



## Combination of Multiple organ Dysfunction and Anaphylaxis in a case of Mass Wasp envenomation: A case report

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### ABSTRACT

Bees, wasps and ants are the common insects to sting. Fatalities due to wasp sting are uncommon. The wasp venom contains various biologically active compounds like histamine, phospholipase, hyaluronidase, adrenaline and noradrenaline. Various factors predispose the outcome of envenomation. Usually within 48 hours the victim recovers but when there is massive envenomation, serious complications like rhabdomyolysis, acute renal failure and anaphylaxis may develop. An elderly female was stung by a swarm of wasps. She presented to hospital with hypotension, stridor and swelling of the face. Biochemical investigations indicated azotemia. The creatinine kinase and immunoglobulin E level had increased twenty and 14 folds respectively. Histopathology report revealed acute tubular necrosis with red blood cell casts and eosinophilic infiltrates in the kidney, edema and intra alveolar hemorrhage in the lungs. Within 30 hours of the incident, the victim succumbed to the complications of the venom. Death in wasp envenomation may be due to anaphylaxis or multiple organ dysfunction. It is difficult to delineate the exact mechanism of death due to massive envenomation. The present case had a combination of multiple organ dysfunction and anaphylaxis.

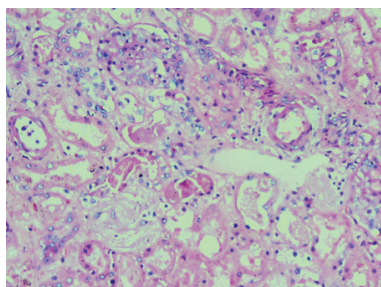
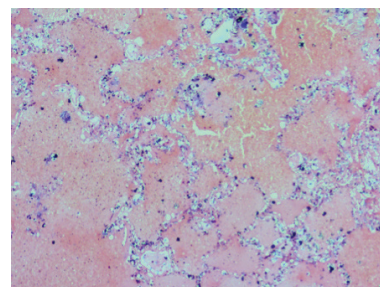
### INTRODUCTION

Bees, wasps and ants are the common insects to sting. Fatalities due to wasp sting are uncommon. Studies reveal that the 56% to 94% of people are stung at least once in their life time by these insects.<sup>1</sup> Fatality due to insect sting varies from 0.03-0.48 for every 1,000,000 inhabitants per year. There is a possibility that the incidence may be high due to the deaths complicated by these stinging insects could be reported as unexplained death.<sup>2</sup> The suborder Aculeate of the order Hymenoptera includes the stinging insect families namely Apidae (bees), Vespidae (wasps, hornets and yellow jackets) and Formicidae (ants).<sup>3</sup> Wasp colonies are more commonly encountered in rural regions.

Usually, the female wasp, with a modified ovipositor, stings its prey to paralyze it.<sup>4,5</sup> The quantity of venom injected per sting ranges from 1.7 µg to 17 µg in various wasp species.<sup>6</sup> The death due to envenomation can be due to anaphylaxis or due to systemic effect of venom.<sup>7</sup> The present article describes fatality due to wasp envenomation where there is multi organ dysfunction and anaphylactic reaction.

### CASE REPORT

An elderly female (85 years old) brought to the hospital with the history of stung by a swarm of wasps over face,

**Fig. 1:** Pitting edema over the face.**Fig. 2:** Hematoxylin & Eosin staining of kidney section showing eosinophilic infiltrate and red blood cell casts (H&E,400x magnification).**Fig. 2:** Hematoxylin & Eosin staining of the lung showing intra alveolar Haemorrhage (H&E,200x magnification).

neck and upper limbs while gardening. She was referred to our institute after first aid by a health care center. The victim presented with complaints of facial swelling, difficulty in breathing and stridor. On examination, the pulse was weak and rapid, blood pressure was not recordable and the respiratory rate was 30 per minute accompanied by wheeze and stridor. There was no previous history of diabetes, hypertension, ischemic heart disease, kidney-related disease, and any history of prior sensitization to wasp venom. She was treated with intravenous steroids, vasopressors and calcium gluconate. Biochemical investigations suggested azotemia and high level of Creatinine kinase (CK). Despite all supportive measures, she succumbed to the complications of wasp envenomation after thirty hours of admission. A medico-legal case (MLC) was registered and post-mortem was conducted. At autopsy, external examination showed pitting edema over face including lips and tongue (**Fig.1**). Stingers could not be identified. There was mild edema and congestion of larynx, vocal cord and trachea. Pleural cavities contained 200 ml of serosanguinous fluid. Lungs and brain were congested and edematous. The samples were sent for biochemistry, nephelometry, histopathology and chemical analysis. Kidney showed acute tubular necrosis with eosinophilic and red blood cells cast (**Fig.2**), lungs were edematous with intra alveolar hemorrhage

(**Fig.3**), adrenals were congested and rest of organs were unremarkable. Nephelometry revealed increase in serum IgE levels 1440kIU/L (baseline value <100kIU/L) high-sensitive C-reactive protein 42.2mg/l and normal complement C3 level. Post-mortem biochemical investigations showed elevated total CK —39763 IU/L, CK (MB) —975 IU/L, lactate dehydrogenase —759 IU/L. Chemical analysis of viscera and blood was negative for any toxic substances including alcohol.

## DISCUSSION

The wasp stings to paralyze and kill its prey or to defend the colony.<sup>8</sup> When the wasp stings the humans, the venom provokes pain, redness and edema. A typical wasp sting produces a local reaction and resolves within 48 hrs.<sup>9</sup> Pain is caused by kinins, edema is caused by vasoactive amines, and various enzymes causes tissue damage. The venom acts on smooth muscle and produces hypotension. Chemotaxis of macrophages, cytolysis, hemolysis are also induced by the venom.<sup>10</sup> Various risk factors for severe sting reactions are pre-existing mast cell disorders, anti-hypertensive medications, old age, cardiovascular diseases and elevated mast cell tryptase. The severity of sting reaction increases when the victim is on beta blockers and angiotensin converting enzyme inhibitors therapy.<sup>9,11,12</sup> The venom of wasp contains

enzymes like Phospholipases, hyaluronidase, biologically active substances like acetylcholine, histamine, serotonin, adrenaline, noradrenaline, dopamine, mastoparans and kinins.<sup>10</sup> The phospholipases damage the biological membranes and causes lysis of cell which in turn causes inflammation and tissue damage.<sup>13</sup> The mastoparans are peptide molecules when injected causes pain, edema and inflammation. They are also implicated in cell lysis.<sup>14</sup> They stimulate exocytosis and releases various biologically active compounds like histamine, proteases, lipid mediators and various cytokines.<sup>15</sup> Many of the wasp venoms contains kinin which has a similar morphology to pain producing bradykinin.<sup>16</sup> These, when injected to the prey, will paralyse it<sup>15</sup> and when injected into humans produces severe pain, induces inflammatory response causing increased vascular permeability and vasodilatation.<sup>17</sup> The major biologically active compound in the wasp venom is histamine<sup>18</sup> and other compounds like acetylcholine, serotonin, are also present in appreciable quantities. Histamine induces vessel dilatation and increases vascular permeability. Adrenaline, nor adrenaline and dopamine induce severe pain and increase the venom spread by accentuating the heart rate.<sup>9</sup> The serpin component in the venom has inhibitory effect on trypsin and thrombin and may cause coagulation disorder.<sup>19</sup> In a case, when the individual is stung by the swarm of wasps the individual presents with swelling of body regions, nausea, vomiting, elevated body temperature and fatigability. The wasp venom especially phospholipase, hyaluronidase is hemotoxic and myotoxic.<sup>20</sup> Massive envenomation can cause cell lysis leading to hemoglobinemia and hemoglobinuria.<sup>21</sup> Rhabdomyolysis may develop<sup>22</sup> and reflected is as elevated blood CK levels. The kidney damage may be due to the direct effect of the venom or indirectly due to hemoglobinuria and rhabdomyolysis. The envenomation also causes multiple organ dysfunction.<sup>23,24</sup> In the present case the total CK levels were elevated about 20 folds than the normal level suggestive of rhabdomyolysis. The lungs were edematous and had intra alveolar hemorrhage. The biochemical investigation revealed azotemia and kidneys had red blood cell cast. All the above findings suggested that the victim had a systemic involvement due to envenomation. Multi organ involvement usually occurs in cases of multiple stings due to the toxicity of the venom.

The other rare complication of wasp sting is stroke, acute myocardial infarction, soft tissue necrosis, acute renal failure and interstitial nephritis.<sup>9</sup> Studies reported that

the death could happen between 4 days to 9 days after wasp envenomation.<sup>21</sup> Another lethal complication of the sting is generalised allergic reaction. The chance of systemic reaction after a previous sting ranges from 25% to 50%.<sup>25</sup> The anaphylaxis is characterised by laryngeal edema, spasm of bronchus and decrease in blood pressure.<sup>26</sup> Many allergen compounds are identified in wasp venom yet their function are not identified. The antigen 5 is the major venom allergen and can induce acute hypersensitivity in humans.<sup>27</sup> The phospholipase and hyaluronidase also have allergenic properties.<sup>10,14</sup> The mast cell on its surface has high affinity IgE receptors. The allergens from the venom bound to the receptor and the mast cell is activated. The activated mast cell releases biologically active compounds like histamine, leukotrienes, prostaglandins and platelet activating factor. The systemic reactions and local reactions depend on the threshold of mast cell and basophil activation.<sup>28</sup> An elevated total serum IgE of more than 250kIU/L can occur in mild to moderate anaphylactic reaction.<sup>29</sup> The antigen-antibody complex preferably involving IgE attracts eosinophils. The eosinophils have high affinity to phagocytize IgE containing antigen-antibody complex. This can explain the eosinophilic infiltrate of the kidney in various IgE mediated hypersensitivity reaction.<sup>30</sup> The victim in the present scenario had hypotension, stridor and edema during admission, very high serum IgE levels, and eosinophilic infiltrates in kidney. These features are suggestive of allergic or anaphylactic reaction. Usually death due to anaphylaxis may be caused by a single wasp sting.<sup>21</sup> Fitzgerald et al. reported that an anaphylactic reaction did not depend on the dose of wasp venom as well as a number of stings.<sup>31</sup> Xie C et al. reported that out of 1091 cases wasp sting fatalities of 50% died from multi organ dysfunction, and 31.5 % died due to shock which includes 11.1% due to anaphylactic shock, 20.4% due to non-anaphylactic shock.<sup>23</sup> Studies have shown that fatality due to multi-organ failure, anaphylactic reaction due to sting may not be differentiated and in such scenario, various ancillary investigations like elevated tryptase and IgE levels can aid in differentiating the two.<sup>7</sup> But the validity of serum tryptase in post-mortem samples is questionable. The half-life of tryptase is two hours and peaks within two hours of onset on anaphylaxis. Studies have shown that the tryptase level drastically decline in ante-mortem and post-mortem samples.<sup>32,33</sup> Further actual elevation of tryptase compared with baseline tryptase could be ascertained only after a repeating the test tryptase level fourty eight to seventy two hours later.<sup>33</sup>

The kinetics of various parameters should be considered for diagnosing a case of wasp envenomation.

## CONCLUSION

The victims of envenomation usually recover with supportive measures but certain cases due to the pre-existing risk factors or due to toxicity of the venom, the victim may succumb to complications of envenomation. Death may be due to anaphylaxis or multiple organ

dysfunction or both. It is difficult to delineate the exact mechanism of death due to massive envenomation. If the incidence is not witnessed the death may be reported as unexplained death. A thorough investigation is required to confirm the exact mechanism of death. Our case report has supporting evidence of anaphylaxis and systemic involvement. In case of unexplained death, investigations to rule out insect envenomation are recommended.

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