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CASE REPORT

ACUTE RENAL FAILURE AFTER MASSIVE HONEYBEE STINGS

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SUMMARY

Two clinical cases of patients who survived after numerous attacks of Africanized bees (600 and 1500 bee stings, respectively) are reported. Clinical manifestation was characterized by diffuse and widespread edema, a burning sensation in the skin, headache, weakness, dizziness, generalized paresthesia, somnolence and hypotension. Acute renal failure developed and was attributed to hypotension, intravascular hemolysis, myoglobinuria due to rhabdomyolysis and probably to direct toxic effect of the massive quantity of injected venom. They were treated with antihistaminic, corticosteroids and fluid infusion. One of them had severe acute renal failure and dialysis was required. No clinical complication was observed during hospital stay and complete renal function recovery was observed in both patients. In conclusion, acute renal failure after bee stings is probably due to pigment nephropathy associated with hypovolemia. Early recognition of this syndrome is crucial to the successful management of these patients.

KEYWORDS: Multiple stings; Acute renal failure; Rhabdomyolysis; Bee venom.

INTRODUCTION

The Africanized bee (*Apis Mellifera*) was originated from an apiculture laboratory in Brazil and subsequently extended its range to the rest of Americas[3]. An increasing frequency of Africanized bee attacks has been recently reported in Mexico and in the southern United States[16]. In Brazil, the great majority of accidents involving insect stings remain unreported[9,14]. Accidents involving venomous animals are very common in the State of Ceará, northeast of Brazil (data from CEATOX - Toxicological Center of Ceará). The Africanized bee attacks are characteristically massive, and, excluding the cases of anaphylaxis, the injected venom intensity and the prognosis are directly associated with the number of bee stings[2,3,10,11]. It has been observed that multiple bee stings are capable of causing death, in an adult man, which is probably due to a direct toxic effect of the venom[5,7].

There are several studies about the effects of honeybee venom in human organism[1,3,4,15,16]. The incidence of anaphylaxis caused by insect stings has been estimated from 0.3 to 3% in the general population[15]. Allergic manifestations to honeybee and wasp stings are well recognized, but more serious complications like intravascular hemolysis, rhabdomyolysis, thrombocytopenia, acute renal failure, liver impairment and myocardial infarction are less common[8,13,17,19]. Acute renal failure would occur due to toxic-ischemic-type mechanism as hypovolemia, myoglobinuria, hemoglobinuria, renal ischemia, or direct venom toxicity[4,12,18,20].

After the approved consent of the ethical committee, we report two patients who suffered multiple bee stings from Africanized bees. The first patient developed severe acute renal failure and the second one presented mild acute renal failure.

CASE REPORTS

Case 1: A 17-year-old boy from countryside of Ceará, Northeast of Brazil, was previously healthy when was attacked by America's Africanized bees in a rural area. Immediately after the massive attack, he presented nausea, vomiting, muscular weakness, generalized paresthesia and diffuse edema. The boy became unconscious under the sunbeam for at least six hours. He received emergency treatment in the nearest hospital seven hours after the bees attack. Twenty-four hours later he was transferred to the General Hospital of Fortaleza for further treatment. At admission the patient was semi-conscious, with dyspnea, generalized edema, arterial hypotension (blood pressure of 70/40 mmHg), tachycardia (pulse rate of 120 bpm) and with dark colored urine. More than 1500 bee stings were observed all over his body. Treatment was started as soon as he was admitted and consisted of saline solution infusion, hydrocortisone and parenteral anti-histaminic type 2-receptor.

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Twenty-four hours later, after fluid infusion, blood pressure was 140/90 mmHg and the patient was still anuric (50ml/24 h) even after abundant hydration and diuretic administration. His renal function continued to deteriorate although her blood pressure remained well preserved and no evidence of systemic infection was observed. There was some evidence for hemolysis and rhabdomyolysis, and no disseminated intravascular coagulation was detected. The laboratorial data during hospitalization are summarized in Table 1. The ultrasound showed kidneys with increased size, compatible with acute renal failure. The constant increasing in the serum urea and creatinine levels, and persistent anuria, were indication for dialytic treatment (Fig. 1). Ten hemodialysis sessions were performed during hospitalization. Twenty-six days after the initial event the patient was discharged with partial renal function recovery. Two weeks after discharger the renal function was normal.

Table 1
Laboratory findings (Case 1)

Day	1	6	9	18	20	26
Urea (mg/dL)	177	254	268	267	163	52
Creatinine (mg/dL)	5.9	9.3	10	7.7	4.4	1.5
Potassium (mEq/L)	5.6	5.0	5.1	5.8	3.9	4.1
Sodium (mEq/L)	128	129	130	133	134	143
Hematocrit (%)	36	27	19	20		28
Hemoglobin (g/dl)	14	10	7.4	7.2		8.2
Platelets (x10^3 mm^3)	278	264	220			
Prothrombin time (control:13")	14.4	13.7	13.6			
Partial thromboplastin time (control:28")	24.6	32.3	27.6			
AST (IU/L)	1164	128	22			
ALT (IU/L)	214	68	50			
Direct bilirubin (mg/dL)	0.22					
Indirect bilirubin (mg/dL)	2.41					
LDH (IU/L)		1101				
Creatine kinase (IU/L)		588				
pH	7.32	7.35	7.43			
Bicarbonate (mEq/L)	14	8	18			
PCO_2 (mmHg)	28	15	28			
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.

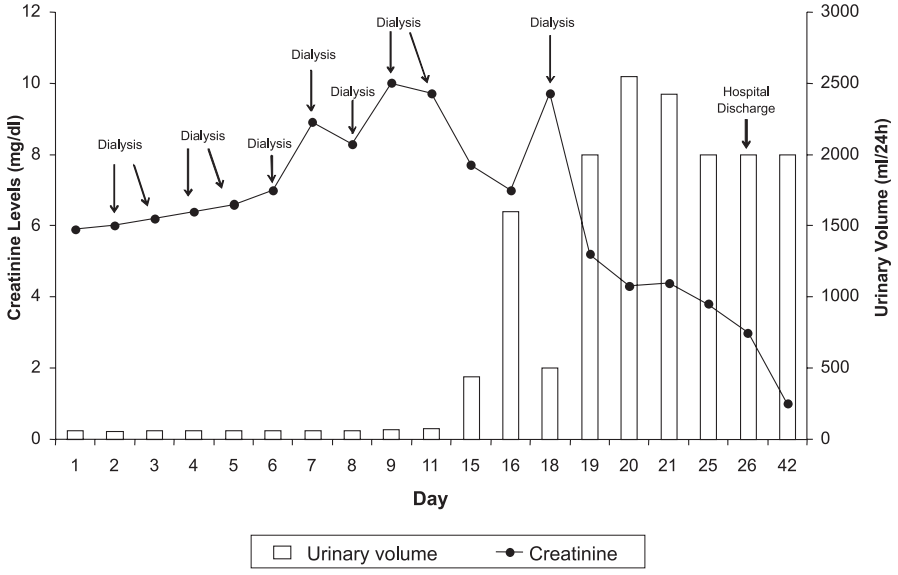

Fig. 1 – Urinary volume, serum creatinine levels and dialysis sessions during hospitalization (Case 1).

Case 2: A 4-year-old child from Fortaleza City, Ceará State, Northeast of Brazil, was in a forest with his father hunting honeybees when both were attacked. His father immediately took him to an emergency hospital (Center of Toxicological Care – José Frota Institute). He received emergency treatment half an hour after the bees attack. At arrival he was sleepy, with bouts of agitation, generalized edema, and signs of multiple bee stings, estimated in 600 stings. His father also presented bee stings, but was stable and did not need aggressive treatment. The little boy was dehydrated, with abdominal pain, dark colored urine, glottis edema and oliguria at admission. He was then submitted to mechanical ventilation due to respiratory failure. The blood pressure was 80 x 50 mmHg and heart rate was 130 bpm. The laboratorial data during hospital stay are expressed in table 2. The urinary volume was 60 ml/day at the first hospital day. The treatment consisted of hydrocortisone and vigorous hydration with alkaline solution. Three days after admission diuresis was spontaneously increased and the levels of urea and creatinine progressively decreased (Fig. 2). There was some evidence for hemolysis and rhabdomyolysis but no disseminated intravascular coagulation was

Table 2
Laboratory findings (Case 2)

Day	1	2	3	4	6	7	9	12
Urea (mg/dL)	48	53	80	83	36	33	33	13
Creatinine (mg/dL)	0.9	0.8	0.6	0.7	0.4	0.5	0.4	0.4
Potassium (mEq/L)	3.5	3.4	3.9	3.6	3.6	2.9	3.6	3.5
Sodium (mEq/L)	138	135	149		152	141	142	144
Hematocrit (%)	39.3	30.9		21				23
Hemoglobin (g/dl)	12.4	10.1	12	7.1				7.9
Leukocyte count (mm^3)	25200	17200			20300			25400
Platelets ($x10^3$ mm^3)		398			296			637
Prothrombin time (control:13")	19.8	22.4			15		16.6	15
Partial thromboplastin time (control:28")	70.2	43.7			24.7		23	29.7
AST (IU/L)	431	2085					107	34
ALT (IU/L)	179	530					366	107
Direct bilirubin (mg/dL)			0.24					
Indirect bilirubin (mg/dL)			0.60					
Creatine kinase (IU/L)				41600	50000			
pH	7.3		7.3	7.4				
Bicarbonate (mEq/L)	16		20	27				
PCO_2 (mmHg)	29		36	44				
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.

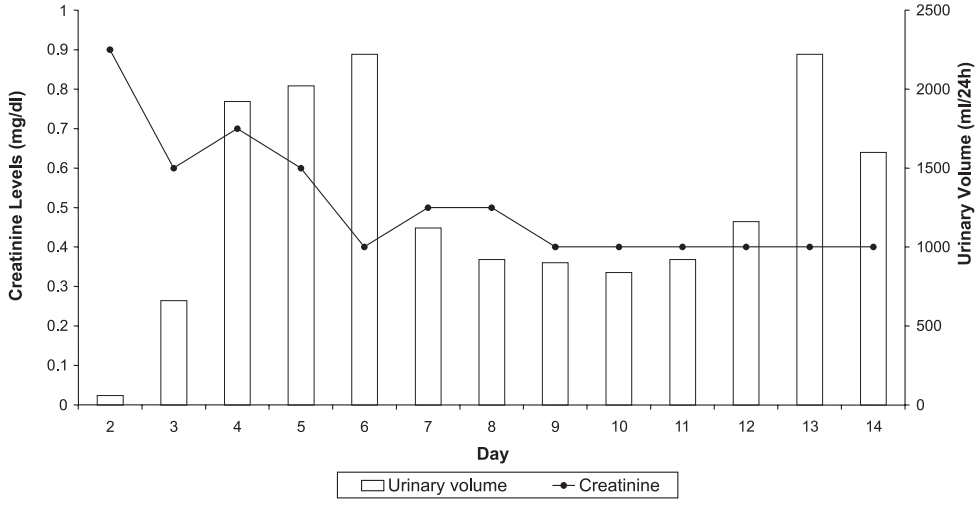

Fig. 2 – Urinary volume and serum creatinine levels during hospitalization (Case 2).

detected. He was transferred clinical stable to the medical ward after fifteen days at the intensive care unit (Fig. 3 and 4). No dialysis was required and complete renal function recovery was recorded.

DISCUSSION

Massive attacks by honeybees have been reported in studies from different parts of the world and there is a consensus that severe complications as arterial hypotension, hemolysis, rhabdomyolysis, coagulation disturbance and hepatic involvement are directly related to the number of stings[2,3,9,19]. Systemic toxic effects of bee venom are generally seen on patients with more than 50 stings[19]. The potentially lethal number of stings has been estimated at 500, and death is probably due to a direct systemic effect of the venom[2]. The most frequent clinical findings seen in these cases were generalized edema, arterial hypotension, hemolysis, rhabdomyolysis and acute renal failure.

The honeybee venom contains several active components such as mellitin, which is the main component, and, associated with phospholipase A_2 (PLA_2), have hemolytic and vasoactive properties[4]. The PLA_2 triggers the release of arachidonic acid from lipid in the cell membrane, which probably proceeds to production of inflammatory eicosanoids. Hyaluronidase breaks down chondroitins and hyaluronic acid in connective tissues, facilitating the rapid spread and vascular uptake of venom[4]. There are others small-molecular-weight components that may contribute to its toxic effects, including apamin (a neurotoxin), mast cell-degranulating peptide and histamine[4]. These substances could be responsible for lyse of red blood cells, leukocytes, platelets and damage to vascular endothelium[4]. It has also been reported rhabdomyolysis and myocardial necrosis[8,18]. The lesions are probably caused by a direct toxic effect of the venom, but an anaphylactic component can play an important role, causing hypotension and hypoperfusion to many important organs, including the kidneys[11,15].

The two reported patients presented low levels of hemoglobin and hematocrit and high level of LDH, corroborating the hypothesis of hemolysis. There was a significant increase in prothrombin time and partial thromboplastin time in the second case but the number of platelets was normal in both cases. There was no clinical manifestation of disseminated intravascular coagulation. Thrombocytopenia is less common and when it occurs is likely to be due to a direct toxic effect on platelets[4].

Acute renal failure in these patients is likely to be secondary to arterial hypotension due to direct vasoactive toxic effect of the venom, hemoglobinuria due to intravascular hemolysis and myoglobinuria due to rhabdomyolysis. Clinical evidence suggests that some bee toxins may directly damage renal tubule[5,7,10,17]. The association between rhabdomyolysis and acute renal failure is well known. Myoglobinuria-induced acute renal failure has been observed in patients with dehydration, hypotension and increased serum CK level[6]. In the two reported cases elevated serum CK, dehydration and arterial hypotension were recorded. The laboratorial tests were not performed daily, so we could not observe the progression of some prognostic parameters like serum CK level. However we could demonstrate evidence of rhabdomyolysis by one occasional elevation of serum CK level. Acute tubular necrosis (ATN) was the most common biopsy histological finding in cases of acute renal failure induced by wasp stings[19]. The pathogenesis of ATN is mediated

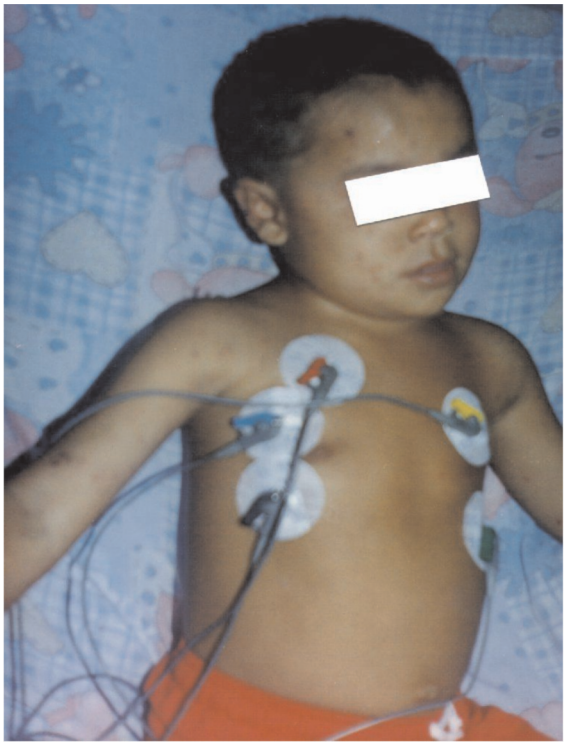

Fig. 3 – Multiple bee stings over the child's face, trunks and arms (case 2).

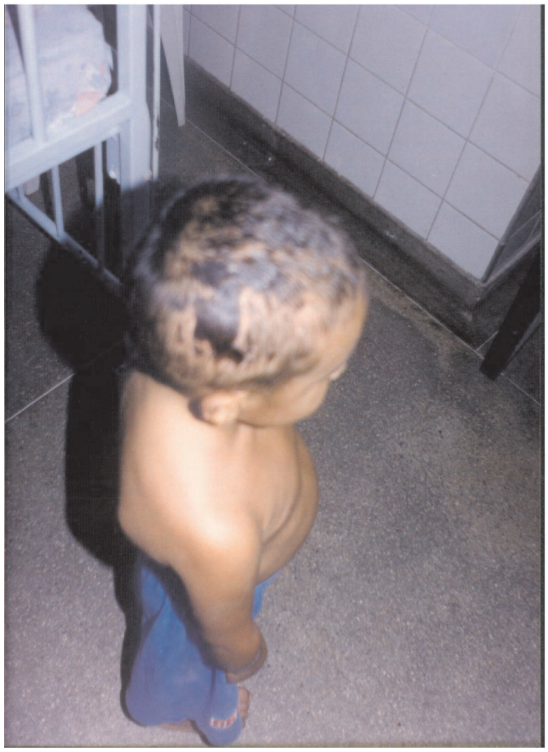

Fig. 4 – Multiple bee stings all over the child's scalp (case 2).

partially by pigment nephropathy caused by precipitation of myoglobin and hemoglobin casts in renal tubule[19].

The first reported patient presented arterial hypotension and anuria with increased persistent levels of urea and creatinine, suggesting the occurrence of ATN and dialytic treatment was required. The second patient presented a mild acute renal failure, with only slight increasing in serum creatinine. He presented oligoanuria at admission and his urinary output spontaneously reached normal levels in the fourth hospital day and no dialysis was required. It seems that the levels of creatinine did not have a definite correlation with the number of stings[19]. It is probable that the renal deterioration can be avoided if treatment is given early. The time between the accident and medical treatment seems to be important in determining the patient's prognosis in these cases. The patient who received medical support seven hours after the bee stings had severe acute renal failure whereas in the patient whose treatment was given half an hour after the attack the renal dysfunction was mild and rapidly reversed after aggressive fluid infusion.

Another point to consider is the removal of bee stings. The sting continue to inject venom after be detached from the insect body. The patients should remove it as quickly as possible in order to reduce the amount of venom inoculated. The method of removal does not seem to affect the quantity of venom received[21]. In the cases presented here the removal of the stings were made in the hospitals. The first patient had this performed seven hours after be stung, and the second after half an hour. This made the first case more serious, because a larger quantity of venom must be injected.

The venom component responsible for hepatic damage is unknown, but it has been established that hornet venom has a direct hepatotoxic effect in rats[13]. Liver impairment has been described through post-mortem findings as centrilobular necrosis and pericholangitis[12]. The two reported cases presented increased levels of liver enzymes due to a liver dysfunction, even though part of serum AST elevation was caused by rhabdomyolysis.

Several cases of death due to massive insect stings have been reported, and the mortality rates has been estimated from 15 to 25 percent[3,9,10,11,17,19]. The cause of death was not described in most cases. In one study involving a small group of patients the cause of death following honeybee stings was respiratory failure[10].

In summary, the pathogenesis of acute renal failure in these patients is probably in part due to pigment nephropathy caused by precipitation of myoglobin and hemoglobin in renal tubules associated with hypovolemia. Early recognition of this syndrome is crucial to the successful management of these patients. Mortality remains significant but there is generally complete recovery of renal function in those who survive.

RESUMO

Insuficiência renal aguda após numerosas picadas de abelhas

Foram relatados dois casos clínicos de pacientes que sobreviveram a ataques maciços de abelhas africanizadas (600 e 1500 picadas). As reações caracterizaram-se por edema difuso e generalizado, sensação de queimação na pele, cefaléia, fraqueza, parestesia generalizada, sonolência e hipotensão. A insuficiência renal aguda desenvolveu-se, tendo sido atribuída à hipotensão, hemólise intravascular, mioglobinúria devido à rabdomiólise e provavelmente ao efeito tóxico direto da grande quantidade de veneno injetada. Os pacientes foram tratados com agentes anti-histamínicos, corticosteróides e reposição hídrica. Um paciente apresentou quadro grave de insuficiência renal aguda necessitando de tratamento dialítico. Nenhuma complicação clínica foi observada durante a internação e ambos evoluíram bem com recuperação completa da função renal. Assim, a insuficiência renal aguda após picadas de abelhas ocorre provavelmente devido a nefropatia por pigmentos associada à hipovolemia. O rápido reconhecimento desta síndrome é crucial para o sucesso terapêutico destes pacientes.

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