Multi-organ dysfunction following honeybee bite—A rare entity

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Abstract

Honeybee bites have been known to cause localized allergic reactions and anaphylaxis but systemic toxic reactions leading to multiorgan dysfunction is very rare. Serious complications like acute renal failure, acute myocardial infarction (Kounis syndrome) and even death have been reported as the complication of honeybee bite. Herein, we report a case of multiorgan dysfunction following honeybee bite, which was complicated with acute kidney injury, thrombocytopenia, bradycardia, keratitis, and deranged liver function along with localized allergic reaction and pain.

Keywords: Bradycardia, honeybee, multi-organ dysfunction, thrombocytopenia

Introduction

Honeybees are a common public health hazard, the incidence of which is gradually increasing. The bee species causing human envenoming are Apis mellifera mellifera (A. m. mellifera) and A. m. ligustica, and A. m. Scutellata.⁴ Massive envenomation is defined as stings more than 50 in number.⁵ The clinical manifestations of honey bee bites may be divided into localized reactions, allergic reactions, anaphylaxis, and systemic toxic reactions. Systemic reactions are due to large dose of the venom being injected into the body by a large number of bee bites. Localized reactions include erythema, oedema, and pain whereas allergic reactions triggered by IgE, may cause urticaria, angioedema, bronchoconstriction, and anaphylactic shock. Systemic toxic reactions may cause acute kidney injury (AKI),⁶ acute myocardial infarction (Kounis syndrome),⁷ stroke,⁸ peripheral neuropathy, glomerulonephritis, and even death. Mortality rates in various studies are as high as 15–25 percent.⁹ Amongst all the complications, stroke,⁸ and multiorgan dysfunction are extremely rare manifestations. The toxic effects of the venom are due to various substances like phospholipase A2, melittin, peptide 401, histamine, hyaluronidase, and apamine. Of these melittin has been found to be the most toxic and is incriminated for most of the severe complications of the bee sting.⁸ Allergen-specific immunotherapy has been employed in treatment of insect venom bites to prevent severe allergic reactions. But beta-blockers and ACE inhibitors should be avoided in such patients, as they may worsen allergic reactions.⁹

Case Summary

A 23-year-old male came to the emergency of our hospital with a history of multiple bee bites, two days back. Patient was initially managed at local health center with anti-histaminic and steroids and was discharged after removal of the barbed stingers. He complained of repeated vomiting two days after the bite and got...
admitted. On examination he was conscious, oriented, afebrile with facial puffiness, congestion of the eyes, pulse-120/min regular, blood pressure-120/80 mmHg and multiple bites all over the body including face and eyelids [Figure 1]. His urine was normal, electrolytes were normal, urinary albumin-creatinine ratio was 42.05. His urine output varied between 1500 and 2500 ml per day. His reports were as follows: [Table 1].

ECG on day 1 showed sinus tachycardia [Figure 2]. On day 4 of admission, he developed transient bradycardia [Figure 3] which reverted to sinus rhythm spontaneously, the next day. The patient developed multi-organ dysfunction (haematological- thrombocytopenia, acute kidney injury, cardiac rhythm abnormalities, liver dysfunction) and arterial blood gas showed mild metabolic acidosis. He was treated with anti-histaminic, steroids, antibiotics, and intravenous fluids. He then developed keratitis which was treated with topical steroid and atropine eye drops and the sting was removed. He improved with conservative treatment and was discharged on 7th day of admission. On follow-up, he is doing well.

**Discussion**

Bee stings commonly cause localized allergic reactions and anaphylaxis but severe systemic toxic reactions can occur, though infrequently. Severity of systemic reactions usually corresponds to the amount of venom injected, which in turn is related to number of bites. Severe systemic complications include acute kidney injury (AKI), acute myocardial infarction, stroke, immune thrombocytopenia, and multiorgan dysfunction syndrome (MODS). Of these, stroke and MODS are very rare. Our case is rare, as the patient had AKI, bradycardia, thrombocytopenia, liver dysfunction, and keratitis apart from the localized allergic reaction. Very few such cases have been reported in literature. Luana Ferrià Martin de Toledo et al. had reported a similar case of multiorgan involvement in a 3-year-old child who developed anaphylactic shock, cardiac dysfunction, rhabdomyolysis, and AKI following honeybee bite. Several cases of AKI following bee stings have been reported. Acute kidney injury (AKI) from bee stings is due to multiple factors, such as intravascular hemolysis, rhabdomyolysis, hypotension, and direct toxicity of the venom components (melittin and apamin) to the renal tubules.

Our case also had transient bradycardia which developed 4 days after bee sting. In literature, the association of acute coronary syndrome/myocardial infarction with hymenopteran sting has been called Kounis Syndrome. In a study of 152 patients of honeybee bite done by Laxmegowda et al., bradycardia was reported in <0.7 percent patients. Our case, though, had only transient bradycardia and did not require pacing. The most likely explanation for bradycardia was a transient spasm of the...
right coronary artery. Other possible causes of bradycardia and heart block are immune mediated heart block by IgE, action of tetraipine on myocardial potassium channels and apamin-mediated bradycardia.

An elevation of serum creatine phosphokinase and serum lactate dehydrogenase levels was also observed which correlated with muscle damage.

Phospholipase A2 has been incriminated for the hematological manifestations of bee sting and may be the cause of thrombocytopenia in our case. Several cases of immune thrombocytopenia have been reported following honeybee bites.\(^{10}\)

Our patient also had raised ALT and AST level. Hepatotoxicity in bee bite may be due to the direct effect of the toxin or may be immune mediated and the level of hepatic damage correlates directly with the amount of the venom injected. Liver cell damage due to venom is of the cholangiocellular type.

In a series of 322 cases, only two patients had to be referred to tertiary care center, of whom one had ocular stings. Our case also had ocular stings, which was removed.\(^3\) This case is being reported after getting permission from the institute ethics committee.

### Conclusion

This index case is unique in the sense that multiple organ systems were involved and very few cases have been reported. Our patient developed AKI, bradycardia, liver dysfunction, thrombocytopenia, and keratitis. Bradycardia has been found in less than 0.7% cases only. He improved with conservative management and did not require hemodialysis or pacing. We suggest that all patients with multiple honeybee bites should be admitted and kept under observation for 4-7 days to monitor for development of delayed complications. Beta blockers should be avoided in view of the worsening of bradycardia due to bee bite. In the primary care settings, all cases coming with multiple bee bites, a possibility of multi-organ failure should be kept in mind by the primary care physician.

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### Conflicts of interest
There are no conflicts of interest.

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### Table 1: Serial laboratory reports of the patient during his hospital stay

| Day 1   | Day 3   | Day 4   | Day 5   | Day 6   | Day 7   |
|---------|---------|---------|---------|---------|---------|
| Hemoglobin (gm/dl) | 16.2    | 11.1    | 12.6    | 12.3    | 12.5    |
| TLC (per cumm)      | 26000   | 23700   | 19800   | 12900   | 9700    |
| Platelets (per cumm) | 2 lacs  | 87000   | 85000   | 78000   | 1.2 lacs|
| Bilirubin (Total - mg/dl) | 2.21     | 0.91    | 0.76    | 0.76    | 0.76    |
| Creatinine (mg/dl)  | 1.69    | 2.13    | 1.92    | 1.6     | 1.1     |
| LDH (U/l)           | 1557.2  | 606.7   |         |         |         |
| ALT                 | 46.9    | 74.6    | 95.6    | 35.5    | 40.2    |
| AST                 | 327.4   | 211     | 64.5    | 1218    |         |
| CPK                 |         |         |         |         |         |