

Acute Renal Failure following Multiple Hornet Stings

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Abstract. Five patients who developed acute renal failure due to acute tubular necrosis following multiple hornet (*Vespa orientalis*) stings are described. All of them had intravascular hemolysis. Evidence for rhabdomyolysis was present in 2 patients. Two patients had elevated transaminase and alkaline phosphatase levels and in 1 of these, liver biopsy showed centrilobular necrosis. Two patients had thrombocytopenia in the absence of disseminated intravascular coagulation. Two patients died of infections while the remaining 3 recovered completely. Acute renal failure following multiple hornet stings appears to result mainly from intravascular hemolysis or rhabdomyolysis although a direct nephrotoxic effect of venom cannot be excluded.

Introduction

The order Hymenoptera consists of the stinging insects including the honey bees, yellow jackets, hornets and paper wasps [1]. In most instances, stings by these insects are followed by only allergic reactions. Though the direct toxic effects of venoms of these insects have been studied in experimental animals and by in vitro studies [2], such effects in humans have been infrequently reported. Isolated case reports have documented the occurrence of intravascular hemolysis [3–5], rhabdomyolysis [5, 6], thrombocytopenia [5], acute tubular necrosis [3,4,6], acute hepatic injury [6–8] and myocardial infarction [9] following multiple stings. The clinical and laboratory data and renal histologic lesions of 5 patients who presented with acute renal failure following multiple hornet (*Vespa orientalis*) stings are presented in this report and the relevant literature is reviewed.

Material and Methods

Over a period of 12 years (1975–1986), 5 patients were referred to the Artificial Kidney Unit of this Institute with acute renal failure following multiple hornet (*V. Orientalis*) stings. A detailed physical examination was carried out and the total number of stings was

recorded in each patient. At admission, hematological parameters, serum biochemistry, urinalysis, chest radiogram and electrocardiogram were obtained. The presence of intravascular hemolysis was documented by a fall in hemoglobin levels, raised plasma-free hemoglobin, reticulocytosis, hemoglobinuria and altered red cell morphology in the peripheral blood smear. Glucose-6-phosphate dehydrogenase (G6PD) levels were estimated by the methemoglobin reduction method. A platelet count and complete coagulation profile were studied to look for the presence of disseminated intravascular coagulation. Muscle enzymes, i.e. lactate dehydrogenase (LDH), aldolase and creatinine phosphokinase (CPK) levels were estimated in the serum as evidence for rhabdomyolysis. A daily record of the fluid intake, urine output, body weight and serum biochemistry of all patients was maintained. The serum creatinine was kept below 8 mg/dl with the support of hemodialysis or peritoneal dialysis. A kidney biopsy was performed during the diuretic phase in 2 of 3 patients who recovered. In addition post mortem liver and kidney biopsies were obtained in 1 of the 2 patients who died.

Results

Clinical profile and laboratory data are shown in table I and II. All patients had evidence to suggest intravascular hemolysis. G6PD levels were normal in all. All of them required dialytic support during the oliguric phase.

Renal histology studied in 3 patients revealed feature of acute tubular necrosis. There was widespread necrosis of tubular epithelium with foci of regeneration and inter-

Table I. Clinical profile of patients

	Case 1	Case 2	Case 3	Case 4	Case 5
Age, years	38	65	45	8	28
Number of stings	55	46	22	63	24
Onset of oliguria, h	24	48	24	24	48
Peak blood urea					
mg/dl	427	160	240	260	171
μmol/l	152.4	57.1	85.7	92.8	61
Peak serum creatinine					
mg/dl	13.2	9.0	17.0	7.5	9.0
μmol/l	1,166.9	795.6	1,502.8	663	759.6
Intravascular hemolysis	+	+	+	+	+
Rhabdomyolysis	NI	NI	NI	+	+
Duration of oliguria, days	12	22	16	11	11
Number of dialyses	3	4	7	2	2
Renal histology	ATN	ATN	biopsy not done	biopsy not done	ATN
Outcome	recovered	died	died	recovered	recovered

All the cases were men. NI = Not investigated; ATN = acute tubular necrosis.

Table II. Laboratory data

	Case 1	Case 2	Case 3	Case 4	Case 5
Hemoglobin					
g/dl	4.5	6.4	4.4	5.3	7.6
mmol/l	2.79	3.97	2.73	3.29	4.71
Reticulocytes, %	7.8	0.2	4.6	2.5	2
Plasma free hemoglobin					
mg/dl	43	20	11	107	13
μmol/l	26.7	12.4	6.82	66.3	8.1
Urine hemoglobin	+	—	—	+	—
Serum bilirubin					
mg/dl	1.0	1.0	6.	15	0.5
μmol/l	17.1	17.1	102.6	256.5	8.5
Platelet count × 10 ⁹ /l	160	150	40	40	200
PTI					
%	100	100	100	100	100
arb units	1.0	1.0	1.0	1.0	1.0
Features of hemolysis on peripheral blood smear	+	+	+	+	+
Serum LDH ^a					
mU/ml	ND	ND	ND	1,296	475
μmol/l				21.64	7.93
Serum aldolase ^b					
mU/ml	ND	ND	ND	50	6.5
nmol/l				833.5	108.4
Serum CPK ^c					
IU/ml	ND	ND	ND	5,376	252
μmol/l				89.7	4.2

ND = Not done; PTI = prothrombin index

^a Normal range 70–240 mU/ml, 1.5–4.17 μmol/l.

^b Normal range 2–8 mU/ml, 25–135 nmol/l.

^c Normal range 24–145 IU/ml or 0.42–2.42 μmol/l.

stitial edema. In addition, pigment casts were present in the tubular lumina in all 3 patients. In the 2 patients who did not undergo a renal biopsy, the clinical course was consistent with acute tubular necrosis.

Skin biopsy from the site of one of the stings (case 1) showed evidence of mild vasculitis. Two patients (cases 3 and 4) had evidence of liver injury. Both had elevated serum transaminase and alkaline phosphatase levels. Of these, 1 patient (case 4) recovered and liver function tests also returned to normal. The other patient (case 3) died and a postmortem liver biopsy revealed foci of centrilobular necrosis. There was a prominent collection of lipofuchsin in the Kupffer cells. Mild portal triaditis and pericholangitis were also seen.

Discussion

Because of the small dose of venom injected during isolated stings, overt intravascular hemolysis occurs only with multiple stings [10]. All of our patients had significant hemolysis, and the absence of hemoglobinuria and normal plasma-free hemoglobin in 3 of them was not unexpected since they presented more than 5 days after the stings. The hemolytic properties of oriental hornet venom have been investigated by in vitro studies and have been attributed to a basic protein fraction which has direct lytic activity and phospholipase A which is an indirect hemolysin [2]. Hemolysis has also been reported

with bee stings because of the presence of melittin (which is a direct hemolysin) and phospholipase A in bee venom [11]. However, intravascular hemolysis and acute renal failure are apparently more frequently seen with hornet and wasp stings than with bee stings [5, 12].

Rhabdomyolysis has been observed following multiple stings by hornets (*V. affinis*) [6] and yellow jackets (*Vespula germanica*) [5] but not with bee stings. Evidence for rhabdomyolysis was present in both of our patients in whom it was looked for. Rhabdomyolysis has been attributed to polypeptides, histamine, serotonin and acetylcholine present in hornet and wasp venom [13]. Acetylcholine, which constitutes as much as 10% by weight of dried *V. Orientalis* venom, is not present in bee venom.

Acute renal failure due to multiple stings appears to result mainly from intravascular hemolysis but may also be a consequence of rhabdomyolysis, hypotension during an anaphylactic reaction, or rarely disseminated intravascular coagulation [14]. Although definite evidence for a direct nephrotoxic effect of venom is lacking, this possibility cannot be completely excluded. Sandbank et al. [15] have shown changes in mouse proximal tubular epithelium 45 min after intravenous administration of 1 mg of venom sac extract of *V. Orientalis* even in the absence of hemoglobinuria; the changes were qualitatively different from those observed with experimentally produced hemoglobinuria. Renal biopsy invariably reveals acute tubular necrosis [3, 4, 6] and acute cortical necrosis has never been observed. Although the occurrence of a nephrotic syndrome following bee stings has been reported by Venters et al. [16], a cause and effect relationship between the two was not established and this is likely to have been only a coincidence. Thrombocytopenia, which occurred in 2 patients, was most probably due to a direct effect of venom on platelets [5].

Hepatic damage, for which there was evidence in 2 of our patients, is a rare manifestation of wasp and hornet stings [6–8]. Shilkin et al. [6] reported the occurrence of widespread focal hepatic necrosis in a patient who sustained 250 stings by the hornet *V. affinis*. They also found elevated transaminase levels in another patient who had 180 stings by the same hornet species. The venom component that is responsible for hepatic damage is unknown but it has been established that hornet venom has a direct hepatotoxic effect in rats [17].

Thus, acute renal failure due to acute tubular necrosis which mostly results from intravascular hemolysis and rhabdomyolysis, alone or in combination, can complicate the course of patients who suffer multiple stings by hornets.

References

- 1 Ewan, P.W.: Allergy to insect stings: a review. *J. R. Soc. Med.* 78: 234–239 (1985).
- 2 Joshua, H.; Ishay, J.: The hemolytic properties of the oriental hornet venom. *Acta pharmac. tox.* 33: 42–52 (1973).
- 3 Chugh, K.S.; Sharma, B.K.; Singhal, P.C.: Acute renal failure following hornet stings. *J. trop. Med. Hyg.* 79: 42–44 (1976).
- 4 Tan, K.H.; Chew, I.S.; Chao, T.C.: Fatal hemolysis from wasp and hornet stings. *Singapore med. J.* 77: 112–114 (1966).
- 5 Bousquet, J.; Huchard, G.; Michel, F.-B.: Toxic reactions induced by Hymenoptera venom. *Ann. Allergy* 52: 371–374 (1984).
- 6 Shilkin, K.B.; Chen, B.T.M.; Khoo, O.T.: Rhabdomyolysis caused by hornet venom. *Br. med. J. i:* 156–157 (1972).
- 7 Jonas, W.; Shugar, M.: Severe hepatic and renal damage following wasp stings. *Dapim Refuim (Folia Medica)* 22: 353–356 (1964).
- 8 Glaser, M.: A fatal case after hornet stings and Benadril medication. *Harefuah* 50: 175–176 (1956).
- 9 Levine, H.D.: Acute myocardial infarction following wasp sting. *Am. Heart J.* 91: 365–374 (1976).
- 10 Dacie, J.V.: The hemolytic anemias. IV. Drug-induced hemolytic anemias, p. 1091 (Churchill, London 1967).
- 11 Habermann, E.: Bee and wasp venoms. *Science* 177: 314–322 (1972).
- 12 Bousquet, J.; Coulomb, Y.; Robinet-Levy, M.; Michel, F.B.: Clinical and immunological survey in beekeepers. *Clin. Allergy* 10: 331 (1982).
- 13 Habermann, E.: Recent advances in the pharmacology of toxins; in Raudonat, vol. 9, p. 53 (Pergamon Press, Prague 1963).
- 14 Barnard, J.H.: Study of 400 Hymenoptera sting deaths in the United States. *J. Allergy clin. Immunol.* 52: 259–264 (1973).
- 15 Sandbank, U.; Ishay, J.; Gitter, S.: Kidney changes in mice due to oriental hornet venom: histological and electron microscopic study. *Acta pharmac. tox.* 32: 442–448 (1973).
- 16 Venters, H.D.; Vernier, R.L.; Worthen, H.G.; Good, R.A.: Beesting nephrosis: a study of immunopathologic mechanisms. *Am. J. Dis. Child.* 102: 688–689 (1961).
- 17 Neuman, M.G.; Eshchar, J.; Cotariu, D.; Ishay, J.S.; Bar-Nea, L.: Hepatotoxicity of hornet's venom sac extract after repeated in vivo and in vitro envenomation. *Acta pharmac. tox.* 53: 314–319 (1983).

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