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Case Report

Multiple bee stings, multiple organs involved: a case report

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Abstract

Accidents related to Africanized honey bees are growing globally and are associated with multiple stings owing to the aggressive behavior of this species. The massive inoculation of venom causes skin necrosis and rhabdomyolysis leading to renal failure. Anaphylactic manifestations are more common and are treated using well-defined treatment protocols. However, bee venom-induced toxic reactions may be serious and require a different approach. We report the case of a 3-year-old child, which would help clinicians to focus on the treatment approach required after an incident involving multiple bee stings.

Keywords: Africanized honeybee stings. Treatment guidelines. Apis mellifera.

INTRODUCTION

European honey bees (EHB) were introduced in Brazil in 1839. African queen bees brought in 1956 to optimize honey production, accidentally escaped in 1957 causing wild hybridization, reaching the Americas at a rate of 300-500km/year[1,2] .

Although more productive, Africanized honey bees (AHB) are more defensive[2]. They sting 4-10 times more than the EHB given the same stimulus[3]. They usually pursue intruders as large groups traveling over several miles and include approximately 10-30 times more bees and also show a larger defensive perimeter (distances ≥100 meters from the colony) than EHB[3].

AHB have spread throughout the Americas and their aggressiveness emphasizes the need for adequate knowledge regarding the optimal management of these attacks.

We report a case of massive AHB envenomation in a 3-year-old child who developed multiorgan system involvement (ocular, integumentary, renal, cardiac, and hepatic) and describe the management in the pediatric intensive care unit (ICU).

CASE REPORT

A 3-year-old boy was attacked by a large swarm of AHB (approximately 1,000 stings) affecting his entire body - primarily his head, the trunk and the upper limbs. The child, still awake, was rescued by his father and following transfer to the hospital, was intubated in the ICU and diagnosed with probable anaphylactic shock. His condition deteriorated, and he developed hypodynamic shock with severe cardiac dysfunction (ejection fraction 43%) and arterial hypotension. He was treated with adrenaline (0.3mcg/kg/min), dobutamine (5mcg/kg/min), noradrenaline (1mcg/kg/min), hyperhydration (3,000mL/m^2/day), bicarbonate replacement, and continuous diuretic and aminophylline infusions. Initially, he received hydrocortisone 250mg/m^2/day for 5 days, which was reduced to 150mg/m^2 over the subsequent 5 days, followed by slow dose reduction. He showed thrombocytopenia (54,000/mm^3) and liver dysfunction with alanine aminotransferase elevated to 257U/L, aspartate aminotransferase to 1,348U/L, international normalized ratio of 2.35, and *lactate dehydrogenase* (LDH) of 3132 U/L.

He developed rhabdomyolysis with creatine phosphokinase (CPK) levels of 28,700U/L, creatine kinase-MB fraction (CK-MB) 589U/L, troponin 15.96ng/L, and myoglobin >3,781mg/L. The consequent oligoanuria (<0.5mL/h), anasarca, hyperuricemia with a maximum uric acid level of 8mg/dL, and hyperphosphatemia with a maximum phosphate of 11.4mg/dL necessitated treatment with prolonged hemodialysis (6-8h/day) on the 3rd day of ICU admission. The bee stings were removed. Skin lesions evolved to vasculitis and resolved following treatment with potassium permanganate baths and topical essential fatty acids (**Figure 1**). Stings were identified in both eyes, with corneal involvement of the left eye. The stings were removed by the ophthalmology. Secondary eye infection was treated using moxifloxacin eye drops, topical corticosteroids, and atropine (**Figure 2**). He developed bacteremia and leukocytosis of 33.8 x 10^9/L, left shift with 10% of metamyelocytes and was empirically treated with meropenem, teicoplanin, and amphotericin B.

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FIGURE 1: Skin lesions that evolved into vasculitis.

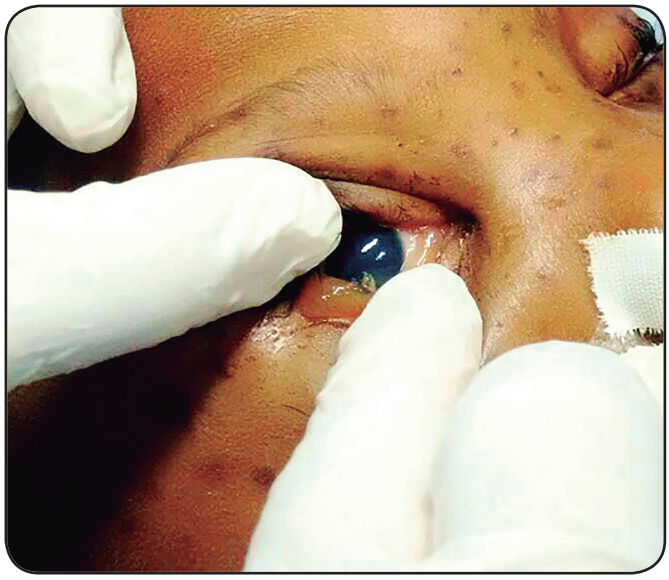

FIGURE 2: Eye involvement showing a bee sting present in the eye.

On the 5th day, his cardiac function stabilized, (ejection fraction 69%, troponin 0.1ng/mL), and his inotropic and vasoactive drugs were reduced. Liver function normalized on the 13th day of hospitalization. The CPK level dropped only after the 8th day (1,499U/L), CK-MB (45U/L), myoglobin (119.5mg/L), and LDH (1,193U/L). Normal diuresis was re-established on the 10th day of hospitalization, and dialysis was discontinued. The patient was extubated on the 15th day of hospitalization after appropriate management of his multiorgan dysfunction.

He was discharged from the ICU on the 18th day of hospitalization with CPK levels of 60U/L and CK-MB 19U/L. Subcapsular cataract of the left eye and a few hypertrophic scars were observed 60 days after discharge.

The study was approved by the Ethics Committee Review Board of the Institution.

DISCUSSION

Clinical manifestations after bee attacks may vary. A few individuals may develop only local inflammatory reactions (few stings), whereas allergic manifestations and anaphylactic shock may occur in those previously sensitized after even a single sting. A few individuals may develop secondary toxic reactions to envenomation (multiple stings)[4]. The massive inoculation of venom containing different molecules, including phospholipase A2, hyaluronidase, melittin, and apamine can produce skin necrosis at the sting site and rhabdomyolysis causing renal failure[4]. In this case, in addition to the manifestations of anaphylaxis, we observed secondary toxic reactions to poisoning.

Initial symptoms of poisoning are fatigue, dizziness, nausea, vomiting and diarrhea, which evolve into hemolysis, hemoglobinuria, rhabdomyolysis, and elevated hepatic transaminases culminating in acute renal insufficiency. Owing to the large number of stings (approximately 1,000), the patient was comatose upon arrival at the hospital, similar to a 9-year-old girl who presented with approximately 800 stings[5], and a 17-year-old male adolescent who presented with 1,500 stings[6]. A retrospective analysis reported 11 survivors of multiple bee stings (number of stings 20-500 in individuals aged 5-87 years). However, no patient was in a comatose state[4]. Although animal studies have estimated 3.5mg/kg[7] as the mean lethal dose of venom, the estimated lethal dose in humans remains unknown. Age, body weight, number of stings, and individual characteristics of the victim (immune status, comorbidities, and previous sensitization) determine the severity of the condition.

The CPK peaked to an extremely high level within the first 48 hours after the attack, similar to the findings in a 13-year-old boy affected by 700 stings[8]. However, other studies have reported CPK levels peaking between the 4th and 6th day, followed by a slow decrease[4,5].

Renal impairment occurs secondary to toxic-ischemic mechanisms, with hypovolemic and anaphylactic shock associated with acute tubular injury following muscle injury, hemolysis, and/or acute tubular necrosis and the direct toxicity of the venom[4]. Our patient was treated with vigorous hydration to minimize hemoglobinuria and myoglobinuria-induced renal lesions[4]. Despite this treatment, he developed oligoanuria, hyperuricemia, and hyperphosphatemia necessitating intermittent hemodialysis (6-8h/day) initiated on the 3rd day of ICU admission. A study performed by Mejía-Vélez observed that 7 of 43 patients presenting with acute renal failure secondary to multiple AHB stings did not recover their renal function and died, emphasizing the importance of prompt determination of the severity of renal impairment and early treatment for renal dysfunction[9]. This study also showed that hematuria was observed within the first 24h of presentation. A previous case report showed that a 13-year-old boy presented to the Emergency Department and was

discharged following treatment; however, he returned 4h later with features consistent with envenomation[8]. Thus, even those who appear oligosymptomatic in the early hours of presentation require long-term monitoring to avoid possible complications.

Although we did not determine electrocardiographic changes that could have been transient, we observed cardiac dysfunction indicated by the elevated cardiac enzymes and the reduced ejection fraction. Kounis syndrome, also called allergic angina syndrome or allergic myocardial infarction comprises acute coronary syndrome, including coronary spasm, acute myocardial infarction, and stent thrombosis. This condition involves mast cell and platelet activation and the action of inflammatory cells (macrophages and T lymphocytes) causing allergic reactions, hypersensitivity, and anaphylactic/anaphylactoid symptoms[10]. Therefore, it is important to assess troponin levels and obtain electrocardiograms and echocardiograms in these patients.

Other studies have reported hepatic complications indicated by elevated transaminases[5,6,8]. The liver could possibly be affected by the direct toxicity of the venom, autoimmune reaction and causes poisoning-induced anaphylactic shock[4].

The optimal method to remove the stings remains controversial; thus, this was not the priority here, and most stings were removed by shaving the skin using a razor rather than extracting them[4]. However, some portion of the venom reservoir persisted.

Bee stings can cause corneal injury and venom-related toxic or immunological inflammation with visual sequelae including corneal opacities, bullous keratopathy, and optic neuropathy[11]. In this patient, appropriate removal of the stings, and the use of a topical antibiotic and high-dose topical corticosteroids ensured good recovery of his vision, and he developed only subcapsular cataract in the left eye.

This case concurs with the report by Almeida et al. indicating that accidents related to multiple AHB stings constitute a medical emergency[4], and the potential severity of the condition must not be underestimated. Since October 1957, when 26 swarms of AHB escaped from an apiary in Rio Claro, Brazil, and then spread through the Americas[1]. Thus, AHB attacks are now considered a public health issue not only in Brazil but in other American countries[1]. Bee sting accidents have been under-reported over the years. Diniz et al. indicated the importance of epidemiological data to improve the existing knowledge regarding honeybee envenomation at regional levels[1]. Improved data collection requires appropriate differentiation between secondary allergic reactions and envenomation and ascertaining whether the reaction occurs after a single or multiple stings.

Researchers from the Center for the Study of Venoms and Venomous Animals of the São Paulo State University have provided useful perspectives regarding the treatment of honey bee attacks with evenomation and in partnership with the Vital Brazil Institute, Brazil, have developed the apilic antivenom[12]. Recently, a clinical protocol was developed for application in a multicenter non-randomized and open phase I/II clinical trial to address the safety, to determine the pharmacokinetic and proteomic profile, and confirm the lowest antivenom dose, based on the severity in each case[12]. The protocol will include participants aged >18 years; however, the inclusion of children has not yet been considered.

In conclusion, multiple bee stings can cause multiorgan injuries and serious clinical manifestations secondary to envenomation induced-anaphylactic and toxic reactions. Thus, these patients require prompt and appropriate treatment. Even in patients without early symptoms, long-term monitoring is essential to avoid morbidities and more severe outcomes including death. Improved collection of epidemiological data related to these attacks is required to ensure improved care in severe cases. Clinical trials to evaluate apilic antivenom can potentially offer perspectives on better treatment in such patients[12].

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Conflict of interest

The authors declare that there is no conflict of interest.

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