Revised: 23 November 2021

Fatal outcome following multiple bee stings: A rare case

Mahdi Fakhar¹ | Zakaria Zakariaei^{1,2} | Ali Sharifpour^{1,3} | Mostafa Soleymani¹ | Ashkan Zakariaei⁴

¹Toxoplasmosis Research Center, Communicable Diseases Institute, Iranian National Registry Center for Lophomoniasis and Toxoplasmosis, Mazandaran University of Medical Sciences, Sari, Iran

²Toxicology and Forensic Medicine Division, Toxoplasmosis Research Center, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

³Pulmonary and Critical Care Division, Iranian National Registry Center for Lophomoniasis (INRCL), Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, Iran

⁴Babol Branch, Islamic Azad University, Babol, Iran

Correspondence

Zakaria Zakariaei, Toxicology and Forensic Medicine Division, Toxoplasmosis Research Center, Imam Khomeini Hospital, Mazandaran University of Medical Sciences, Sari, P.O box: 48166-33131, Iran. Email: ali.zakariaei@yahoo.com

Funding information

None

Abstract

Anaphylactic shock is an unexpected, life-threatening, and sometimes fatal occurrence that affects patients in 75% of instances without a prior history of allergies. The severity of the reaction can vary among individuals. We report a case who died suddenly after being stung by bees in various parts of his body.

K E Y W O R D S

anaphylactic shock, bee stings, sudden death

1 | INTRODUCTION

Insect stings can induce local or systemic symptoms that are usually moderate, but can also be severe and fatal.¹ The reaction to bee stings is one of the most common causes of anaphylaxis and sudden death. Each year, approximately 3% of adults' experience anaphylaxis as a result of insect bites.^{2,3} Bee stings are quite common all over the world and may be considered dangerous, but they rarely cause cardiac arrest.

Anaphylactic shock is an unexpected, life-threatening, and sometimes fatal occurrence that affects patients in 75% of instances without a prior history of allergies. According to current theory, the most common causes of hypersensitivity are drugs, hymenoptera toxins, and nutrients.⁴ The severity and duration of the reaction to bee venom and the incidence of symptoms can vary among individuals. Most people in the world experience a mild, non-serious

allergic reaction to bee venom. However, depending on the location and number of bee stings, a previous history of allergic reactions may increase the risk of serious lifethreatening outcomes. Insects of the order Hymenoptera, such as honey bees, wasps, ants, and hornets, are commonly involved in accidental stings of human beings all over the world. Hymenoptera venom consists of a combination of biologically active substances and enzymes, which cause localized and systemic reactions and can be fatal in rare cases. The prognosis and severity of the envenomation are directly related to the number of stings. Therefore, 50-500 stings can cause the death of an adult man.⁵ Simple stings are responsible for a mild reaction such as skin rash and urticaria, even occasionally with anaphylaxis, and multiple stings cause toxic shock syndrome with systemic symptoms.⁶

In most cases, patients who are referred to the emergency room after a bee sting, the first steps are

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made. © 2022 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd. WILEY_Clinical Case Reports

resuscitation and hydration with vascular expansion solutions. Morphine and acetaminophen are used to control pain, while antihistamines and corticosteroids in high doses are used to prevent anaphylaxis, and epinephrine is used in severe cases.⁷

2 | CASE PRESENTATION

On September 19, 2021, a 42-year-old man with a history of hypersensitivity to bee venom was referred to the emergency ward of a local hospital in Mazandaran Province, northern Iran. The patient was a smoker and an opium addict, with no history of dyslipidemia, hypertension, diabetes mellitus, coronary artery disease, or other significant illness.

The patient and his family were working on a farm when he suddenly became envenomated by a few bee stings in various parts of his body, including his neck and right leg. After 15 min, he developed vomiting, weakness, fatigue, dizziness, itch, urticaria, respiratory discomfort, and chest pain. He did not refer to the emergency department. After half to 1 h, he suffered hypotension and severe dyspnea due to anaphylactic shock, followed by cardiopulmonary arrest. The patient had no vital signs at the time of admission to the emergency room.

Immediately, cardiopulmonary resuscitation (CPR) processes were started. Unfortunately, after an hour, no suitable response was detected and the patient died. On examination, the conjunctiva of the eyes was congested as well as having a generalized erythematous rash over the face, neck, thorax, and lower limbs. One punctured sting with oozing of straw-colored fluid was seen on the right side of the neck. Also, the biochemical test results were normal except for Troponin-T positivity (> 0.10 IU/L) and high CPK and CPK-MB levels. On admission, the CPK and CPK-MB levels were 1408 and 180 units/L, respectively. Laboratory tests are shown in Table 1. Written informed consent was obtained from the patient's parents for the publication of this report. This study was conducted according to the Declaration of Helsinki principles. Also, CARE guidelines and methodology were followed in this study.

3 | DISCUSSION

Bee sting hypersensitivity reactions can range from mild urticaria and subcutaneous angioedema to severe anaphylaxis and are mediated by various immunologic mechanisms.⁸ Although cardiac involvement is rare, it is the most significant and life-threatening complication. Since 1991, the Kounis syndrome has been used to describe the

TABLE 1 Results of laboratory tests

	Initial blood sample in	
Parameter	our emergency room	Normal range
Na	143	135–145 mEq/L
К	4.5	3.5-5.5 mEq/L
BS	191	<200 mg/dl
BUN	18	13–43 mg/dl
Creatinine	1.2	0.6–1.2 mg/dl
Ca	10	8–12 mg/dl
AST	43	50-40 U/L
ALT	35	<45 U/L
ALP	150	80-306 U/L
pH	6.80	7.35-7.45
PCO ₂	84	35–45 mmHg
HCO ₃	18.5	20–28 mmol/L
Troponin-T	>0.10 IU/L	<0.01 IU/L
СРК	1408 units/L	32–267 IU/L
СРК-МВ	180 units/L	<16 IU/L

coronary vasospasm and myocardial infarction caused by bee sting allergies.^{9,10} It has now been associated with several factors which may activate hypersensitivity pathways and cause mast cell degranulation.¹¹ Drugs, stings from ants, bees, wasps, and jellyfish, as well as grass cutting, poison ivy, latex contact, limpet ingestion, millet allergy, shellfish eating, and viper venom poisoning, have been reported to be associated with Kunis syndrome.

In Europe and the United States, up to 5% of the population has allergic reactions to honey bee or wasp stings of any grade.^{12,13} For reasons that are now being investigated, these reactions vary in severity, with symptoms ranging from skin reactions such as rash and itching to respiratory discomfort, gastrointestinal disorders, and cardiovascular collapse, as in our case. In a few patients, particularly those who have had severe anaphylactic reactions, an association with mastocytosis has been reported.¹⁴ Although the majority of severe reactions to hymenoptera stings occur with the initial sting, patients who have previously been stung by insects are at a higher risk of having more severe allergic reactions to future stings.

Bee venom consists of various enzymes and biologically toxic substances such as mellitin, phospholipase A_2 , hyaluronidase, histamine, and apamin. The main component of bee venom (50%) is mellitin, which causes inflammatory reactions, cytolysis, intravascular hemolysis, and rhabdomyolysis, all of which can exacerbate and lead to acute kidney injury. Phospholipase A2 can cause disseminated intravascular coagulation (DIC). Hyaluronidase with increased capillary permeability facilitates the spread of toxins. Apamine is neurotoxic.

WILEY

Histamine is a chemical compound that dilates blood vessels, promotes fluid secretion, and stimulates nerves that cause bronchospasm and local muscle spasms.¹⁵⁻¹⁷ Therefore, phospholipase A2 and mellitin with destruction of the cell membrane cause hemolysis, thrombo-cytopenia, liver damage, kidney failure, cardiac arrest, and death.²

Histamine receptors affect the heart tissue differently in four ways, all of which contribute to the severity of myocardial injury.¹⁸ H1-histamine receptors have vasoconstrictive effects, while H2-histamine receptors have vasodilatory effects on coronary arteries. The interaction of H1 and H2-receptor stimulation mediates decreased diastolic pressure and increased pulse pressure. H3histamine receptors inhibit endogenous norepinephrine release, thereby causing shock during allergic reactions. H4-histamine receptors affect blood cells such as mast cells, eosinophils, and lymphocytes.

Local reactions such as pain, burning, redness, itching, urticaria, and flare reactions are caused by Hymenoptera stings, and they usually disappear completely within a few hours. Accidental stings from a variety of bees can cause life-threatening upper-airway edema, such as angioedema and bronchospasm. Multiple stings can lead to nausea, vomiting, diarrhea, dizziness, generalized edema, dyspnea, rhabdomyolysis, intravascular hemolysis, and renal injury.¹⁷ Neurologic disorders, including strokes following bee stings, are very rare.^{19,20} Bee stings have also been associated with cardiovascular disorders, including acute myocardial infarction in patients with both normal and abnormal coronary arteries.^{21,22} In our patient, it seems anaphylactic shock and ventricular arrhythmia were related to the release of vasoactive amines and thrombogenic substances in the bee venom, the first able to produce vasospasm and the second able to cause ventricular dysrhythmia.

4 | CONCLUSION

Bee stings can lead to anaphylactic shock and sudden death. Therefore, it is necessary for patients who suffer from being envenomated by a bee sting to be referred to medical centers promptly and receive appropriate treatments to prevent undesirable complications.

ACKNOWLEDGEMENT

Declared none.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

AUTHOR CONTRIBUTIONS

ZZ and MF were involved in the interpretation and collecting of data and editing of the manuscript. ASH involved in writing, editing, and preparing the final version of the manuscript. AZ and MS were responsible for collecting data and submitting the manuscript. All authors reviewed the paper and approved the final version of the manuscript.

CONSENT

Informed consent for publication of this case report was obtained from the patient's parents. Written informed consent was obtained from the patient's next of kin to publish this report in accordance with the journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The data are available to the correspondent author and can be obtained upon request.

ORCID

Zakaria Zakariaei D https://orcid. org/0000-0003-4835-9349

REFERENCES

- 1. Golden DB. Insect sting allergy and venom immunotherapy: a model and a mystery. *J Allergy Clin Immunol*. 2005;115(3):439-447.
- Shahidi S, Ashrafi F, Adilipour H. Patients with massive honeybee stings: report of four cases. *Tehran Univ Med J*. 2008;66(8):611-615. [In Persian].
- 3. Moffitt JE, Golden DB, Reisman RE, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol.* 2004;114(4):869-886.
- 4. White J. Bites and stings from venomous animals: a global overview. *Ther Drug Monit.* 2000;22(1):65-68.
- Bresolin NL, Carvalho FC, Goes JC, Fernandes V, Barotto AM. Acute renal failure following massive attack by Africanized bee stings. *Pediatr Nephrol.* 2002;17(8):625-627. doi:10.1007/s0046 7-002-0888-0
- Chapsa M, Roensch H, Langner M, Beissert S, Bauer A. Predictors of severe anaphylaxis in hymenoptera venom allergy: the importance of absence of urticaria and angioedema. *Ann Allergy Asthma Immunol.* 2020;125(1):72-77.
- Kouame EK, Brouh Y, Boua N. Envenimation massive par un essaim d'abeilles chez un nourrisson. *Arch Pediatr.* 2004;11:1333-1335. doi:10.1016/S0929-693X(04)00386-0
- 8. Freeman TM. Clinical practice. Hypersensitivity to hymenoptera stings. *N Engl J Med*. 2004;351:1978-1984.
- Kounis NG, Zavras GM. Histamine-induced coronary artery spasm: theconcept of allergic angina. Br J Clin Pract. 1991;45:121-128.
- Kounis NG. Kounis syndrome (allergic angina and allergic myocardialinfarction): a natural paradigm? *Int J Cardiol.* 2006;110:7-14.

V_Clinical Case Reports _____

- 11. Nikolaidis LA, Kounis NG, Gradman AH. Allergic angina and allergicmyocardial infarction: a new twist on an old syndrome. *Can J Cardiol.* 2002;18:508-511.
- 12. Brown SGA. Clinical features and severity grading of anaphylaxis. *J Allergy Clin Immunol.* 2004;114:371-376.
- 13. Ludolph-Hauser D, Rueff F, Fries C, Schopf P, Przybilla B. Constitutively raised serum concentrations of mast-cell tryptase and severe an applyactic reactions to hymenoptera stings. *Lancet*. 2001;357:361-362.
- 14. Rohr SM, Rich MW, Silver KH. Shortness of breath, syncope andcardiac arrest caused by systemic mastocytosis. *Ann Emerg Med*. 2005;45:592-594.
- Munoz-Arizpe R, Velasquez-Jones L, Romero-Navarro B, Gomez-Chico R. Acute kidney failure due to stings by Africanized bees. *Bol Méd Hosp Infant Méx.* 1992;49(6): 388-390.
- Betten DP, Richardson WH, Tong TC, Clark RF. Massive honey bee envenomation-induced rhabdomyolysis in an adolescent. *Pediatrics*. 2006;117(1):231-235., 117, 231-235. doi:10.1542/ peds.2005-1075
- Mackler BF, Kreil G. Honey bee venom melittin. Correlation of nonspecific inflammatory activities with amino acid sequences. *Inflammation*. 1977;2(1):55-65. doi:10.1007/BF00920875

- Kounis NG. Kounis syndrome (allergic angina and allergic myocardialinfarction. A natural paradigm?). *Int J Cardiol.* 2006;110(1):7-14.
- Bilir O, Ersunan G, Kalkan A, Ozmen T, Yigit Y. A different reason for erebrovascular disease. *Am J Emerg Med.* 2013;31:891. e5-e6 Google Scholar.
- 20. An JY, Kim JS, Min JH, et al. Hemicho-rea after ltiple bee stings. *Am J Emerg Med.* 2014;32:196.e1-e2. Google Scholar.
- 21. Wagdi P, Mehan VK, Bürgi H, Salzmann C. Acute myocardial infarction after wasp stings in a patient with normal coronary arteries. *Am Heart J.* 1994;128(4):820-823. Article Download PDFView Record in ScopusGoogle Scholar.
- 22. Jones EL, Joy M. Acute myocardial infarction after a wasp sting. *Heart.* 1988;59(4):506-508.

How to cite this article: Fakhar M, Zakariaei Z, Sharifpour A, Soleymani M, Zakariaei A. Fatal outcome following multiple bee stings: A rare case. *Clin Case Rep.* 2022;10:e05303. doi:<u>10.1002/</u>ccr3.5303