CASE REPORT

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Adrenal hemorrhage and rhabdomyolysis following mass bee sting envenomation : An autopsy based case report.

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ABSTRACT

Hymenoptera stings causes variety of sting reactions ranging from subtle allergic reactions to multiple-organ failure leading to death with a mortality rate of 1-5 % in various countries. We report a case of elderly male who was stung by multiple bees. During the course of treatment, he developed multiple organ failure and succumbed to death. Medicolegal autopsy reveal congested of all internal organs and adrenal hemorrhage. Histopathological examination revealed acute tubular necrosis with myoglobin casts. Postmortem serum IgE levels and creatine kinase levels were elevated. Adrenal haemorrhage in bee sting fatalities is rarely reported in literature.

INTRODUCTION

Honey bees (Apis mellifera) belong to subfamily Apinae and family Apidae grouped under Order hymenoptera. [1] In temperate countries there is a greater incidence of reaction to hymenoptera sting.[2] About 50 – 90% the general population have been stung minimum once in their lifetime.[3] The mortality rate is estimated to be approximately 1-5% in different countries.[4] In the US, an estimated 60 deaths annually are due to stings from hornets, bees, and wasps.[5] The estimated number of deaths per year ranges 0.03–0.45 per million inhabitants. [6] The consequences of envenomation ranges from a subtle allergic reactions, mild to severe anaphylaxis and shock, and multiple-organ dysfunction and death.[7] The elucidation regarding the diagnosis and the cause of death in cases of hymenoptera stings is challenging in medicolegal scenario due to various factors like absence of sting marks, absence of sting and postmortem degradation of Immunoglobulin E (IgE) and tryptase.

CASE REPORT

A 59-years-old-male as admitted in the casualty with history of multiple bee stings followed by vomiting, diarrhea and altered sensorium with blood pressure of 200/110 mmHg. He was suffering from Parkinson's disease for the past five years and was under treatment with SynDOPA. He had generalized edema with decreased urine output. Investigations revealed azotemia with elevated lactate dehydrogenase (LDH-2891IU/L) and creatine kinase (>2000IU/L) levels. He succumbed to envenomation within five days of hospitalization after

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bee sting. Since it was a case of unnatural death, the deceased body was brought to the department of Forensic Medicine for autopsy. The deceased was a moderately built male with body length 165 cm and weight 90 kg. Multiple black sting marks were present over face (Figure 1A), upper limbs, lower limbs and front of trunk. Three stings were recovered from left thigh (Figure 1B,1C &1D). Larynx & trachea were edematous and congested. Lungs were congested and edematous with multiple petechiae present over all the surfaces. Middle lobe of right lung was consolidated. Kidneys appeared pale with patchy effacement in both cortex and medulla. Both adrenal glands were hemorrhagic. On microscopy, lungs showed interstitial congestion, focal alveolar rupture and features of lobar pneumonia. Centrilobular necrosis and periportal preservation of hepatocytes consistent with chronic venous congestion of liver was seen. Acute tubular necrosis with myoglobin casts (Fig.2A,2B,2C) was found in kidneys. Adrenal glands showed areas of haemorrhage (Fig. 2D). Postmortem serum IgE level was elevated to 1210 IU/m. C Reactive Protein level was elevated to 86.8 mg/L which is around 28 times the high normal value. Serum IgM level was below 0.168 g/L. Blood LDH levels & CK-MB (Creatine Kinase MB) were elevated to 5347 IU/L & 223 IU/L respectively.

DISCUSSION

Honeybees have a stinger which is a modified ovipositor present in abdomen. The stinger have a barb and once stung the stinger gets implanted into the skin and the bee is disemboweled.[1] Hence honeybees can sting only once.[8] Each bee sting releases around 140 µg of venom.[1,9] Bee venom comprises of enzymes like phospholipase, hyaluronidase, phosphatase and α-glucosidase, peptides like mellitin, apamin, tertiapin, secapin, cardiopep & vasoactive amines like histamine, dopamine and noradrenaline.[10] Hyaluronidase causes systemic envenomation which enables the venom to perfuse into the tissues by altering cell permeability.[11] Bee venom acid phosphatase stimulates histamine release from previously sensitized basophils.[12] Melittin causes membranolysis and further release of histamine, thereby causing severe pain. It forms a synergistic complex with PLA2 by activating it, thereby increasing catecholamine secretion and inducing skin mast cell lysis & intravascular haemolysis.[13,14] Apamin, an octapeptide neurotoxin, crosses the blood-brain barrier leading to motor hyperexcitability with selective inhibition of small conductance calcium-activated potassium (SK) channels.[15] MCD peptide, due to interaction with cell-bound specific IgE, after fusion with the membranes of the mast cell granules leads to exocytosis of granule releasing more histamine.[16] It is the dose of venom but not the number of stings that influences an anaphylactic reaction.[9] The severity of the rection is inversely proportional to the time interval between sting and symptom onset. The patient may present with vomiting, diarrhea syncope, generalized urticaria, facial edema, stridor, fever with chills, pain in the limbs, and shortness of breath. Clinical evaluation may reveal cyanosis and laryngeal edema, hypotension and poor left ventricular function.[1,17-19] Rarely patchy subarachnoid hemorrhage, ecchymotic subendocardial hemorrhage, extracardiac infarction with emboli in lungs, spleen, femoral veins, pulmonary hemorrhage, atelectasis and bullae are reported in bee sting.[19-23] In the present case, the patient presented with generalized edema of body, vomiting and diarrhea Stings were recoverable in few fatal cases at autopsy but only sting marks and local reactions were found in most of the cases.[8,19-23] In the present case, 3 stings were recovered with multiple sting marks present all over the body. Respiratory signs and symptoms were commonly seen.[21] Edema of upper airways, lower airways, limbs, trunk, face and lips were reported. [19-23] Histological sections may reveal mast cells in laryngeal mucosa, eosinophils with intra-alveolar macrophages, dermal edema with inflammatory infiltrate comprising lymphocytes and eosinophils in the dermis with extension into the subcutaneous fat, vascular congestion and some extravasated free red blood cells in the underlying fibro-fatty tissues.[19-23] Delayed deaths may show acute tubular necrosis and multiorgan hypoxic or ischemic damage. In most of the cases, there is no evidence of inflammatory infiltrate in sting sites of skin.[19-24] In the present case, there are myoglobin casts in kidney and adrenal hemorrhage where the latter is to the best of authors' knowledge have not been reported in literature. Diagnosis of anaphylaxis due to sting reaction is dependent on history and estimation of IgE-antibodies (RAST score). A bee venom specific IgE and serum mast cell tryptase obtained at autopsy can help ascertaining the cause of death due to anaphylaxis, particularly in the absence of recoverable stings or visible stings marks.[17,25] Huang et al reported that antibodies to bee venom specific antigen was identified in adrenal glands, heart and sera of persons died of bee stings.[26] Deaths can occur within several minutes while fulminant course may quickly succeed an initial mild course.[18,21] About half of fatal reactions have occurred in people without

any previous allergic reactions to stings.[26] Three types of bee sting related deaths are described in literature (1) deaths not directly caused by bee sting, but may cause accidental injuries or may aggravate the underlying pathological condition like coronary artery disease. (2) deaths due to systemic reaction or anaphylactic deaths as a consequence of IgE-mediated acute hypersensitivity reaction. (3) deaths due to mass envenomation (>500 stings) fatality mainly due to toxin. [20,21,27,28] The rapidity of death is an important feature in hymenoptera sting. About 60% may die within an hour and 75% deaths may happen within 6 hours.[16] Survival duration after cerebral pathology secondary to hymenoptera stings may occur ranges from minutes to 4 months. Deaths may ensue due to respiratory pathology within 60 minutes whereas due to vascular complications between 6 and 96 hours after sting.[21] The complications include acute renal failure which could be due to toxic-ischemic mechanism, pigment tubulopathy and acute tubular necrosis(ATN). Rhabdomyolysis and hemolysis may lead to ATN and pigment tubulopathy. Rhabdomyolysis may progress within 12 hours of massive bee stings resulting in acute renal failure progressing to death within as early as 50 hours.[29,30] In this case, rhabdomyolysis is evidenced by histochemical demonstration of myoglobin casts in kidney in presence of elevated CK MB & LDH enzymes in post-mortem serum samples. Apart from the anaphylactic reaction numerous other causes were reported in literature. Delayed death due to left thalamic hemorrhage, total brain infarction, cardiac hypertrophy with myocardial fibrosis, multiorgan failure & anaphylaxis with bilateral ischemic lesions ending in vegetative state.[31-33] Robinson reported a single case of adrenal insufficiency and adrenal mass following massive bee envenomation.[34] The studies conducted by Robinson, Huang et al and the present case reveal that the bee venom may have an effect on adrenal gland. The exact mechanism of venom leading to adrenal hemorrhage and its clinical outcome on the deceased is not clear. It is not feasible to sharply state the mechanism of death in cases of massive hymenoptera sting envenomation as in most cases it may be due to combination of multiple organ dysfunction and anaphylaxis.[27,35] With marginal similarity, in present case scenario with the available autopsy findings and postmortem lab investigations and tissue microscopy, the death could be due to multiple organ failure.

Fig-1A : Multiple sting marks present over the face; 1B, one of the recovered stings from deceased; 1C&1D, Microscopic view of a recovered sting with residual abdominal wall (40X microscopic view)

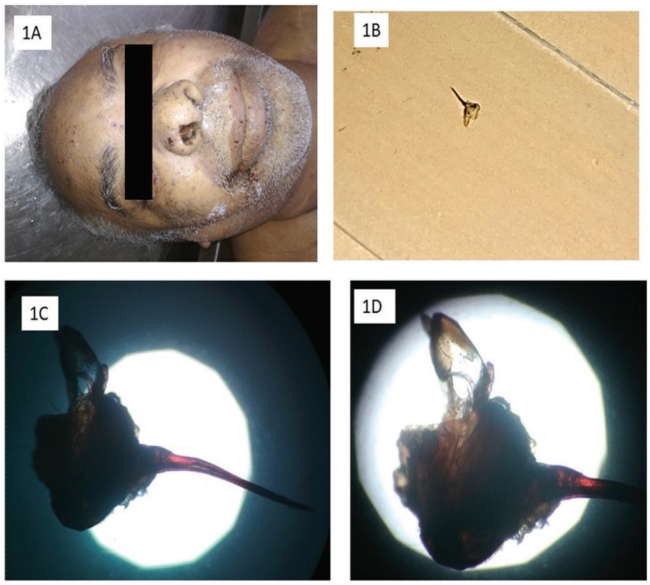
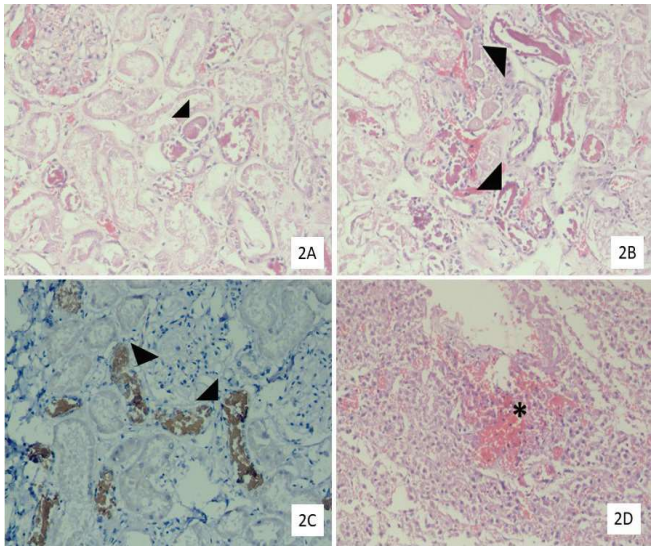


Fig-2A : Kidney shows acute tubular necrosis. Some of tubules show Casts (arrow head) (200x view); 2B, High Power shows tubules with myoglobin casts (arrow heads) (400x); 2C, Immunohistochemistry with myoglobin highlighting myoglobin casts (arrow heads) (DAB 400x); 2D, Adrenal gland shows areas of Hemorrhage (*) (200x)



CONCLUSION

The postmortem diagnosis of bee stings lacks specificity in delineation while opining cause of death in medicolegal cases. Devising a new diagnostic score in relation to clinical,

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autopsy, postmortem histopathology, & laboratory sero-immunological findings may be considered. Various internal organs are affected by massive bee envenomation. The treating physician shall also consider adrenal hemorrhage and adrenal insufficiency while treating cases of massive bee envenomation.

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