Clin Kidney J (2012) 5: 158–161
doi: 10.1093/ckj/sfr171
Advance Access publication 22 February 2012

Clinical Report

CKJ

Acute renal failure following multiple hornet stings

Yashad Dongol[1], Yadab Prasad Paudel[1], Rakesh Kumar Shrestha[2] and Gopi Aryal[3]

[1]Department of Biochemistry, KIST Medical College and Teaching Hospital, Lalitpur, Nepal, [2]Department of Biochemistry, Little Angels' College of Higher Studies, JF Institute of Health Education, Lalitpur, Nepal and [3]Department of Pathology, KIST Medical College and Teaching Hospital, Lalitpur, Nepal

Correspondence and offprint requests to: Yashad Dongol; E-mail: theyashad_02@hotmail.com

Abstract

Hornet stings are medically important stings which can cause allergic manifestations and, in severe cases, may lead to the unusual complication of acute renal failure (ARF) and other systemic complications. ARF results from toxic or ischaemic acute tubular necrosis in a setting of haemolysis or rhabdomyolysis or both and acute allergic interstitial nephritis. Venom from hornet stings can also contribute to myocardial injury or liver impairment. Here, we report three cases of hornet stings leading to ARF. Case #1 and Case #3 recovered their renal function and body physiology after a 38-day and 15-day stay in the hospital, respectively, whereas Case #2 died. They were meticulously supported by haemodialysis along with the combination of various drug regimens.

Keywords: acute renal failure; acute tubular necrosis; haemolysis; multiple hornet stings; rhabdomyolysis

Introduction

The insect order Hymenoptera consists of many medically important groups of stinging insects—Apoidea (bees), Vespoidea (paper wasps, hornets and yellow jackets commonly referred as wasps [1]) and Formicidae (ants) [2]. Hymenoptera venoms are concentrated and highly complicated mixtures of biochemically active agents [3]. Though allergic manifestations to Hymenoptera stings are well documented, the complication of acute renal failure (ARF) is rare [4, 5]. Severe reactions to 'Hymenoptera' stings are generally attributed to allergic mechanisms. In cases of multiple stings, severe reactions and even death may result from the toxic actions of venom [6]. ARF results mostly from toxic or ischaemic acute tubular necrosis (ATN) in a setting of haemolysis, rhabdomyolysis or both. Rarely, it occurs as a direct nephrotoxic effect of venom [7] or from acute allergic interstitial nephritis (AIN) from hypersensitivity reaction to venom [5, 7, 8]. Besides renal impairment, other systemic complications such as liver impairment, respiratory and cardiac impairments have also been reported [7, 9]. Here, we report three cases of ARF followed by multiple hornet stings during the month of August in 2010.

Case report

Case #1

A 39-year-old man was referred to our hospital with complaints of multiple hornet stings from one of the peripheral hospital near Kathmandu valley after a day of hospitalization. On examination, he was conscious but icteric. There were 50–60 hornet stings over his trunk and limbs. Investigations in the peripheral hospital revealed persistent oliguria (20 mL of bloody urine output over 18 h), serum urea 67 mg/dL (11.12 mmol/L), serum creatinine 1.8 mg/dL (159.12 μmol/L), serum sodium and potassium 134 and 4.7 mmol/L, respectively, serum creatine phosphokinase (CPK) 15 200 IU/L, serum alanine transaminase (ALT) 1810 IU/L, serum aspartate transaminase (AST) 400 IU/L, prothrombin time (PT) 23 s, activated partial thromboplastin time (APTT) 198 s, haemoglobin (Hb) 17.8 g/dL (178 g/L), total leucocyte count (TLC) 31 000/mm^3 and platelets 175 000/mm^3. On arrival to our hospital (Day 2), his blood pressure was 140/100 mmHg. Stool occult blood test was positive. The routine examination of urine revealed 3+ albumin and plenty of red blood cells (RBC) and white blood cells. His serum glucose was 150 mg/dL (8.34 mmol/L), serum urea and creatinine were 99 mg/dL (16.43 mmol/L) and 2.9 mg/dL (256.36 μmol/L). The extreme abnormal laboratory values reported during the patient's stay in hospital are shown in Table 1. The case was diagnosed as ARF along with ischaemic liver injury, haemolysis and rhabdomyolysis. The first session of haemodialysis was undertaken on Day 4. The course of renal function during his hospital stay is shown in Figure 1. With sessions of haemodialysis and medication, serum urea and creatinine subsequently regressed to 53 mg/dL (8.8 mmol/L) and 2.8 mg/dL (247.52 μmol/L), respectively, on Day 38; serum CPK, ALT, AST and bilirubin level returned to the physiological range. He had increased total count till Day 31 and neutrophilia till Day 23. Besides haemodialysis, he was managed with various combinations of drugs, such as diuretics, vitamin K, polystyrene sulphonate, hydrocortisone and chlorpheniramine, antacids, antibiotics, antihypertensives and ondansetron. The patient underwent

Table 1. Laboratory investigation report[a]

Parameter	Normal range	Case #1	Case #2	Case #3
Hb	13–18 g/dL (130–180g/L)	7.8 (78)	NA	8.5 (85)
TLC	4500–11 000/mm^3	31 000	NA	9100
Platelets	150–400 $\times$ 10^3/mm^3	36 000	NA	363 000
PT	11–13 s	23	NA	16
APTT	35–45 s	198	NA	-
Urea	10–40 mg/dL (1.66–6.64 mmol/L)	252 (41)	99 (16.43)	440 (73)
Creatinine	0.5–1.4 mg/dL (44.2–123.76 μmol/L)	9.7 (857.48)	3 (265.2)	26.8 (2369.12)
Sodium	136–145 mmol/L	134	132	127
Potassium	3.5–5.0 mmol/L	5.2	6.3	7.1
Calcium	9–11.5 mg/dL (2.24–2.87 mmol/L)	NA	NA	6.2 (1.54)
Phosphorus	2.5–4.5 mg/dL (0.80–1.45 mmol/L)	NA	NA	17 (5.48)
Uric acid	2–7 mg/dL (119–416 μmol/L)	NA	NA	14.6 (868.4)
Total protein	5.5–8.0 mg/dL (55–80 g/L)	NA	NA	5.7 (57)
Albumin	3.5–5.5 mg/dL (35–55 g/L)	NA	NA	1.1 (11)
Bilirubin total	0.3–1.0 mg/dL (5.13–17.1 μmol/L)	10.3 (176.13)	NA	NA
Bilirubin direct	0.1–0.3 mg/dL (1.7–5.13 μmol/L)	7 (119.7)	NA	NA
AST	0–35 IU/L	400	NA	NA
ALT	10–40 IU/L	1810	NA	NA
Random blood glucose	60–140 mg/dL (3.3–7.7 mmol/L)	150 (8.34)	206 (11.45)	NA
CPK	24–170 IU/L	15 200	9080	362
CPK–MB	$<$24 IU/L	NA	570	NA

[a]Conversion factors for units: albumin in g/dL to g/L, $\times$10; bilirubin in mg/dL to μmol/L, $\times$17.1; calcium in mg/dL to mmol/L, $\times$0.2495; creatinine in mg/dL to μmol/L, $\times$88.4; glucose in mg/dL to mmol/L, $\times$0.0556; haemoglobin in g/dL to g/L, $\times$10; phosphorus in mg/dL to mmol/L, $\times$0.3229; total protein in g/dL to g/L, $\times$10; urea in mg/dL to mmol/L, $\times$0.166; uric acid in mg/dL to μmol/L, $\times$59.48; NA - Not Available.

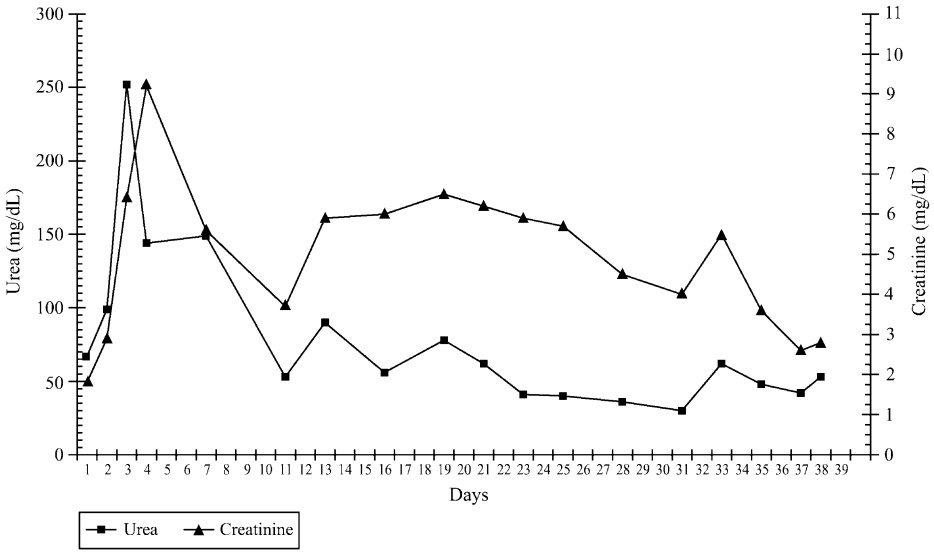

Fig. 1. A line graph showing the record of the serum urea level and serum creatinine level of the Case #1 during his hospital stay. Conversion factors for units: serum creatinine in mg/dL to μmol/L, $\times$88.4; serum urea in mg/dL to mmol/L, $\times$0.166.

14 sessions of haemodialysis during his 38 days of hospital stay. He resumed his normal urinary output from Day 33. He was discharged on Day 39 with the advice to continue with a renal diet and a follow-up visit in nephrology outpatient department (OPD) after one week.

Case #2

A 30-year-old man was rushed to the emergency department of our hospital with complaint of multiple hornet stings. The biochemistry investigation revealed random blood glucose 206 mg/dL (11.45 mmol/L), serum urea 99 mg/dL (16.43 mmol/L), serum creatinine 3.0 mg/dL (265.2 μmol/L), serum sodium 132 mmol/L, serum potassium 6.3 mmol/L, serum CPK 9080 IU/L, creatinine phosphokinase–MB (CPK–MB) 570 IU/L and cardiac Troponin I (cTnI) negative. The blood sample was icteric. Urine was reddish in colour. Urinalysis revealed 3+ albumin, plenty of RBC and positive for myoglobin. The case was diagnosed as ARF and urgently referred for haemodialysis. Unfortunately, the patient died before haemodialysis was undertaken.

Case #3

A 35-year-old man was rushed to the emergency department of our hospital with complaint of hornet stings. Twenty days previously, he was attacked by a swarm of hornets. For 5 days after the hornet stings, reddish urine was observed which regressed there after. He was treated by a traditional healer in the village for 20 days. On arrival to our hospital, he had decreased urinary output and yellowish discolouration of sclera. There were ~50 stings over his body.

His blood pressure was 140/90 mmHg. The laboratory investigations revealed serum urea 252 mg/dL (41.83 mmol/L), serum creatinine 4.9 mg/dL (433.16 μmol/L), serum sodium and potassium 126 mmol/L and 6.7 mmol/L, respectively, Hb 8.5 g/dL (85 g/L), PT 16 s, platelets 363 000/mm^3 and TLC 8500/mm^3. Table 1 shows the extreme abnormal laboratory values reported during the patient's stay in the hospital. The diagnosis was made as ARF due to hornet sting with dyselectrolytaemia and anaemia. The first session of haemodialysis was performed on Day 2. With sessions of haemodialysis, serum potassium level returned to the physiological range of 4.4 mmol/L on Day 7, serum urea and creatinine level regressed down to 129 mg/dL (21.41 mmol/L) and 3.7 mg/dL (327.08 μmol/L), respectively, and haemoglobin level increased to 9.5 g/dL (95 g/L) on Day 15. The course of renal function during his hospital stay is shown in Figure 2. The patient underwent a total of total six sessions of haemodialysis. Besides haemodialysis, he was managed with a combinations of various drugs such as diuretics, vitamin K, polystyrene sulphonate, hydrocortisone, antacids, antibiotics, ondansetron, allopurinol and calcium supplement with vitamin D. He was discharged on the 16th day of hospital admission with the advice to continue with the renal diet and follow-up in the nephrology OPD after a week.

Discussion

Hymenoptera stinging events usually occur during late summer or early fall with the numbers reaching a peak in August [10]. In a previously sensitized person, a single sting may result in a spectrum of clinical manifestations ranging from non-fatal, non-specific skin manifestations and non-specific urinary abnormalities to anaphylactic shock [4]. IgE-mediated Type I anaphylaxis in hornet stings results in clinically important incidents [10]. However, an unexposed person can get a toxic effect from systemic envenomation following multiple stings which leads to cellular damage presenting a diverse clinical sequelae, such as intravascular haemolysis, disseminated intravascular coagulopathy, rhabdomyolysis, liver damage, ATN and acute myocardial infarction [4]. Toxic ingredients in hornet venom are active amines, such as serotonin, histamine, tyramine, catecholamines; wasp kinins; allergens like antigen 5; enzymes, such as phospholipase A and B, hyaluronidase [2, 3, 5, 10] and mastoparan—a peptide which causes secretion of histamine from mast cells, serotonin from platelets and catecholamines from chromaffin cells [11]. Some species might have neurotoxins like mandaratoxin and a few species contain acetylcholine [2, 3, 10]. These toxic effects of venom are normally seen in patients with >50 stings [4]. However, Sakhuja *et al.* reported toxic effects from as few as 22 stings [4, 6]. The venom dose lethal to 50% of victims (LD_{50}) differs among the insects [10]. In our study, there were ~50–60 stings in Case #1 and ~50 stings in Case #3. The number of stings in Case #2 could not be evaluated.

ATN and AIN cause ARF after wasp stings [5, 8, 12]. Haemoglobin and/or myoglobin in urine and diffuse tubular necrosis in renal biopsy specimens suggest ATN due to pigment tubulopathy [5]. Along with this pigment tubulopathy, hypovolaemic or anaphylactic shock also causes ATN [5, 8, 12]. The absence of rhabdomyolysis and haemolysis resulting in renal impairment is suggestive of direct nephrotoxic effect of venom [7]. AIN results from hypersensitivity reaction to venom [5, 7, 8].

All the three cases in this study developed ARF with intravascular haemolysis and rhabdomyolysis. Renal biopsies were not performed in any of the cases. The diagnosis was made on the basis of laboratory investigation (Table 1) and typical clinical history. Case #1 was anuric at the time of hospital admission, whereas Case #3 was oliguric. Besides ARF, in Case #1, increased serum liver enzymes suggest acute hepatic injury and increased serum CPK level suggests rhabdomyolysis [7]. Case #2 also showed increased serum CPK and myoglobin in urine referring towards the evidence of rhabdomyolysis [7]. There was an increased level of CPK–MB isoform with undetected Troponin I in the serum of Case #2, which possibly indicates progression towards acute allergic myocardial infarction [13] at its early stage. Myocardial infarction followed by wasp sting was reported for the first time by Levine in 1976 [8]. Follow-up investigations could not be carried out due to the death of the patient on the same day of hospital admission. The concurrence of

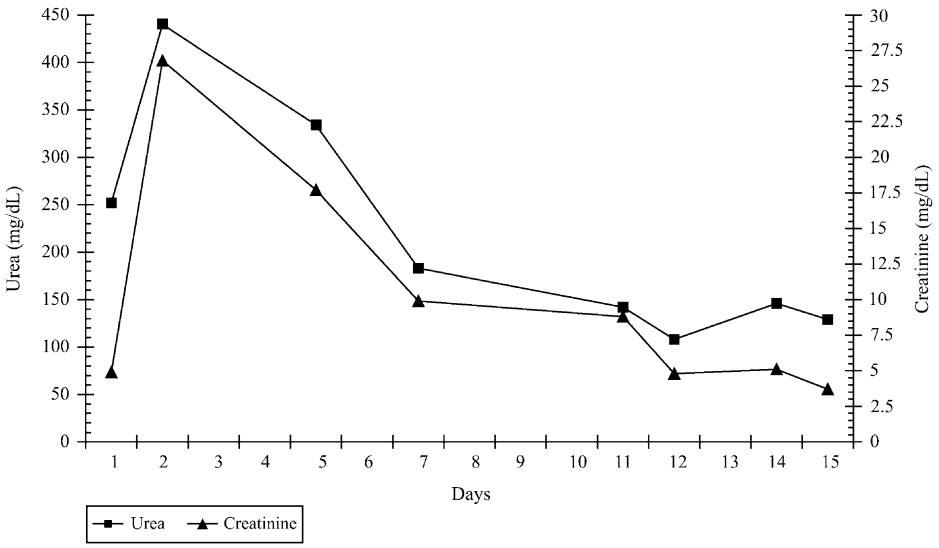

Fig. 2. A line graph showing the record of the serum urea level and serum creatinine level of Case #3 during his hospital stay. Conversion factors for units: serum creatinine in mg/dL to μmol/L, ×88.4; serum urea in mg/dL to mmol/L, ×0.166.

acute coronary syndromes with allergy or hypersensitivity as well as with anaphylactic reactions is well known as Kounis syndrome. The inflammatory response is essentially due to mast cell degranulation [13]. In Case #3, increased serum CPK and uric acid possibly suggests rhabdomyolysis. Case #1 and Case #3, although, advised to have a follow-up in the nephrology OPD, did not show up for follow-up to our hospital.

In conclusion, multiple hornet stings cause a wide spectrum of clinical sequelae ranging from intravascular haemolysis, rhabdomyolysis, ARF, hepatic dysfunction, myocardial necrosis, thrombocytopaenia and coagulopathy. ATN and AIN are the major causes of ARF in multiple hornet stings. Intensive haemodialysis support and therapy of steroids and diuretics resulted in the good recovery of renal functions in two of the three cases.

Conflict of interest statement. None declared.

References

1. Vetter RS, Visscher PK. Bites and stings of medically important venomous arthropods. *Int J Dermatol* 1998; 37: 481–496
2. Fitzgerald KT, Flood AA. Hymenoptera stings. *Clin Tech Small Anim Pract* 2006; 21: 194–204
3. Habermann E. Bee and wasp venoms. *Science* 1972; 177: 314–322
4. Thiruventhiran T, Goh BL, Leong CL *et al.* Acute renal failure following multiple wasp stings. *Nephrol Dial Transplant* 1999; 14: 214–217
5. Chao YW, Yang AH, Ng YY *et al.* Acute interstitial nephritis and pigmented tubulopathy in a patient after wasp stings. *Am J Kidney Dis* 2004; 43: e15–e18
6. Sakhuja V, Bhalla A, Pereira BJG *et al.* Acute renal failure following multiple hornet stings. *Nephron* 1988; 49: 319–321
7. Vikrant S, Pandey D, Machhan P *et al.* Wasp envenomation-induced acute renal failure: a report of three cases. *Nephrology* 2005; 10: 548–552
8. Zhang R, Meleg-Smith S, Batuman V. Acute tubulointerstitial nephritis after wasp stings. *Am J Kidney Dis* 2001; 38: E33
9. Levine HD. Acute myocardial infarction following wasp sting report of two cases and critical survey of the literature. *Am Heart J* 1976; 91: 365–374
10. Vetter RS, Visscher PK, Camazine S. Mass envenomations by honey bees and wasps. *West J Med* 1999; 170: 223–227
11. Higashijima T, Uzu S, Nakajima T *et al.* Mastoparan, a peptide toxin from wasp venom, mimics receptors by activating GTP-binding regulatory proteins (G proteins). *J Biol Chem* 1988; 263: 6491–6494
12. Sharma A, Wanchu A, Mahesha V *et al.* Acute tubulo-interstitial nephritis leading to acute renal failure following multiple hornet stings. *BMC Nephrol* 2006; 7: 18
13. Kounis NG. Kounis syndrome (allergic angina and allergic myocardial infarction): a natural paradigm? *Int J Cardiol* 2006; 110: 7–14

Received for publication: 17.10.11; Accepted in revised form: 4.12.11