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The Interesting Case

Acute renal failure following multiple wasp stings

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Introduction

The order *Hymenoptera* consists of a variety of stinging insects which include honey bees, yellow jackets, hornets, and wasps. Although allergic manifestation to their stings is well recognized [1], complications resulting in acute renal failure occur less commonly [2]. The pathomechanisms involved may include hypotension as part of anaphylactoid reactions, intravascular haemolysis, rhabdomyolysis, and a direct toxic effect of the insect venom [2]. We report on a patient who suffered multiple wasp stings and subsequently developed acute renal and liver impairment. Her son who was also bitten many times, quickly succumbed and died on arrival at the local hospital. Cases of renal failure due to insect stings reported in the English literature are reviewed and the syndrome of acute renal failure, intravascular haemolysis, rhabdomyolysis, and abnormal liver function tests, which is now recognized as a unique complication of multiple insect stings from the order *Hymenoptera* are discussed.

Case report

A 29-year-old female and her 10-year-old son, both previously healthy, were attacked by a swarm of wasps near a beach. Both of them suffered multiple stings, in particular the mother as she attempted to shield her son from the attacking bees. Unfortunately, the boy succumbed and died on arrival at the local hospital. The cause of death was not determined but is likely to be related to anaphylatic shock or overwhelming toxaemia. The mother was stable with normal blood pressure and had no symptoms of anaphylactic shock. Her main complaints were of local pain at sites where she had been bitten and generalized muscle ache. She had had one episode of dark coloured urine. Subsequent investigations showed her to be in acute renal failure with impaired liver function (Table 1) and she was transferred to the University Hospital for further treatment. Following transfer, her renal function continued to deteriorate although her blood pressure remained well preserved and there was no evidence of systemic sepsis. Her haemoglobin declined $\sim$4 g/dl over the next 10 days, and there was evidence for intravascular haemolysis with elevated bilirubin and LDH in association with a peripheral reticulocytosis. Complement levels and a clotting screen were normal with no evidence of disseminated intravascular coagulation. Her urine output remained well preserved with creatinine peaking at 598 μmol/l 14 days after she was first attacked. Renal replacement therapy with dialysis was not required. Renal biopsy (Figure 1), which was performed at the peak of her creatinine concentration, showed features of acute tubular necrosis with myoglobin casts in the tubules, consistent with tubular damage due to rhabdomyolysis. Subsequent recovery was uncomplicated with renal function eventually returning to normal.

Discussion

Most of the clinical sequelae [3] typically resulting from multiple stings of various stinging insects from the order *Hymenoptera*, was seen in our two cases. There was evidence for intravascular haemolysis, abnormal liver function tests, and acute renal failure in the mother, and sudden death in her child, possibly due to overwhelming toxaemia from the venom which has been reported to cause acute myocardial infarction in human [4] and myocardial necrosis in animal studies [5]. In hypersensitive persons, a single sting may result in death due to anaphylactic shock or cause other non fatal complications including serum sickness-like reaction [1,6], delayed skin eruptions, haematuria, and short-lived proteinuria [1]. In persons not previously sensitized, toxic effects, such as those seen in our

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Table 1. Laboratory results

Day	1	14	21	28	42
Haemoglobin (g/dl)	13.2	9.1	8.4	10.8	
Reticulocyte count (%)	4.6%	2.4%			
Urea (mmol/l)	11.7	21.9	15.6	12.1	6.2
Creatinine (μmol/l)	223	598	470	254	112
Bilirubin (μmol/l)	66	4			
Alk. phos (iu/l)	282	102			
ALT (iu/l)	2144	107			
AST (iu/l)	1224	31			
LDH (iu/l)	1073	430			

Alk. phos, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; LDH, lactate dehydrogenase.

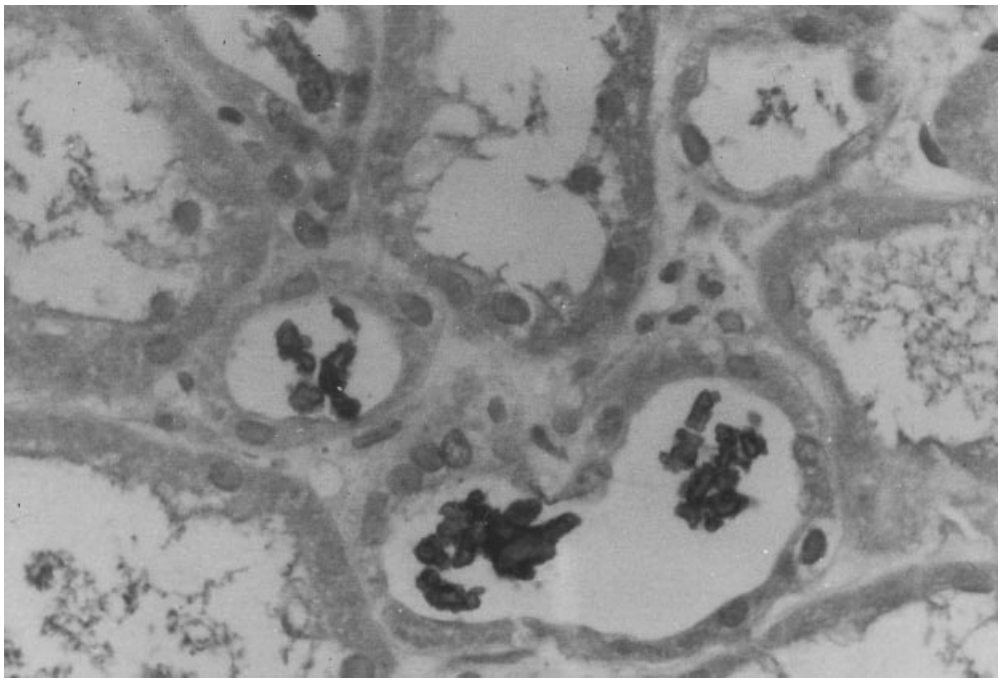

Fig. 1. Photomicrograph showing beaded coagulated proteinaceous casts within tubules exhibiting immunoreactivity (dark colour) for myoglobin. Avidin–biotin complex immunoperoxidase stain for myoglobin (×400)

surviving patient and previous cases reported in the English literature, are reviewed and summarized in Table 2. These toxic effects are normally seen only in patients with >50 stings [7], although they occurred in one patient with as few as 22 stings in one report [3]. The potentially lethal number of stings has been estimated at 500, and death is probably due to a direct toxic effect of the venom [8].

Among the several active substances of venom, mellitin is its main component and has haemolytic and vasoactive properties. Histamine, hyaluronidase and apamin, which are all potentially neurotoxic, and phospholipase A, are other toxins present in the venom of these insects [1,8,9]. Phospholipase A and surface agents such as mellitin and apamine act on red cell membranes, provoking haemolysis which may contribute to the development of acute tubular necrosis [10], the most common histological finding in cases where biopsies were performed (Table 2). Other toxins may cause rhabdomyolysis [11], myocardial necrosis [5], and centrilobular necrosis of the liver [3]. Acute renal failure is however likely to be secondary, and mediated by a combination of haemolysis and/or rhabdomyolysis. Indeed, there was evidence for intravascular haemolysis and rhabdomyolysis, in all reported cases where such a direct cellular toxic effect was sought (Table 2). Pigment casts in renal tubules [3], probably due to myoglobin and haemoglobin have been documented in addition to acute tubular necrosis, supporting the view that renal complications are likely to be a secondary rather than primary effect of venomous toxins. In our surviving patient, myoglobin casts within renal tubules was detected by specific immunostaining with anti-myoglobin antibodies (Figure 1). However, experimental evidence suggests that some toxins may directly damage renal tubules [12]. The mainstay of management of renal failure in these patients is

Table 2. Summary of clinical and laboratory findings of the 24 cases reviewed

Authors	Year	No. of cases	Type of insect	Haemolysis	Rhabdomyolysis	Hypotension	Abn LFTs	Renal biopsy	Dialysis	Outcome
Sitprija *et al.* [17]	1972	1	Wasp	NI	Yes	Absent	NI	ATN	Yes	Recovered
Chugh *et al.* [18]	1976	1	Hornet	Yes	NI	NI	NI	ATN	Not known	Recovered
Loasombat V *et al.* [19]	1982	1	Wasp	Yes	NI	Absent	NI	NI	No	Died
Humblet *et al.* [10]	1982	1	Bee	Yes	Yes	Yes	Yes	NI	Yes	Recovered
Bousquet *et al.* [20]	1984	1	Yellow jacket	Yes	Yes	Yes	Yes	NI	Yes	Recovered
Mejia *et al.* [16]	1986	5	Bee	NI	Yes (2/2)	Yes (4/5)	Yes (2/2)	ATN[a]	Yes (5/5)	Recovered (4/5) Died (1/5)
Sakhuja *et al.* [3]	1988	5	Hornet	Yes (5/5)	Yes (2/2)	NI	Yes (2/5)	ATN[a] (3/5)	Yes (5/5)	Recovered (3/5) Died (2/5)
Barss P [21]	1989	1	Wasp	Yes	NI	Absent	NI	NI	No	Died
Ramanathan *et al.* [22]	1990	2	Bee	NI	Yes (2/2)	Absent	NI	NI	Yes (2/2)	Recovered (2/2)
Nace L *et al.* [23]	1992	1	Wasp	Absent	Absent	NI	NI	NI	Yes	Recovered
Munoz *et al.* [2]	1992	1	Bee	Yes	NI	Absent	Yes	ATN	Yes	Recovered
Beccari M *et al.* [24]	1993	1	Bee	Absent	Absent	Absent	NI	ATN	Not known	Recovered
Sert *et al.* [25]	1993	1	Bee	Yes	Yes	Absent	Yes	NI	No	Died
Hiran *et al.* [11]	1994	1	Bee	Yes	Yes	Absent	NI	NI	No	Recovered
Present case	1998	1	Wasp	Yes	NI	Absent	Yes	ATN	No	Recovered
Total		24								Recovered 18/24 Died 6/24

NI, not investigated; ATN, acute tubular necrosis; [a]dense proteinaceous deposits within tubules.

supportive and to encourage alkaline diuresis (to reduce dissociation and precipitation of myoglobin to its nephrotoxic metabolite ferrihemate) with the help of sodium bicarbonate and mannitol or frusemide [13]. Further deterioration in renal function may be averted if treatment is given early. Indeed, some of these early-treated patients did not require dialysis, supporting the notion that the acute renal failure is mediated by pigment casts released by destruction of red blood cells and muscle fibres in these cases.

Liver involvement is relatively common in cases where liver function tests were evaluated. In most patients, elevated liver enzymes were the only evidence for hepatic damage as hepatomegaly, tenderness or signs of overt liver failure were not observed. There were post-mortem findings of centrilobular necrosis, together with mild portal triaditis and pericholangitis in one patient who died [3]. The venom component responsible for hepatic damage is unknown, but it has been established that hornet venom has a direct hepatotoxic effect in rats [14]. Less commonly, there may be thrombocytopaenia, and this is likely to be due to a direct toxic effect on platelets [10,15], especially in the absence of disseminated intravascular coagulation.

There was a mortality rate of 25% (six fatalities) in the 24 cases of acute renal failure associated with insect stings. The cause of death was not reported in most cases except one where death was apparently due to respiratory failure [16]. There were no obvious predictors of poor prognosis in this small group of patients. The level of creatinine did not correlate with number of stings (which ranged from 22 to >1000) or presence of hypotension. In addition, concentration of creatinine, dialysis dependence, age or number of stings did not correlate with mortality, although attacks involving >500 stings are likely to be lethal [8]. In those who survive, there is generally complete recovery without residual renal impairment.

In summary, the syndrome of acute renal failure in association with intravascular haemolysis, rhabdomyolysis and abnormal liver function tests, occasionally accompanied by thrombocytopaenia, is now increasingly recognized as a unique complication of multiple insect stings from the order *Hymenoptera*. The pathogenesis of acute renal failure in these patients is likely to be mediated at least in part by pigment nephropathy caused by precipitation of haemoglobin and myoglobin casts in renal tubules. The most common renal histological findings are compatible with acute tubular necrosis with pigment casts in the renal tubules. Early recognition of this syndrome is crucial in the management of these patients. In particular, forced alkaline diuresis may help avert the need for dialysis and reduce morbidity. Mortality remains significant, but in the majority who survive, the prognosis is good with satisfactory recovery of renal function.

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