Bee venom is a complex substance, which acts in several tissues\(^1\). Although severe allergic reactions have occurred after one or more stings, several deaths have been reported without allergic manifestations, emphasizing the toxic effects of massive poisoning. A number of about 100-1000 stings have been considered necessary to cause death by direct toxicity, but as few as 30-50 stings have proved lethal in children.\(^1,2\) On the other hand LD\(_{50}\) = 2.8 ml/kg or 19 stings/kg is reported fatal\(^3\). According to this count, 760 honey bee stings were fatal dose for our patient. We report a fatal case involving multiorgan failure due to the highest number of honey bee stings to date.

**Case Report**

A ten-year-old boy was attacked by a large number of honey bees while playing with a beehive. He was initially treated with subcutaneous adrenalin at a district hospital and referred because of massive honey bee stings. He had 5989 sting marks all over the body and more prominent on his face. Severe petechia and ecchymosus were seen on his body (Figs. 1A, 1B). The embedded stings were removed after arrival and then tetanus vaccine was given (Fig. 2). Initial laboratory was normal except white blood cell count 31.6\(\times 10^9\)/L. Forty-eight-hours after the hemoglobin level had fallen to 7.2 g/dl, the peripheral smear showed evidence of hemolysis with anisopoikilocytosis and polychromatic erythrocytes, platelet count was 59\(\times 10^9\)/µL. Prothrombin time, partial thromboplastin time and fibrinogen concentration were normal. Troponin Ths level was 3.4 ng/ml. Blood urea, serum creatinine, AST and LDH had risen to 94 mg/dl, 2.2 mg/dl, 2485 U/L and 2942 U/L respectively. CPK had also risen 46750 U/L, CPK-MB 8900 U/L (Table I). Serum tryptase level was not evaluated. Patient was treated with intravenous fluid, diuretic, antibiotic, steroid, antihistaminic drug and sodium bicarbonate. Plasmapheresis was started
to remove venoms from body circulation and to control severe hemolysis, progressing to organ failure on the 2nd days. Plasmapheresis was repeated twice daily for 3 days. Hemodialysis was performed for renal failure. The patient had severe generalized tonic-clonic convulsion and respiratory failure on the 3rd day. He was followed by mechanical ventilation after this event. In cranial MR imaging with diffusion weight scene, bilaretal isemic infarcts were detected in basal ganglion and parietooccipital cortex (Fig. 3). Low molecular weight heparin was started for intracranial infarct in addition to treatment. Systemic hypertension resistant to nitroprusside, nitroglycerin, captopril and minoxidil was developed on the fifth day. It persisted for 3 days. After 2 hours of hypertensive–hypotensive episodes, spontaneous respiration efforts were lost on 10th day. In his neurologic exam, brain stem reflexes were negative. Bilateral dilated pupil and no light response were detected. He died on the 12th day of hospitalization because of the multiorgan failure.

**Discussion**

It is of paramount importantance that parents warn their children to keep them away from bee hives. By this way one could avoid potential worrisome results due to bee stings. Various manifestations after bee sting have been described. Generally, three major reactions occur after bee inoculation as 1) local reactions at the site of stings such as edema, erythema, burn-like sensation, pruritus, 2) generalized anaphylactic responses, and 3) serum sickness like symptoms, which include hemolysis, disseminated intravascular coagulation, rhabdomyolisis, etc. Components

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Admission</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>7</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count, x10^9/L</td>
<td>31.6</td>
<td>28.3</td>
<td>25.9</td>
<td>23.2</td>
<td>18.0</td>
<td>12.0</td>
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<tr>
<td>Hemoglobin, g/dl</td>
<td>15.0</td>
<td>12.9</td>
<td>7.2</td>
<td>10.6</td>
<td>9.8</td>
<td>10.5</td>
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<tr>
<td>Hematocrit, %</td>
<td>44.9</td>
<td>38.9</td>
<td>22.4</td>
<td>31.0</td>
<td>29.5</td>
<td>31.3</td>
</tr>
<tr>
<td>Platelet counts, x10^9/L</td>
<td>344</td>
<td>273</td>
<td>59</td>
<td>85</td>
<td>102</td>
<td>96</td>
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<tr>
<td>Aspartate aminotransferase, U/L</td>
<td>278</td>
<td>1122</td>
<td>2485</td>
<td>1950</td>
<td>129</td>
<td>73</td>
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<tr>
<td>Lactate dehydrogenase, U/L</td>
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<td>2154</td>
<td>2942</td>
<td>832</td>
<td>430</td>
<td>254</td>
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<tr>
<td>Creatine phosphokinase, U/L</td>
<td>3034</td>
<td>6066</td>
<td>46750^a</td>
<td>25055</td>
<td>2724</td>
<td>560</td>
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<tr>
<td>Blood urea nitrogen, mg/dl</td>
<td>35</td>
<td>42</td>
<td>94^b</td>
<td>58</td>
<td>21</td>
<td>18</td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
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<td>1.7</td>
<td>2.2</td>
<td>1.4</td>
<td>0.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Troponine, ng/ml</td>
<td>3.4</td>
<td>2.1</td>
<td>0.6</td>
<td>0.05</td>
<td>0.01</td>
<td></td>
</tr>
</tbody>
</table>

^a, b: initial values of plasmapheresis and hemodialysis

Figs 1A-1B. 5989 bee stings more prominent on his face and severe petechia and ecchymosis on his body.
of the venom responsible of these clinical presentations include toxic surface-active polypeptides (mellitin and apamin), enzymes (phospholipase A₂ and hyaluronidase), and low molecular weight agents (histamine and amino acids). Mellitin and phospholipase A₂ are important components causing rhabdomyolysis following a toxic action on striated muscles and also act on the red cell membrane and provoke hemolysis. PLA₂ is also known to cause coagulation abnormalities as a rare complication of bee stings. We thought that the patient’s clinical findings associated with systemic toxic effects of bee stings. Hence, serum tryptase level was not evaluated. A raised tryptase may be a useful clue to the diagnosis of anaphylaxis but should only be ordered if the diagnosis is unclear such as in unexplained and life-threatening cardiac or respiratory collapse. Serum tryptase returns to normal within hours of anaphylaxis, and a normal serum tryptase does not exclude anaphylaxis. Serum tryptase is unstable and must be transported to the laboratory quickly.

Systemic toxic reactions due to venom compounds are usually observed after 50 to 100 bee stings. In our case, exposed to many bee stings: hemolysis, rhabdomyolysis, and elevation of serum hepatic transaminase developed within 48 hours. Finally multiorgan failure occurred due to possible toxic effects of the venom. In the literature, it is recommended that plasmapheresis should be used for the treatment of life-threatening multisystem organ failure due to stings of members of the order Hymenoptera (honey bee, bumble bee, wasp, hornet, yellow jacket). We performed plasmapheresis earlier than literature recommendation due to excessive circulating venom load and severe hemolysis. It was administrated twice daily for 3 days. Renal failure progressed despite urine alkalization and enough output due to severe rhabdomyolysis and hemolysis. We also started hemodialysis in addition to the other treatments. Besides, intracranial infarct was detected on the 3rd days of admission. Bee venom itself contains histamine, thromboxane, leukotrienes, and other vasoactive and inflammatory mediators. Both thromboxane and leukotrienes have been shown to cause vasoconstriction resulting in cerebral ischemia. Additionally, releasing endogenous cathecolamines by phospholipase and mellitin can cause hypertension and cerebral infarct. Despite of the antihypertensive treatment such as nitroprusside, nitroglycerin and minoxidil, our patient remained severe hypertensive for 3 days. We failed the case despite of all treatments because of multiorgan failure. There were only two fatal pediatric cases due to delayed toxic reactions except our case. Additionally, our case report enclosed the major complications reported in the literature due to bee stings such as renal failure, intracranial infarct, hypertension, and convulsion, hepatic failure, peripheral neuropathy, etc.

As a conclusion, pediatricians dealing with emergent conditions should be aware about
delayed toxic reactions for all children who have more than 50 stings.

REFERENCES