Clinical Case Report

Disseminated intravascular coagulation after multiple honeybee stings

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ABSTRACT
Honeybee venom contains apitoxin which can cause anaphylaxis, cardiovascular collapse and death. Disseminated intravascular coagulation is rare following honeybee stings. We describe the case of a farmer who developed this complication.

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INTRODUCTION
Disseminated intravascular coagulation (DIC) is a clinicopathological syndrome characterized by widespread intravascular fibrin formation in response to excessive blood protease activity that overcomes the natural anticoagulant mechanisms.1 The most common causes are bacterial sepsis, malignant disorders such as solid tumours or acute promyelocytic leukaemia, obstetric causes, and insect and snake envenomations.1

Bee stings are painful and cause a local inflammatory response. Honeybee venom (apitoxin) can induce immediate anaphylaxis, cardiovascular collapse and death. Envenomation of apitoxin can cause DIC, thrombotic microangiopathy, acute encephalopathy, peripheral neuritis, acute renal failure, nephrotic syndrome, silent myocardial infarction, rhabdomyolysis, conjunctivitis, corneal peripheral neuritis, acute renal failure, nephrotic syndrome, silent DIC, thrombotic microangiopathy, acute encephalopathy, Honeybee venom (apitoxin) can induce immediate anaphylaxis.

THE CASE
A 40-year-old agricultural labourer was brought to the emergency room of our hospital in an unconscious state. He had sustained multiple honeybee stings 3 days ago while working in his farm at Pandurangapuram village, Khammam, a rural area of Telangana, India. He was immediately taken to a local hospital, where he received primary care. He was stung predominantly on the face, neck and trunk. About 25–30 stingers were removed, swelling was noticed at the sting sites and he did not have any signs of anaphylaxis or hypotension. He was treated with intravenous hydrocortisone, pheneramine maleate and analgesics for symptomatic relief, and was sent home. The next day, he had intense body pain, easy fatiguability, malaise and fever with chills. The family members found the patient unconscious on his bed early on the morning of day 3 following the sting and brought him to our hospital.

At the time of presentation, the patient was unconscious with a Glasgow Coma Scale score of 5. Multiple sting sites were observed over the arms and the face but the stingers could not be retrieved. Examination revealed a temperature of 101 °F, tachycardia (120/minute), tachypnoea (26/minute), blood pressure 100/70 mmHg and heart sounds were normal on auscultation. Neurological examination revealed no focal deficits.

Serum-specific bee IgE could not be evaluated due to lack of facilities. Electrocardiogram and computed tomography scan of the brain showed no abnormal findings on the day of admission. His APACHE II score was 19. He was treated with intravenous broad-spectrum antibiotics. He developed bleeding from the oronasal cavity and the gastrointestinal tract. Anaemia and coagulopathy were corrected with fresh whole blood, fresh frozen plasma and platelet concentrates. A diagnosis of DIC was made on the basis of clinical and laboratory findings (Table I).

On day 2 of admission, his blood pressure was 80/50 mmHg with tachycardia and profuse bleeding from the upper gastrointestinal tract. Despite transfusion of blood products, mechanical ventilation, intravenous ionotropes and all supportive care his vital signs could not be stabilized. Blood and urine cultures were negative. On day 3 of admission the patient died due to hypovolaemic shock and multi-organ dysfunction syndrome due to DIC.

Postmortem biopsies of the liver and the lung showed anoxic damage. Brain tissue (Fig. 1) showed areas of circumscribed haemorrhage and inflammatory cells. The spleen (Fig. 2) had haemorrhagic necrosis and the liver and lungs (Fig. 3) showed congestion.

DISCUSSION
A fatal reaction after honeybee stings can occur within a few hours to a few days. Honeybee stings are common in rural India. Local reactions are limited to pain and swelling at the sting site, whereas systemic allergic reactions can cause death. A fulminant multi-organ failure is usually observed in previously sensitized individuals. In an Australian study, a fatality rate of 0.02% per year was reported due to systemic reactions within an hour of bee sting.

Bee venom contains components such as apamin, melittin, phospholipase A2 (PLA2), mast cell degranulation peptide, hyaluronidase, histamine and dopamine.4 The most common serious systemic reaction is anaphylaxis.5–7 Coagulation abnormalities are relatively rare. PLA2 in bee venom is known to cause coagulation abnormalities.6 Petroianu et al reported that in human plasma, several parameters of coagulation were affected due to an increase in concentration of PLA2.7 This peptide catalyses the hydrolysis of 2-acyl bonds in structural membrane phospholipids of cells, mitochondria, and other cellular constituents, and thereby inhibits cellular functions.9 Melittin is involved in intravascular haemolysis caused by interactions with PLA2.10 The anaphylactic reaction leads to the release of kallikrein and bradykinin into the circulation, and these may cause coagulation abnormalities.11 There are few reports of intravascular coagulopathy after a bee sting and most cases did not have any features of anaphylaxis.12,13 Gawlik et al reported a patient who presented with coagulation abnormalities after a honeybee sting.14 Jung et al reported a fatal case of intravascular coagulation after bee sting acupuncture.15 George et al reported a rare case of acute tubular necrosis and thrombotic microangiopathy after multiple wasp stings.16
First aid and subsequent treatment should include removal of honeybee stingers embedded in the skin as early as possible to limit the quantity of venom delivered. The site should be cleansed and disinfected and ice packs applied to slow the spread of venom. Elevation of the affected site and administration of analgesics, oral antihistamines and topical calamine lotion relieve symptoms. Large local reactions may require a short course of oral therapy with glucocorticoids. Patients with numerous stings should be monitored for 24 hours for evidence of renal failure or coagulopathy.

Anaphylaxis is treated with subcutaneous injection of 0.3–0.5 ml of epinephrine hydrochloride in a 1:1000 dilution; treatment is repeated every 20–30 minutes as necessary. Intravenous epinephrine (2–5 ml of a 1:10 000 solution administered by slow push) is indicated for profound shock. A tourniquet may slow the spread of venom. Parenteral antihistamines, fluid resuscitation, bronchodilators, oxygen, intubation and vasopressors may be required. Patients should be observed for 24 hours for recurrent anaphylaxis.

The diagnosis of DIC is based on the presence of clinical and/or laboratory abnormalities of coagulation or thrombocytopenia. The laboratory investigation should include coagulation tests (activated partial thromboplastin time [aPTT], prothrombin time [PT]) and markers of fibrin degradation products (FDPs), in addition to platelet and red cell count and analysis of the blood smear. Common findings include the prolongation of PT and/or aPTT; thrombocytopenia or a rapid decline in platelet numbers; the presence of schistocytes in the blood smear (may or may not be seen in the smear16); and elevated levels of FDP. The most sensitive test for DIC is the FDP level. DIC is an unlikely diagnosis in the presence of normal levels of FDP. The D-dimer test is more specific for detection of FDPs.1

The control of bleeding in patients with DIC who have marked thrombocytopenia and low levels of coagulation factors requires replacement therapy. Replacement with fresh frozen plasma (FFP) is indicated if the PT is >1.5 times the normal. Low levels of fibrinogen (<100 mg/dl) or brisk hyperfibrinolysis will require infusion of cryoprecipitate (plasma fraction enriched for fibrinogen, factor VIII, and von Willebrand factor [vWF]). The transfusion scheme must be adjusted according to the patient’s clinical and laboratory parameters. Platelet concentrates at a dose of 1–2 U/10 kg body weight are sufficient for most DIC patients with severe thrombocytopenia.1

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<th>Table I. Investigations during the course of stay in hospital</th>
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<td>Peripheral blood smear for schistocytes</td>
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<td>Prothrombin time (patient/control)</td>
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<td>Activated partial thromboplastin time in seconds (patient/control)</td>
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<td>Bleeding time (minutes)</td>
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<td>Erythrocyte sedimentation rate (mm/hour)</td>
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Fig 1. Cut section of the brain showing multiple petechiae (arrow)
Fig 2. Congested spleen
Fig 3. Congestion and haemorrhage in lung tissue
Our patient died due to DIC leading to hypovolaemia and multi-organ failure. Early diagnosis and management are important for reducing morbidity and mortality in such patients. This experience emphasizes the importance of considering coagulation abnormalities in a patient who develops clinical deterioration and bleeding tendencies following bee stings.

REFERENCES


