Rev. Inst. Med. Trop. Sao Paulo
55(1):61-64, January-February, 2013
doi: 10.1590/S0036-46652013000100011

CASE REPORT

RRH: ENVENOMING SYNDROME DUE TO 200 STINGS FROM AFRICANIZED HONEYBEES

Guilherme Almeida Rosa da SILVA, Karina Lebeis PIRES, Diogo Cerqueira de Salles SOARES, Marcos Rosa FERREIRA, Fernando Raphael de Almeida FERRY, Rogerio Neves MOTTA & Marcelo Costa Velho Mendes de AZEVEDO

SUMMARY

Envenoming syndrome from Africanized bee stings is a toxic syndrome caused by the inoculation of large amounts of venom from multiple bee stings, generally more than five hundred. The incidence of severe toxicity from Africanized bee stings is rare but deadly. This report reveals that because of the small volume of distribution, having fewer stings does not exempt a patient from experiencing an unfavorable outcome, particularly in children, elderly people or underweight people.

KEYWORDS: Envenoming syndrome; Stings; Africanized honeybees; Review.

INTRODUCTION

Envenoming syndrome by multiple Africanized bee stings is a toxic syndrome caused by the large amount of venom inoculated. The incidence of envenoming syndrome is rare. Treatment is not specific and it does not determine the prognosis of the envenomation[2]. European honey bees, *Apis mellifera mellifera* and *Apis mellifera ligustica*, were introduced to Brazil in 1839 and 1870, respectively. They were poorly adapted to Brazilian climatic conditions and had low honey production. In 1956, the African bee, *Apis mellifera scutellata*, characterized by an aggressive nature and high honey production, was introduced to Brazil. In 1957, there was an accidental release of some African queen bees, which resulted in the hybridization or Africanization of European honey bees in the Brazilian environment and uncontrolled mixed breeding of the species[12].

Africanized bees are fully adapted to the tropical climate of Brazil. They are aggressive and attack in large numbers when they sense a threat to their hive. The persistent nature of their attack means that when an individual is stung, he or she will likely be inoculated with a large quantity of venom, which can result in envenoming syndrome (Gonçalves LS, unpublished data). Herein, we report a case of envenoming syndrome from Africanized bee stings that presented a favorable outcome for our service. We also review literature on the management and prognosis of this rare syndrome.

CASE REPORT

A 76-year-old retired Army sergeant with type 2 diabetes and prostate cancer was attacked by a swarm of bees after lifting a stone located in a construction area. Because of a bilateral periorbital angiodema, he was treated with intravenous steroids and promethazine in the emergency hospital. He was subsequently transferred to the 10th Ward of the Gaffrée Guinle University Hospital for clinical observation and evaluation, where they determined that he presented near two hundred stings. He was admitted in good general condition. The patient was non febrile, stable and without respiratory complaints or altered mental status. He was diagnosed as having bilateral periorbital angioedema, papules, blisters and tubercles with a confluent erythematous base on the chest, upper limbs and head (Fig. 1 and 2). Upon admission, he was prescribed intravenous hydration at 2.000

Fig. 1 - Bilateral periorbital angioedema.

Nacional School of Medicine and Surgery, Federal University of Rio de Janeiro State (UNIRIO)/Gaffrée e Guinle Universitary Hospital, Rua Mariz e Barros 775, Tijuca, 20270-004 Rio de Janeiro, RJ, Brazil.
Correspondence to: Guilherme Almeida Rosa da Silva. E-mail: drguialmeida@gmail.com

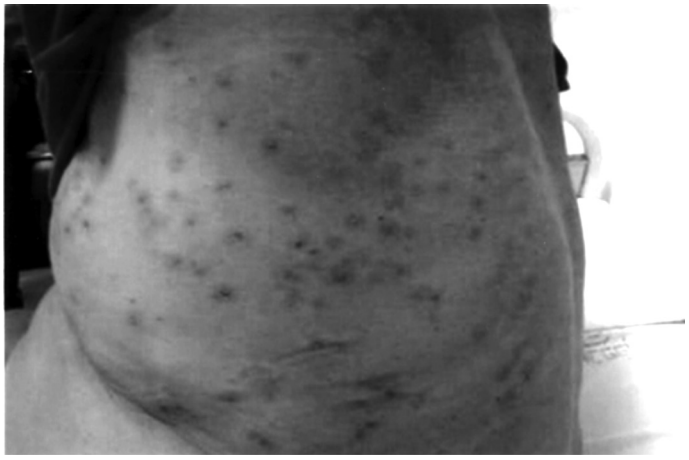

Fig. 2 - Papules, blisters and tubercles with a confluent erythematous base.

mililiter/d, analgesia, selective H1-antihistamine and 1 milligram/kilograms of weight of prednisone.

Twenty hours after admission, he unexpectedly progressed to obnubilation and seizures, scoring an 8 on the Glasgow coma scale, which indicated that he was in a postictal state. He was promptly intubated by the medical team and transferred to the Intensive Care Unit (ICU). Upon admission to the ICU, he was prescribed phenytoin as a prophylactic anticonvulsant, and cranial computed tomography was performed without contrast; the result was normal.

The laboratory tests showed increased lactate dehydrogenase (LDH; 437 international units/liter) and creatine kinase (CK; 525 international units/liter), consequent to hemolysis and muscle damage. He also exhibited a slight increase in indirect bilirubin (0.7 milligrams/deciliter), mild anemia, leukocytosis (14,100 cells/mm³), neutrophilia, hyperglycemia and increased blood urea nitrogen (40 milligrams/deciliter).

In 24 hours, the patient's skin lesions and angioedema showed improvement. However, there was a decrease in urine output and a positive fluid balance accompanied by mild pulmonary congestion. The oliguria persisted for over 24-48 hr, with a good response to the use of loop diuretics. On the fourth day of hospitalization, the ventilatory assistance was withdrawn, and the corticosteroid therapy dosage was reduced. The skin lesions had involuted and appeared only as papular and crusted lesions that were slightly erythematous. On the seventh day of hospitalization, the patient was transferred from the ICU to the ward, where he remained for two days. After nine days in the hospital, the patient was discharged, fully lucid and oriented, with normal muscle enzyme, bilirubin and nitrogenous compound levels. The laboratory findings are listed in Table 1.

Table 1
Laboratory findings

Day	1	3	5	7	9
Urea (mg/dL)	**79.9**	**78**	**63.1**	32.5	24
Creatinine (mg/dL	1.1	0.9	0.7	1.0	1.1
Glucose (mg/dL)	**370**	94	**189**	**205**	**186**
Potassium (mEq/L)	4.28	3.86	4.12	3.88	4.2
Sodium (mEq/L)	136	137	140	140	137
Hematocrit (%)	**28**	**25**	**30**	**30**	**36**
Hemoglobin (g/dL)	**9.6**	**8.5**	**10.2**	**10**	**12.1**
Platelets (x10³/mm³)	156	150	**148**	152	**148**
Prothrombin time (control:13``)	**14**	**14**	**15**	**15**	**15**
Partial thromboplastin time (control:28``)	26	26	28	28	28
AST (IU/L)	35	20	11	18	18
ALT (IU/L)	19	15	17	12	11
Direct bilirubin (mg/dL)	0.2	0.1	0.2	0.2	0.2
Indirect bilirubin (mg/dL)	**0.7**	0.4	0.3	0.2	0.2
LDH (IU/L)	**437**	**358**	**324**	**280**	**283**
Creatine kinase (IU/L)	**525**	**274**	**159**	107	51
PH	7.35	7.38	7.38	7.37	
Bicarbonate (mEq/L)	22	23	24	23	
PCO_2 (mmHg)	42	20	38	39	
Hydric balance	+	+	-	-	
Urine – Red blood cells	++	+	+		
White blood cells	+	+			
Proteinuria	+	+	+		

LDH- lactate dehydrogenase; AST- aspartate amino transaminase; ALT- alanine amino transaminase; PCO_2 - partial pressure of CO_2.

DISCUSSION

Africanized bee venom is made up of degradative enzymes, such as phospholipase A2, hyaluronic acid, phospholipase B and esterases. The large peptides present in bee venom are melittin (50% of the total venom composition), apamin and mast cell-degranulating peptides. Small peptides present in bee venom include secarpin, tertiapin, procamine and biogenic amines (histamine, dopamine, serotonin and norepinephrine)[15]. The degradative enzymes contribute to the penetration of the toxin into the bloodstream and the lysis of cells, including erythrocytes, leukocytes, platelets and endothelial cells. This can result in intravascular hemolysis with increased bilirubin, increased LDH, decreased haptoglobin, hemoglobinuria and thrombocytopenia, and in more severe cases, disseminated intravascular coagulation (DIV). The patient of the present case developed a mild hemolysis without DIV, since the number of stings was low. Other possible manifestations include hepatitis, rhabdomyolysis with myoglobinuria, increased CK, increased aldolase and acute tubular necrosis[6,16]. The main reports of envenoming syndrome by multiple bee stings and information on the cases are listed in the Table 2[1-10,13,16,17,20,21].

Seizures are a rare manifestation in envenoming syndrome by multiple Africanized bee stings, and are associated with a greater number of stings. In the present case, hyperglycemia or hypoglycemia associated to *diabetes mellitus* and the patient age are some factors that may influence the neurologic symptoms. Obnubilation is frequent and may be associated with electrolyte disorders, shock and direct action of the Africanized bee venom. It is not clearly associated with a large number of stings[23].

Apamin is a large peptide that is most likely responsible for neurotoxicity. Experimental models demonstrate its role in synapses and neuromuscular junctions, resulting in hyperexcitability and seizures[2,18]. Mast cell-degranulating peptide promotes the release of serotonin, histamine and arachidonic acid derivatives, stimulating inflammation and the increased absorption of the toxin as well as headaches, flushing, hypotension and cardiovascular changes[18]. Treatment of this condition is based on support and attention by the medical team, especially regarding hemodynamic and respiratory problems. An assessment of renal function, urine output and electrolytes should be performed in addition to cardiac monitoring, oximetry and intravenous access. Intravenous hydration (2,000 milliliters) should be administered early after admission with epinephrine, immunosuppressive corticosteroids and antihistamines (one class or a combination of two classes).

It is difficult to differentiate between the effects of systemic envenoming syndrome by bee stings and an anaphylactic reaction. Both conditions can occur in a patient sensitized to bee venom. When the patient in the case was admitted, he was non febrile, stable, without respiratory complaints and only presented bilateral angioedema as a mild anaphylactic reaction. Severe reactions usually begin within 10 min of the sting and only rarely develop after five hours. All the later symptoms presented in the case were assigned as part of envenoming syndrome. With greater amounts of venom (more than five hundred stings), the risk of developing envenoming syndrome increases[8,16,18].

In the present case, the stings were not removed and this may have contributed to the serious complications. The early removal of stings by clamping or scraping can reduce the amount of venom injected. However, scraping is believed to decrease the risk of venom inoculation during the subsequent clamping procedure[2,22]. A study at the University of California showed no change in the blood levels of the toxin content 10 min after removing the stings, as the venom content had been completely released from the stings by this time[22]. SCHUMACHER demonstrated that antibodies against the venom of Africanized bees obtained from the serum of beekeepers were effective in counteracting the deleterious

Table 2
Reported cases of envenoming syndrome by multiple bee stings

Author	Age (years)	Gender	Stings	Complications	Outcome
Penteado JOP	33	Male	3200	Shock, rhabdomiolysis, ARF	Died
Díaz-Sánchez	30	Male	>2000	Shock, coma, anemia, ARF	Survived
Azevedo RV	19	Male	2000	Shock, rhabdomiolysis, ARF	Died
Humblet Y	61	Male	>1000	Rhabdomyolysis, ARF	Survived
Sert M	68	Male	>1000	Rhabdomyolysis, ARF	Died
Daher EF (2 cases)	4-17	Males	600-1500	Rhabdomyolysis, ARF	Survived
França FOS (5 cases)	8-64	Males	200-1000	Shock, coma, rhabdomiolysis, ARF	3 Died
Mejia G (43 cases)	Mean 56	38 Males 5 Females	Mean 900	ARF	7 Died
Bresolin NL	9	Female	800	Seizures, rhabdomiolysis, ARF	Survived
Betten DP	13	Male	700	Rhabdomyolysis, ARF	Survived
Gabriel DP	55	Male	>500	ARF, anemia	Survived
Almeida RAMB	5-87	7 Males 4 Females	20-500	Rhabdomyolysis, ARF	1 Died
da Silva GAR	76	Male	200	Seizures, rhabdomiolysis, ARF	Survived
Oliveira FA (5 cases)	20-53	3 Males 2 Females	2-60	Headache, myalgia, nausea	2 Died
Daher EF (2 cases)	54-61	Males	-	ARF	1 Died
Sena RS	59	Male	-	Rhabdomyolysis, ARF	Survived

ARF- Acute renal failure.

effects of the venom in rats[11]. In 2010, the Butantan Institute (Brazil, São Paulo) developed and patented the first horse serum for use in humans to treat envenoming syndrome by Africanized bee stings. This serum is awaiting authorization from the Brazilian health regulatory agency for testing in humans with acute poisoning[11].

The case discussed in this report shows that a small number of stings can result in an unfavorable health outcome and that children, older people and underweight people may have a higher risk of envenoming, because of the small volume of distribution. The late manifestation of the syndrome (more than 24 h later) may be due to fewer venom inoculations. Because this patient was under observation in the hospital, he was quickly treated by the medical team for the unexpected complications. The treatment is not specific and it does not determine the prognosis of the envenomation. When the envenomation is severe, it is common to result in the death of the patient. Had the patient been discharged when he was asymptomatic, urgent care may have been delayed, resulting in a worse prognosis. While anecdotal, this case would suggest that individuals who are multiply stung should be closely observed for 24-48 h, but this deserves further scientific evaluation.

RESUMO

RRH: síndrome de envenenamento por 200 ferroadas de abelhas africanizadas

A síndrome de envenenamento por ferroadas de abelhas africanizadas é causada pela inoculação de uma grande quantidade de peçonha por múltiplas ferroadas de abelhas, geralmente acima de quinhentas. A incidência de uma intoxicação severa por ferroadas de abelhas africanizadas é rara, porém letal. Este relato de caso aponta que, devido a um menor volume de distribuição do veneno, um número menor de ferroadas por abelhas africanizadas não exime o paciente de apresentar envenenamentos com desfecho desfavorável, principalmente em crianças, idosos e pessoas com baixo peso.

REFERENCES

1. Almeida RAMB, Olivo TET, Mendes RP, Barraviera SRCS, Souza LR, Martins JG, *et al.* Africanized honeybee stings: how to treat them Rev Soc Bras Med Trop. 2011;44:755-61.

2. Azevedo RV, Paiva RB, Ades F, David CM. Síndrome de envenenamento por 2000 picadas de abelhas africanizadas. Relato de caso. Rev Bras Ter Intensiva. 2006;18:99-103.

3. Betten DP, Richardson WH, Tong TC, Clark RF. Massive honey bee envenomation-induced rhabdomyolysis in an adolescent. Pediatrics. 2006;117:231-5.

4. Bresolin NL, Carvalho LC, Goes EC, Fernandes R, Barotto AM. Acute renal failure following massive attack by Africanized bee stings. Pediatr Nephrol. 2002;17:625-7.

5. Daher EF, da Silva Junior GB, Bezerra GP, Pontes LB, Martins AMC, Guimarães JA. Acute renal failure after massive honeybee stings. Rev Inst Med Trop Sao Paulo. 2003;45:45-50.

6. Daher EF, Oliveira RA, Silva LSV, Silva BEM, Morais TP. Insuficiência renal aguda por picada de abelhas: relato de casos. Rev Soc Bras Med Trop. 2009;42:209-12.

7. Diáz-Sánchez CL, Lifshitz-Guinzberg A, Ignacio-Ibarra G, Halabe-Cherem J, Quinones-Galvan A. Survival after massive (>2000) Africanized honeybees stings. Arch Intern Med. 1998;158:925-7.

8. Franca FOS, Benvenuti LA, Fan HW, Dos Santos DR, Hain SH, Picchi-Martins FR, *et al.* Severe and fatal mass attacks by "killer" bees (Africanized honey bees-*Apis mellifera scutellata*) in Brazil: clinicopathological studies with measurement lf serum venom concentrations. Q J Med. 1994;87:269-82.

9. Gabriel DP, Rodrigues AG Jr, Barsante RC, dos Santos-Silva V, Caramori JT, Martim LC, *et al.* Severe acute renal failure after massive attack of Africanized bees. Nephrol Dial Transplant.2004;19:2680.

10. Humble Y, Sonnet J, Van Ypersele de Strihou C. Bee stings and acute tubular necrosis. Nephron. 1982;31:187-8.

11. Jornal da Tarde, 2010, July 6. Butantã produz soro contra picada de abelha. Available from: http://blogs.estadao.com.br/jt-cidades/instituto-butanta-produz-soro-contra-picada-de-abelha/ [Cited: 2011 Dec 1].

12. Kerr WE. Genética e biologia de abelhas. Cien Cult. 1973;25:927-33.

13. Mejia Vélez G. Acute renal failure due to multiple stings by Africanized bees. Report on 43 cases. Nefrologia. 2010;30:531-8.

14. Mello MHSH, Silva EA, Natal D. Abelhas africanas em área metropolitana do Brasil: abrigos e influências climáticas. Rev Saúde Pública. 2003;37:237-41.

15. Mendes RP, Meira DA, Molinari H, Rodrigues OS, Coelho KYR. Acidentes por múltiplas picadas de abelha. Arq Bras Med. 1990;64:81-8.

16. Oliveira FA, Guimarães JV, Reis MA, Teixeira VP. Acidente humano por picadas de abelhas africanizadas. Rev Soc Bras Med Trop. 2000;33:403-5.

17. Penteado JOP, Oliveira CH, D´Angieri A, Graudenz GS, Massucato AE, Castro AB, *et al.* 3200 picadas de abelhas africanizadas. Rev Bras Ter Intensiva. 2003;15:176-9.

18. Schumacher MJ, Schmidt JO, Egen NB. Lethality of "killer" bee stings. Nature. 1989;337(6206):413.

19. Schumacher MJ, Schmidt JO, Egen NB, Lowry JE. Quantity, analysis and lethality of European and Africanized honey bee venoms. Am J Trop Med Hyg. 1990;43:79-86.

20. Sena RS, Neves MR Jr, Honorato PR, Sales MR, Damasceno SA, Elamide BC, *et al.* Insuficiência renal aguda por conta da rabdomiólise por múltiplas picadas de abelhas: relato de caso. Rev Hosp Univ Getúlio Vargas. 2011;10:39-43.

21. Sert M, Tetiker T, Paydas S. Rhabdomyolysis and acute renal failure due to honeybee stings as an uncommon cause. Nephron. 1993;65:647.

22. Visscher PK, Vetter RS, Camazine S. Removing bee stings. Lancet. 1996;348:301-2.

23. Viswanathan S, Muthu V, Singh AP, Rajendran R, George R. Middle cerebral artery infarct following multiple bee stings. J Stroke Cerebrovasc Dis. 2012;21:148-50.

Received: 28 June 2012
Accepted: 6 August 2012