1 INTRODUCTION

Insect stings can induce local or systemic symptoms that are usually moderate, but can also be severe and fatal. 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. 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. 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.
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.\textsuperscript{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.\textsuperscript{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 coronary vasospasm and myocardial infarction caused by bee sting allergies.\textsuperscript{9,10} It has now been associated with several factors which may activate hypersensitivity pathways and cause mast cell degranulation.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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\textsubscript{2}, hyaluronidase, histamine, and apamin. The main component of bee venom (50%) is mellitin, which causes inflammatory reactions, cytolyis, intravascular hemolysis, and rhabdomyolysis, all of which can exacerbate and lead to acute kidney injury. Phospholipase A\textsubscript{2} can cause disseminated intravascular coagulation (DIC). Hyaluronidase with increased capillary permeability facilitates the spread of toxins. Apamine is neurotoxic.

| Parameter | Initial blood sample in our emergency room | Normal range |
|-----------|------------------------------------------|--------------|
| Na        | 143                                      | 135–145 mEq/L |
| K         | 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\textsubscript{2} | 84                          | 35–45 mmHg   |
| HCO\textsubscript{3} | 18.5                          | 20–28 mmol/L |
| Troponin-T | >0.10 IU/L                              | <0.01 IU/L   |
| CPK       | 1408 units/L                             | 32–267 IU/L  |
| CPK-MB    | 180 units/L                              | <16 IU/L     |
Histamine is a chemical compound that dilates blood vessels, promotes fluid secretion, and stimulates nerves that cause bronchospasm and local muscle spasms. Therefore, phospholipase A2 and mellitin with destruction of the cell membrane cause hemolysis, thrombocytopenia, liver damage, kidney failure, cardiac arrest, and death.

Histamine receptors affect the heart tissue differently in four ways, all of which contribute to the severity of myocardial injury. 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. H3-histamine 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, dizziness, generalized edema, dyspnea, rhabdomyolysis, intravascular hemolysis, and renal injury. Neurologic disorders, including strokes following bee stings, are very rare. Bee stings have also been associated with cardiovascular disorders, including acute myocardial infarction in patients with both normal and abnormal coronary arteries. 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.

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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.

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