

Acute renal failure due to multiple stings by Africanized bees. Report on 43 cases

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ABSTRACT

Acute renal failure due to multiple stings by Africanized bees. Report on 43 cases. This study reports on acute renal failure (ARF) due to multiple stings by Africanized bees (AB) occurring in 43 cases collected between 1982 and 2007 (at the Nephrology Section, University of Antioquia School of Medicine and San Vicente de Paul University Hospital, Medellín, Colombia). No intervention on patient care was performed except for responding the Nephrology consult and prescribing dialysis. Data obtained from the medical records included demography; clinical presentation; laboratory results on admission; evolution of renal function to document improvement and normalization; intervals between stings and outcomes; number of dialysis sessions; length of follow-up and hospitalization; survival; and mortality. Not all patients had complete data and therefore, the number of observations is included where required. Mean age was 56 ± 26 yr (range 2–96); 37 (86%) were men; 38 (of 41 cases) came from rural areas (91%); 22 (of 39) were farmers (56.4%); 33 (of 41) lived in Medellín or in the department of Antioquia (80.5%). Number of stings per patient: ~900. Interval between stings and ARF < 48 hours: in 31 cases (72.1%; mean 2.6 ± 2.6 days; range 1-12); 37 (of 43) required dialysis (86%); mean number of sessions: 4.7 ± 3.3 (range 1-12). Survival occurred in 36 cases (83.7%) and mortality, in 7, all > 60 yr (16.3%). At last follow-up, renal function improvement was documented in 36 (83.7%) and normalization in 15 of them (41.7%). Interval until initiation of diuresis: 10.6 ± 6.8 days (range 1-25). Duration of hospitalization: 16.9 ± 8.7 days (range 1-39). Follow-up: 25.2 ± 18.3 days (range 1–75). Hematuria and oliguria occurred before 24 hours; there was an increase of CPK in 90%, of ALT in 96%, of AST in

89%, of DHL in 95%, and of BUN and creatinine in 100%. Based on our findings and on the review of the available information, we propose that this type of ARF occurs as a result of rhabdomyolysis with subsequent myoglobinuria, which lead to nephrotoxic acute tubular necrosis; a variable degree of direct nephrotoxicity, not quantifiable with current diagnostic methods, is also probably involved. A better knowledge of this entity by the medical community could improve care and prognosis of the patients who develop it.

Key words: Acute renal failure. Nephrotoxicity. Rhabdomyolysis. Myoglobinuria. Bee Venom. Multiple Stings by Africanized Bees

Insuficiencia renal aguda por picadura múltiple de abejas africanizadas. Comunicación de 43 casos

RESUMEN

Se comunican 43 casos de insuficiencia renal aguda (IRA) por picadura múltiple de abejas africanizadas (AA) recopilados entre 1982 y 2007 en la Sección de Nefrología de la Universidad de Antioquia y el Hospital San Vicente de Paúl, de Medellín, Colombia. No se realizó ninguna intervención diferente a responder la interconsulta a nefrología y a ordenar los procedimientos de diálisis. Los datos obtenidos de las historias clínicas incluyeron datos demográficos; presentación clínica; exámenes de laboratorio realizados en el momento del ingreso; evolución de función renal para documentar la mejoría y la curación de la IRA; intervalos entre picaduras y desenlaces; número de sesiones de diálisis; duración del seguimiento y la hospitalización; supervivencia, y mortalidad. Los datos no fueron completos en los 43 casos; por ello se expone el número exacto de observaciones cuando corresponde. Edad promedio: 56 ± 26 años (rango, 2-96); 37 (86%) fueron hombres; 38 (de 41 con datos) procedían del área rural (91%); 22 de 39 fueron agricultores (56,4%); 33 de 41 provinieron de la ciudad de Medellín o

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el departamento de Antioquia (80,5%). Número de picaduras por paciente: aproximadamente 900. Intervalo entre picadura múltiple e IRA <48 horas: 31 casos (72,1%; promedio $2,6 \pm 2,6$ días; rango, 1-12); 37 de 43 requirieron diálisis (86%); promedio de sesiones: $4,7 \pm 3,3$ (rango, 1-12). Supervivencia: ocurrió en 36 casos (83,7%); mortalidad: en siete, todos >60 años (16,3%). La mejoría de la función renal se produjo en 36 casos (83,7%) y la normalización en 15 de los 36 casos (41,7%). El intervalo hasta el inicio de la diuresis fue de $10,6 \pm 6,8$ días (rango, 1-25). La duración de la hospitalización fue de $16,9 \pm 8,7$ días (rango, 1-39). El seguimiento fue de $25,2 \pm 18,3$ días (rango, 1-75). Hematuria y oliguria se produjeron antes de 24 horas de las picaduras; hubo elevación de CPK en el 90%, de ALT en el 96%, de AST en el 89%, de láctico-deshidrogenasa en el 95%, y de BUN y creatinina en el 100%. Basándonos en nuestros hallazgos y en la revisión de la información de la que disponemos, postulamos que este tipo de IRA se produce como resultado de rabdomiólisis con mioglobinuria subsiguiente, lo que desencadena una necrosis tubular aguda nefrotóxica; probablemente influye, además, algún grado de nefrotoxicidad directa no cuantificable con los métodos diagnósticos actuales. Un mayor conocimiento de esta entidad por parte de la comunidad médica puede ayudar a mejorar el tratamiento y el pronóstico de los pacientes que la presentan.

Palabras clave: Insuficiencia renal aguda. Nefrotoxicidad. Rabdomiólisis. Mioglobinuria. Veneno de abejas. Picadura múltiple de abejas africanizadas

INTRODUCTION

In 1986, the Nephrology Group of University of Antioquia School of Medicine and San Vicente de Paúl University Hospital in Medellín, Colombia, published data on the first 5 cases of acute kidney failure (AKF) produced by multiple stings from Africanized bees (AB),¹ which was accompanied by an editorial on the subject in the same journal.² Our first patient was seen in 1982, and since then we have continued to compile data on all those referred to our hospital due to AKF as a complication from multiple AB stings. During the last three decades, numerous isolated cases and short studies on this type of alteration of renal function have been published,³⁻¹⁶ but ours, which summarizes data from 43 cases, is the most extensive in the current scientific literature.

This descriptive study presents our findings on the clinical presentation, natural history, and prognosis of this condition, and discusses possible physiopathological mechanisms that are indicated by the existing medical literature and our study suggest that are due to rhabdomyolysis caused by bee venom. Our objective is to

illustrate medical communities about the characteristics of AKF as a complication of multiple AB stings, and so improve its treatment and the prognosis of those patients who present with this condition.

MATERIAL AND METHODS

Between January 1982 and December 2007, we performed a longitudinal compilation of clinical information on 43 cases of patients diagnosed with multiple AB stings with complicated with alteration of kidney function. The author did not participate in the direct medical care of these patients in emergency services, intensive care, internal medicine, or paediatric units where they were hospitalized (39 cases were admitted to the San Vicente de Paúl University Hospital and 4 were referred from other institutions). Not all clinical data from the laboratory analyses or overall patient evolution was available, leading the number of observations for calculating means to be less than 43 in some variables; when this occurred, the corresponding number of observations was given.

Patient anonymity was maintained when collecting data from medical records; for this reason, informed consent was not required and the study was classified as of no-risk for the subjects whose information was used.

Demographic data

For each case (and according to the availability of information, as previously mentioned) we recorded data on age, sex, rural or urban residency, geographic region where the incident occurred, and job or profession of the patient.

Clinical data

We documented the presence or absence of haematuria, hypotension or oliguria/anuria upon patient admission, an estimation of the number of stings, interval of time between stings and hospital admission, duration of oliguria, number of haemodialysis sessions (or peritoneal dialysis in the few cases where it was applied), documented improvement (start of diuresis and/or decreased creatinine, BUN, and/or potassium levels, sufficient to not require dialysis according to the attending physician) or cure (normalization of kidney function), duration of hospital stay and follow-up until the last documented visit, mortality, cause of death when the patient died, and survival.

The follow-up period continued until the patients were discharged from the hospital or from the Nephrology consult (this generally occurred when the patient no longer presented

criteria for dialysis and/or commenced diuresis), or until the final outpatient visit.

Laboratory data

We registered the test results from the patient's hospital admission, evolution during hospital stay, and those following discharge in the small group of patients who continued their follow-up in outpatient offices. The tests used were: haemoglobin, haematocrit, platelets, leukocytes, neutrophils, creatinine, BUN, sodium, potassium, aspartate (AST) and alanine (ALT) aminotransferases, creatine-phosphokinase (CPK), lactate dehydrogenase (LDH), total and direct bilirubins, glycaemia, haematuria, and proteinuria in occasional urine samples. The testing methods were those traditionally used at the hospital clinical laboratory.

Only those laboratory test results from hospital admission that were used for diagnosis were analyzed; the subsequent test results were excluded from the analysis due to the variability in time and frequency with which they were obtained. Kidney function test results during the patient's evolution were used to document improvement and normalization.

Statistical analysis

The data are expressed as a number (\pm standard deviation [SD]) and in total percentages for the 43 patients or for the total number on which the variable was measured; likewise, the means and ranges for each value are also reported.

RESULTS

In the 25-year period, 43 cases of AKF caused by multiple AB stings were recorded. The mean age was 56 ± 26 years (range: 2-96). The distribution of cases by age group is shown in table 1.

The majority of patients (37 cases, 86%) were male and only 6 patients (14%) were female. The residence of the patient ($n = 41$) was rural in 38 cases (91%) and urban in 3 cases (7%). The patient's profession ($n = 39$) was farmer in 22 cases (56.4%); in 3 cases each (7.7%), the patient was retired, a student, housewife, or preschool child, and in one case each was a physician, tractor driver, shoemaker, office worker, and mentally retarded without occupation. The geographical origin of the patient ($n = 41$) was the city of Medellín and/or the province of Antioquia in 33 cases (80.5%) and from other provinces of Colombia in eight cases (19.5%) (table 2).

The patient's clinical presentation included oliguria or anuria in 42 of the 43 cases (97.7%). Macroscopic or microscopic

Table 1. Distribution of cases by age group

Age Group	Number	Percentage
5 years or less	3	7.0
6-15 years	3	7.0
16-30 years	2	4.6
31-45 years	3	7.0
46-60 years	8	18.6
61 years or more	24	55.8

haematuria was found in 34 cases (100%, $n = 34$), and hypotension in 14 cases (60.9%, $n = 23$). These clinical signs appeared within the first 24 hours of the multiple stings. The majority of patients received primary care at the local hospital or health centre, which included various doses of prescribed adrenaline, corticosteroids, antihistamines, antibiotics, and intravenous fluid replacement within the 24 hours prior to being admitted to the reference medical centre.

The interval between the multiple stings and AKF ($n = 43$) was less than 48 hours in 31 cases (72.1%) and greater than 2 days in 12 cases; the mean interval was 2.6 ± 2.6 days (range: 1-12). Of the 43 cases, 37 required dialysis treatment (86%), peritoneal dialysis was administered in two patients, and two others received both peritoneal dialysis and haemodialysis. Four patients improved without dialysis (14%); in the 34 patients that received only haemodialysis, the mean number of sessions was 4.7 ± 3.3 (range: 1-12).

An estimation of the number of stings was performed in the first cases, revealing approximately 900 lesions; this procedure was not continued in later cases due to the wasteful expenditure of time and effort and because the massive damage caused to all exposed areas of skin and those covered with thin layers of material was evident. One patient received a sting to the cornea, which later required a transplant; 2 patients received stings to the glottis that required an urgent intervention in order to stabilize the airway.

On the day of admission the following results were obtained BUN and creatinine levels elevated 100% in 98% of cases (the only patient that did not present this result on the first day did so on the second); anaemia in 53%, leukocytosis in 89%, neutrophilia in 100%, thrombocytopenia in 59%, hyponatremia in 67%, hyperkalemia in 39%, elevated AST in 89%, ALT in 96%, CPK in 90%, LDH in 95%, total bilirubin in 38%, direct bilirubin in 29%, glycaemia in 48%, and proteinuria in occasional urine samples in 100%. Table 3 shows the number of cases with registered data, as well as the means and standard deviations for each laboratory test, and ranges and percentages in which an abnormal value was found.

Seven patients died (16.3% mortality) and 36 survived (83.7%). The causes of death from the clinical histories were

Table 2. Demographic characteristics

Feature	Result (± SD)	Range or percent
Mean age	56 (26)	2-96 years
Men	38	86%
Rural residence	38	91%
Farmers	22	56.4%
From Medellín or Antioquia	33	80.5%
Oliguria or anuria	42	97.7%
Hematuria	34	100%
Hypotension	14	60.9%
Sting-AKF interval <48 h	31	72.1%
Mean interval	2.6 (26)	1-12 days
Dyalysis requirement	37	86%
HD sessions (average)	4.7 (3.3)	1-12 sessions
Survival	36	83.7%
Mortality	7	16.3%
Average interval until death	4 (3)	1-9 days
Mean age of survival patients	50 (26.7)	2-96 years
Mean age of dead patients	75 (7.4)	63-86 years
Renal function improvement	36	83.7%
Normal renal function	15	41.7%
Interval AKF and initiation of diuresis	10.6 (6.8)	1-25 days
Hospital stay period	16.9 (8.7)	1-39 days
Follow-up period	25.2 (18.3)	1-75 days

cardiac arrest in two patients, and respiratory distress syndrome, septic shock, severe acidosis, electrolyte imbalance, and undeclared in one patient each.

Improved kidney function was observed in 36 cases (83.7%); in the 7 cases (16.3%) with no improvement, the patient died. The mean age of surviving patients was 50 ± 26.7 years (range: 2-96), and the mean age of deceased patients was 75 ± 7.4 years (range: 63-86). Normalized kidney function was documented in 15 of the surviving patients (41.7%). The patients who died did so early in the evolution of AKF, and so did not have enough time to show recovery from the kidney damage, as only one patient showed improvements in oliguria, but none in function. The mean time to the start of diuresis was 10.6 ± 6.8 days (n = 35; range: 1-25) (table 2).

The mean hospital stay (until discharge or until the follow-up period started) was 16.9 ± 8.7 days (range: 1-39). The mean

period between hospital admission and the last hospital or outpatient follow-up (including the day in which normal kidney function was documented or of the death of the deceased patients) was 25.2 ± 18.3 days (range: 1-75). Deaths occurred after 4 ± 3 days in the hospital (range: 1-9) (table 2).

DISCUSSION

In 1957, 26 AB swarms with their queens escaped from an apiary located in the city of Rio Claro, state of Sao Paulo, Brazil. A mix of these bees with native species was immediately predicted, but no one speculated that this apparently harmless accident would create risks for the human population. It was predicted that their dissemination throughout the compatible habitat on the American continent would take several years;^{17,18} however, by 1992, they had already arrived at different areas of North and South America in areas above and below the latitudes in which the seasons would not allow them to survive.¹⁸⁻²⁰ At the same time, publications started to appear, communicating the occurrence of isolated cases or small studies on this form of AKF.³⁻¹⁶

In these case descriptions, the authors postulated that the physiopathology of AKF could be associated with rhabdomyolysis, haemolysis, hypotension, anaphylactic shock, or direct toxic effect of the bee venom (the massive dose occurs upon receiving approximately 1,000 stings; with each sting, the bee injects a maximum of 90 µg of venom, which is the amount that an adult insect venom sack can hold,²⁰ but not all bees have the same venom volume, nor do they inject the total amount in a given sting). The majority of these publications establish rhabdomyolysis as the cause of kidney failure;^{3,5,7-9,11,13-16} in many cases, haemolysis is also an associated mechanism.^{3,5,9,11,13-15} Two articles suggest that the direct toxicity is the mechanism associated with rhabdomyolysis and/or haemolysis^{11,14} and only one case was attributed to anaphylactic shock.⁶

Independently of the physiological mechanism that explains acute tubular necrosis (ATN), the majority of cases referred to in these studies were concentrated in either older adults or young children; in these, dialysis treatment was required, except for one patient who did not receive dialysis and who died of hyperkalemia;⁷ in almost all cases, haemodialysis was given, with peritoneal dialysis administered to a few patients according to the availability of the therapeutic resources.

Among the possible risk factors for the development of AKF, the majority of our patients (56%) were older than 60, which corresponds to a reduced ability to escape from swarms, and it was in this group of patients where high mortality occurred (100% of deceased patients were in this category), making older age a negative prognostic factor. A previous alteration in kidney function would be

Table 3. Laboratory data

Laboratory test	Units of measure	No. of cases with data registered (of 43)	Mean (\pm SD)	Range	Cases with abnormal data (%)
Haematology					
Haematocrit (%)	%	38	37.5 (6.1)	24-48	53
Platelets	n/mm ³	34	161,000 (103,000)	31-422	59
Leukocytes	n/mm ³	35	19,140 (8035)	4.3-39.6	89
Neutrophils	%	32	86 (8)	70-96	100
Blood Chemistry					
Creatinine	mg/dl	42	6.6 (4.2)	1.2-20.1	98
BUN	mg/dl	39	95.6 (58.6)	21-264	100
Sodium	mEq/l	39	135 (7.4)	125-148	67
Potassium	mEq/l	38	5.4 (0.93)	2.9-7.4	39
Aspartate aminotransferases (AST)	U	27	689 (613)	11.0-2.404	89
Alanine aminotransferases (ALT)	U	26	330 (455)	7.0-2.429	96
Creatine phosphokinase (CPK)	mg/dl	31	15,913 (25,646)	34-99,999	90
Lactate dehydrogenase (LDH)	mg/dl	19	3,635 (8,483)	125-69,074	95
Glycemia	mg/dl	27	120 (40)	61-215	48
Urine (occasional sample)					
Semiquantitative proteinuria	mg/dl	27	78 (67)	10-300	100

another factor, but this information was not available for our patients; however, the normal reduction in GFR caused by age >60 years would probably favour it. In this study, rhabdomyolysis itself could be considered a high risk factor for the development of oliguric ATN, but the number of cases limited the potential usefulness of stratifying this factor according to CPK or other enzyme levels.

In the cases of AKF due to multiple AB stings that we analyzed for this article, we observed that haematuria and oliguria usually occurred within the first 24 hours; there was an early, rapid, and progressive rise in muscular tissue enzymes (CPK in 90% of cases, ALT in 96%, AST in 89%, LDH in 95%), as well as in the renal function test (BUN and creatinine in 100% of cases). At the same time, thrombocytopenia occurred in 59% of cases, leukocytosis in 89%, neutrophilia in 100%, hyponatremia in 67%, and hyperkalemia in 39%. For these reasons, in our opinion, the mechanisms that cause AKF have no relationship with anaphylactic reactions that are produced when patients receive single stings.

Regarding the physiopathological analysis, haemolysis could play some role given the vasoactive, cytolytic, and haemolytic properties of the various components of bee venom. However, our study only presented two cases of findings compatible with haemolysis, in which jaundice occurred; total bilirubin was elevated in 38% of cases (although important in only one) and direct bilirubin was

elevated in 29%; no cases presented other clinical manifestations of haemolysis.

The haematological findings can be related to the toxic haematological and proinflammatory effects of the bee venom.²¹ Regarding electrolytes, the cases of hyponatremia could be due to the dilution caused by hydration received by the majority of patients, and the low frequency of hyperkalemia could be due to the early initiation of renal replacement therapy.

Bee venom contains 35-50% melittin and 12% phospholipase A, which have cytolytic effects that act on the phospholipid membrane of blood cells and the vascular endothelium; phospholipase produces rhabdomyolysis in skeletal and cardiac muscle, hepatocellular lesions, and the formation of proinflammatory substances; furthermore, it contains 2-3% hyaluronidase, 2% apamin, 2% mastocytolytic peptide, and 1% acid phosphatase and minor quantities of other substances such as histamine, all of which contribute to the physiopathology of the condition.^{20,21} Table 4 presents the chemical composition of bee venom and the principal actions of each component.

Experimental studies from the last 2 or 3 decades, although infrequent, have been sufficient to support the role of rhabdomyolysis as the main physiopathological mechanism in this condition. In one of these, experimental injections of AB venom into adult Wistar rats produced rhabdomyonecrosis indirectly observed by

Table 4. Chemical composition of Africanized bee venom^{20,21}

Substance	Concentration	Action
Melittin	50%	Haemolytic, vasoactive, contractile, and cellular antimembrane properties
Phospholipase A	12%	Cell membrane lysis
Apamin	2%	Neurotoxin
Mastocytolytic peptide	2%	Cytolysis, histamine release
Hyaluronidase	1-3%	Cell membrane lysis
Histamine	0.1-3%	Increased vascular permeability
Dopamine	<1%	Haemodynamic effect
Minimine	<1%	Similar to phospholipases
Phospholipase B	<1%	Cell membrane lysis

the elevation of muscular enzymes and directly by necrosis and inflammation in skeletal muscle as observed by light microscopy.²²

Another study with the same iv injection model of venom in the same animals evaluated renal function after the inoculum and observed a reduction in GFR and an increase in FENa and FEK (reflecting changes in proximal tubules). The histological analysis of samples obtained after 30 hours of observation allowed identification of ATN and the formation of cylinders in distal and collecting tubules. The findings allowed the authors to conclude that the AKF was due to multiple effects of the venom: hemodynamic alterations from systemic vasodilatation, myoglobinuria, and direct nephrotoxicity on tubular cells.²³

Immunohistochemical studies later performed by this same group of researchers in the same experimental model found muscular actin and myoglobin in tubular cylinders. The examination of renal specimens using an electron microscope showed intracytoplasmic vacuolization in the proximal tubular segments with attenuation of cellular "brush borders" as well as cell death and apoptosis with denudation of the basal tubular membrane. Based on these findings, they postulated that ATN was due to the effects of melittin and phospholipases on the biological membranes, associated with direct toxicity, myoglobinuria and possibly some level of ischemia.²⁴

Another case description evaluated the mechanism of renal damage using experimental iv injection of bee venom into rats; they showed a reduction in GFR, renal blood flow, and insulin clearance, as well as increases in CK, LDH, and AST, all without modifying systemic arterial pressure. The histological analysis of the specimens obtained 24 hours after the injection showed acute tubular lesions and massive deposits of myoglobin in the tubules. In a second phase of the experiment, venom was added to an isolated suspension of proximal tubules that was subjected to normoxia and then hypoxia-reoxygenation in order to

evaluate direct nephrotoxicity; they observed a highly significant increase in LDH release. The authors concluded that vasoconstriction, direct nephrotoxicity, and rhabdomyolysis were all important in the process of AKF induced by the venom, and that these effects present themselves in the absence of hypotension and haemolysis.²⁵

In our opinion, these studies are limited by the fact that, at least theoretically, the iv injection of the venom does not replicate the subcutaneous form of injection that takes place when humans are victims of multiple AB stings. The massive inoculation of one iv venom dose favours the development of hemodynamic effects of vasodilator and inflammatory components and hemolytic effects, as well as the toxic action over capillary and tubular endothelial surfaces.

In order to investigate the hypothesis of direct action of venom on cells, the effects of bee venom and its main component, melittin, on the mechanisms of apical membrane transporters of proximal tubular cells was evaluated. The application of dry venom and melittin to isolated cultures of these cells (from rabbits) produced a reduction in cell viability and inhibited the activity of renal transporters (these effects were independent of the dose) and increased Ca²⁺ uptake. These changes were inhibited by mepacrine (transporter blocking substance) and with calcium channel blockers, respectively. The results of experiments with complete venom as well as with melittin alone, indicating that this substance is responsible for the aforementioned effects.²⁶

Due to the complex mix of enzymes and proteins in bee venom, this same group evaluated different venom fractions on apical transporters in their experimental model using proximal tubule cell cultures. Three different fractions were found based on solubility, and of them, BVA (Bee Venom A) produced a reduction in cell viability.

This one was then separated into three sub fractions based on molecular weight (BF1 [Pm >20 kD]; BF2 [Pm 10–20 kD], and BF3 [Pm <10 kD]). Of these, BF3 was the most effective at producing the experimental effects; additionally, these changes were associated with the activity of the phospholipase A₂ and Ca²⁺-dependent oxidative stress cascade.²⁷

Taken together, these experimental studies support both rhabdomyolysis and direct venom toxicity on renal tubular cells as the physiopathological explanation for the AKF produced by AB venom.

A review of the impact that this problem can have on certain geographic areas of the world where its presentation is possible allows for the prediction that these cases will continue to occur and be communicated with increasing frequency. In order to prevent the consequences, various antivenom vaccines are being produced for prophylaxis in people with high risk of suffering massive stings, but their effectiveness is poor.²⁸

Controversy also exists on whether or not the removal of the stings causes increased venom inoculation; one article affirms that no basis exists for removing the stings since 20 seconds after the sting, all of the venom load that the bee can inject has already passed into the victim;²⁹ however, another publication emphasizes that the stings must be removed to prevent further venom injection, regardless of whether or not this removal is done by “shaving” the stings or by “extracting” them.³⁰

We also expect that in the future, with the advent of serum and urine biomarkers from acute tubular lesions such as cystatin C, Neutrophil Gelatinase-Associated Lypocalin (NGAL), Kidney Injury Molecule-1 (KIM-1), and interleukin 18 (IL-18), among others, could elucidate the exact mechanism of these lesions in humans.³¹

It is important that the medical community becomes conscious of the need for rapid referral of patients with multiple AB stings to high-complexity health centres since the renal lesion forms part of the natural history of this type of venom injection; and also because haemodialysis treatment must be started early in order to prevent complications and reduce mortality.²⁸⁻³⁰

In conclusion, according to our analysis and the review of the available information, we believe that the alteration in kidney function is due to a direct toxic effect of the venom on muscular tissue, which triggers rhabdomyolysis with subsequent acute tubular necrosis (nephrotoxic type) caused by myoglobinuria. Furthermore, it is quite possible that some level of direct nephrotoxicity that is not quantifiable with existing diagnostic tests may be involved. Based on the discussed results, we suggest that multiple AB stings should

be added to the list of causes of nephrotoxic-type AKF and rhabdomyolysis. A more adequate elucidation of the physiopathological mechanisms implicated in this condition could lead to the design of therapeutic interventions in order to prevent or reduce the development of the tissue damage produced by the venom.

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