly present following multiple triggers, including food, medications, insect stings, dyes, etc. Patients usually present with a combination of dermatological, cardiovascular, respiratory and gastrointestinal symptoms. This is a rarely encountered case of anaphylactic shock following the spraying of sulphur containing herbicide called “Gulliver” (Azimsulfuron).

Case presentation

This 58-year-old farmer with previously uneventful past medical history was admitted to the emergency unit with an episode of faintishness and urticarial rash while working in a paddy field. There was no shortness of breath, wheezing or angioedema. He revealed that he had sprayed an herbicide call ‘Gulliver’ (Azimsulfuron, a sulphur containing herbicide) in the morning for 3 to 4 hours without using proper protective equipments and cloths. He denied any insect bites or stings. On admission, he was in shock with blood pressure 60/48mmHg, pulse rate 84 beats per minute with bounding pulses and warm peripheries. He was managed as anaphylactic shock according to the national health guideline and hemodyemically stabilized within 20 minutes of initial resuscitation including intramuscular adrenaline.

Conclusions

It is a well-known fact that a significant proportion of the general population has an allergy to sulphur containing medications. However, this was a rare encounter, detected with a high degree of suspicion. In Sri Lanka, a survey in 2016/2017 revealed 27 percent of the total labour force was engaged in the agricultural sector. We emphasize the importance of consideration of allergy and anaphylaxis in similar presentation in an agricultural based country like Sri Lanka.
allergic history. Therefore, high degree of suspicion and early recognition will prevent a fatal outcome as in this case presentation.

**Case Presentation**

58-year-old farmer with previously uneventful past history is admitted to the emergency treatment unit (ETU), teaching hospital Peradeniya, with an episode of faintishness and urticarial rash while working in the paddy field. It was a generalized urticarial rash involving the face, trunk, upper limb and lower limbs. It was gradual in onset over 5 to 10 minutes and 20-30 minutes after the onset of rash, he experienced faintishness. There was no shortness of breath, wheezing or angioedema. He denied nausea, vomiting, diarrhea, abdominal pain or fever. There was no chest pain or palpitation. These symptoms occurred while working in the paddy field in the afternoon on his routine schedule. He denied intake food from outside at least for more than 48 hours and has not taken unfamiliar food items in the morning. He was not on any medication. He revealed that he had sprayed an herbicide by the name of ‘Gulliver’ (Azimsulfuron, a sulphur containing herbicide) in the morning 3 to 4 hours earlier without using proper protective equipments and cloths. He used a manually spraying herbicide tank for about 3 hours in the morning. He denied attempted or accidental intake of poison or possibility of snake bite. There was no past history of allergy to drugs, food, stings or any other unknown substances. He is an alcohol consumer and last drink was two days before.

On admission, he was in shock with blood pressure 60/48mmHg, pulse rate 84 beats per minute with bounding pulses and warm peripheries. There was a generalized erythematous urticarial rash involving the face. There were no swollen lips, tongue, or uvula and no mucosal ulceration including the genital area. He was not pale; the jugular venous pressure was normal and did not have ankle swelling. His respiratory rate was 20 breaths per minute, on air saturation was 98% and there were no broncho spasms. Abdominal examination was normal. He was conscious and rational.

He was managed as anaphylactic shock based on clinical criteria that the presence of urticaria, rash and systolic blood pressure less than 90mmHg with the other supportive clinical features. His basic investigations, including liver enzymes, renal function test and electrocardiogram were within normal range (White blood cell – 10.5×10³/µL, Hemoglobin-16.5g/dL, platelet-312×10³/µL, C reactive protein-9.3mg/dL, Aspartate aminotransferase – 44U/l, Alanine aminotransferase – 34U/l, Na+-142 mmol/L, K+-3.5 mmol/L, Serum creatinine-85µmol/L). Serum tryptase or plasma histamine levels were not done due to non-availability of these tests at Teaching Hospital Peradeniya.

He was managed as anaphylactic shock at the emergency treatment unit. Following standard resuscitation procedures, dual intravenous access was established and one liter of intravenous normal saline bolus was given. Intramuscular adrenaline 1:1000, 0.5ml followed by intravenous hydrocortisone 400mg and intravenous chlorpheniramine 10mg were given. Oxygen via face mask 5L/min was given. Within 20 minutes his blood pressure was stabilized and was transferred to a medical ward. His vitals including blood pressure, pulse rate and saturation were monitored hourly in the high dependency unit for
24 hours and intravenous hydrocortisone 100mg 6 hourly with oral chlorpheniramine 4mg 8 hourly were given. Urticarial rash was disappeared and he was discharged following two days hospital stay on oral chlorpheniramine 4mg daily with oral prednisolone 10mg daily for 3 days. As the possible allergen in this case was the exposure to herbicide called ‘Gulliver’ (Azimsulfuron, a sulphur containing herbicide), he was advised to avoid spraying and exposure of Azimsulfuron and other sulphur containing drugs with written instructions.

**Discussion And Conclusions**

According to The World Allergy Organization (WAO) Anaphylaxis Committee, anaphylaxis is defined as “a serious systemic hypersensitivity reaction that is usually rapid in onset and may cause death. Severe anaphylaxis is characterized by potentially life-threatening compromise in the airway, breathing and/or the circulation, and may occur without typical skin features or circulatory shock being present”. It is a spectrum of disorders with the severity of symptoms ranging from mild, localized skin reaction to fatal anaphylactic shock resulting cardio respiratory arrest (3). Clinical features can be dermatological manifestation including mucocutaneous involvement, cardiorespiratory, gastrointestinal and symptoms and signs of other organ system involvement (4). Urticarial rash, angioedema causing swelling of the lips, tongue, oropharynx and uvula are the common mucocutaneous manifestation of anaphylaxis. Although mucocutaneous manifestations are the common clinical features, which alone is not enough to diagnose anaphylaxis. In fact skin manifestations can be subtle or absent in 10–20% of cases (4). Respiratory features include stridor, hoarse voice, bronchospasm causing cough or wheezing, prolong expiration, low saturation and cardiovascular features are peripheral vasodilation causing warm peripheries, high volume pulses, arrhythmias, low blood pressure postural hypotension leading to collapse and syncope (severe shock can cause pale, clammy peripheries). Common gastrointestinal (GI) symptoms include nausea, vomiting, abdominal cramps and diarrhea. GI symptoms alone are not diagnostic.

Onset of symptoms and fatal anaphylaxis depends on the type of trigger, dose, route and type of reaction (idiosyncratic vs. dose dependent) (4). Deaths caused by intravenous medications occur most commonly within 5 minutes; Insect stings cause collapse from shock after 10–15 minutes; and fatal anaphylaxis due to food reactions typically cause cardiorespiratory arrest after approximately 30 minutes. Cardiorespiratory arrest more than 4 h after the initial allergen exposure is rare (4).

Ig E-mediated anaphylaxis is considered the classic and most frequent mechanism in which complex immunological cascade is triggered by the interaction of an allergen with the allergen-specific Ig E receptor complex expressed on effector cells, predominantly mast cells and basophils resulting in the release of preformed histamine and other mediators (3). These chemical mediators can result in several pathophysiological changes such as; fluid extravasation leading to airway edema and reduced intravascular volume; vasodilatation leading to distributary shock and reduced effective arterial perfusion; Smooth muscle contraction leading to bronchospasm (and abdominal cramps); direct effect on myocardium leading to myocardial dysfunction and cardiogenic shock. These mechanisms altogether, ultimately can cause tissue hypoxia and hypotension (4).
There are multiple common triggers and most of them are natural substances, but few are synthetic chemicals and medicines. However, most common allergens identified can be categorized into food, drugs and venom (5). In this case presentation, the patient did not have past known allergen. However, he has sprayed sulphur containing herbicide call 'Gulliver' (Azimsulfuron) without full protection equipments for about 3 hours that may have led absorption of chemical into circulation via the skin, mucus membrane and respiratory routes resulting in anaphylactic shock. Azimsulfuron is highly soluble in water, semi-volatile and, appears to have potential for leaching to groundwater. Although it has a low mammalian toxicity, it has high potential for bioaccumulation (6). There are no reported cases related to anaphylaxis following spray of Azimsulfuron. However, it is well known fact that a significant proportion of the general population has an allergy to sulphur containing drugs. Figure 1 below illustrates 2D structure diagram of Azimsulfuron (6).

Diagnosis of anaphylaxis is clinical and serum tryptase and histamine levels might support the diagnosis retrospectively. The WAO Anaphylaxis Committee has proposed to amend the current NIAID/FAAN criteria to make two simplified criteria as mentioned bellow (3);

Anaphylaxis is highly likely when any one of the following 2 criteria is full field;

1. Acute onset of an illness (minutes to several hours) with simultaneous involvement of the skin, mucosal tissue, or both (e.g., generalized hives, pruritus, flushing, swollen lips-tongue-uvula)

And at least one of the following:

   a. Respiratory compromise (dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)
   b. Reduced BP or associated symptoms of end-organ dysfunction (hypotonia [collapse], syncope, incontinence)
   c. Severe gastrointestinal symptoms (severe crampy abdominal pain, repetitive vomiting), especially after exposure to non-food allergens

2. Acute onset of hypotension or bronchospasm or laryngeal involvement after exposure to a known or highly probable allergen for that patient (minutes to several hours), even in the absence of typical skin involvement.

   a. Hypotension defined as a decrease in systolic BP greater than 30% from that person's baseline, OR i. Infants and children under 10 years: systolic BP less than (70 mmHg + [2 x age in years]) ii. Adults and children over 10 years: systolic BP less than <90 mmHg.
   b. Excluding lower respiratory symptoms triggered by common inhalant allergens or food allergens perceived to cause "inhalational" reactions in the absence of ingestion.
   c. Laryngeal symptoms include: stridor, vocal changes, odynophagia.
   d. An allergen is a substance (usually a protein) capable of triggering an immune response that can result in an allergic reaction. Most allergens act through an IgE mediated pathway, but some non-
Allergen triggers can act independent of IgE (for example, via direct activation of mast cells).

As in this case presentation, with a high degree of suspicion towards the possible trigger, an early diagnosis of anaphylaxis can reduce fatal outcomes. In Sri Lanka, a survey in 2016/2017 revealed 27 percent of the total labour force was engaged in agricultural sectors (7). We emphasize the importance of consideration of allergy and anaphylaxis in similar presentation in an agricultural based country like Sri Lanka.

**Abbreviations**

US: United state

ETU: Emergency Treatment Unit

WAO: World Allergy Organization

NIAID: National Institute of Allergy and Infectious Disease

FAAN: Food Allergy and Anaphylaxis Network

**Declarations**

**Ethics approval and consent to participate**

This case study was reported in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments. Ethical approval is not applicable because this is a case report, and all personal health information was deidentified.

**Consent for publication**

Written informed consent was obtained from the patient to publish medical information in this case report.

**Availability of data and materials**

Data sharing is not applicable to this article as no datasets were generated or analyzed during this case report.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors’ contributions**

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**Authors’ information**

Dr. Lankarathna is a registrar in general medicine at university professorial medical wards, teaching hospital Peradeniya who played major role with regard to diagnosis and management of this patient under supervision of prof. Arjuna Medagama, consultant physician and senior lecturer at university professorial medical wards, teaching hospital Peradeniya and Faculty of Medicine, University of Peradeniya.

**References**

Figures

Figure 1

Azimsulfuron (6).