Wasp Stings with Multiple Organ Dysfunction in Children

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ABSTRACT

Objective: Allergic reactions from wasp stings usually occur shortly after the stings. Serious and less common systemic manifestations including multiple organ dysfunction can also occur at a later time.

Methods: Medical records of pediatric patients admitted because of wasp stings into the Faculty of Medicine Siriraj Hospital from 2000 to 2009 were reviewed.

Results: Nine cases were admitted because of systemic reactions from wasp stings. Most required only intravenous fluid and antihistamine. Two young children developed multiple organ dysfunction more than 24 hours after multiple stings. Both patients required artificial ventilation. The first patient received 20 days of renal replacement therapy and recovered completely. The second patient developed sepsis during peritoneal dialysis and died on the 34th day.

Conclusion: Clinicians should be aware that young children with multiple stings are at risk of multiple organ dysfunction. We suggest hospitalization for at least 48 hours to provide early detection of complications and management.

Keywords: Wasp stings, multi-organ failure, multi organ dysfunction, acute renal injury, acute kidney injury

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INTRODUCTION

Wasp, hornet and yellow jacket are members of the vespid subgroup in the order Hymenoptera. Wasp stings are usually associated with only local reactions, but may also result in anaphylaxis, hemolysis, rhabdomyolysis, thrombocytopenia, elevated hepatic serum enzymes, acute renal failure and multiple organ dysfunction. Systemic reactions to wasp stings may develop within 24 hours or be delayed.[1-3] In Thailand, the incidence of childhood systemic reactions to wasp stings was not known, as only occasional case reports exist.[4-6]

The purpose of this study is to review and warn clinicians to be aware of systemic involvement caused by wasp stings in children because most children who suffered from multiple wasp stings need medical attention. Initially they may have mild symptoms and develop severe acute clinical manifestation later. Clinicians should be aware of possible complications of wasp stings in order to provide early detection and proper management.

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MATERIALS AND METHODS

Medical records of patients under the age of 15 years admitted because of wasp stings at the Faculty of Medicine Siriraj Hospital over a period of 10 years were reviewed. Statistical analysis of patient characteristics and clinical manifestations was performed using SPSS version 17. This study was approved by Siriraj Institutional Review Board (EC Number 165/2010).

RESULTS

From January 2000 to December 2009, 9 pediatric cases of wasp stings were admitted. The mean age was 8.1+/- 4.1 years. The male to female ratio was 1.3:1. The average number of sting marks was 6.3 (range 1-20). Allergic reactions after wasp stings were the most common manifestations. All nine cases developed allergic reaction, five patients (55.5%) developed anaphylaxis, four patients (44.4%) developed urticaria and two patients (22.2%) developed angioedema. Two patients developed acute kidney injury requiring renal replacement therapy and are described below.

Patients with mild clinical features were admitted for a few days and required only symptomatic treatment. Eight of nine patients survived without long term complication and one patient died of sepsis. Patient characteristics,

TABLE 1. Patient characteristics in this study compare with studies by Watana D, et al[4] (by Visitsunthorn N and Poranwong N unpublished data).

Characteristics	This study	Watana D et al.[4]	Visitsunthorn N and Poranwong N [unpublished data]
Number of patients	9	20	7
Age (years) : mean ± SD	8.1 ± 4.1	5.6 ± 3.1	6.3 ± 3.5
Male : female ratio	1.3 : 1	0.42 : 1	1.5 : 1
Mean sting marks (range)	6.3 (1-20)	NA (5-130)	11.7 (2-50)

NA- not available

clinical manifestations and outcomes are shown in Tables 1 and 2.

Case 1

A previously healthy 3-year-old girl was seen by a general physician shortly after wasp stings. Oral paracetamol, chlorpheniramine, and cloxacillin were prescribed. Twenty five hours later, she developed facial puffiness, respiratory distress and decreased urine output and was referred to Siriraj Hospital.

Physical examination on admission revealed pulse rate 150/min. with weak peripheral pulses with respiratory rate 60/min and blood pressure 100/70 mmHg. She appeared drowsy with periorbital swelling and poor tissue perfusion. Inspiratory stridor, dyspnea, expiratory wheezing lungs, mild icterus and mild hepatomegaly were noted. Twenty sting marks were recorded. Urine catheterization revealed only a small amount of red urine.

She was immediately intubated and artificially ventilated. Adrenaline, methylprednisolone and antihistamine were given.

Blood chemistries revealed urea nitrogen of 68.8 mg/dl, creatinine of 3.2 mg/dl, wide anion gap metabolic acidosis, hyperuricemia and hyperphosphatemia (Na^+ 131 mmol/L, K^+ 4.2 mmol/L, Cl^- 97 mmol/L, HCO_3^- 14 mmol/L, uric acid 13.1 mg/dl and phosphate 9.9 mmol/L). Complete blood count showed leukocytosis, adequate platelets and no features of hemolysis. Urinary examination showed blood 3+ and RBC 10-20/HPF. Liver function test revealed SGOT 7,386 U/L, SGPT 3,470 U/L, total bilirubin 12.4 mg/dl and direct bilirubin 9.8 mg/dl. Prothrombine time and partial thromboplastin time were prolonged (PT=15.9 sec, aPTT=62.4 sec). Creatine phosphokinase levels were markedly elevated. A chest radiograph showed bilateral pulmonary edema. Anaphylactoid reaction, rhabdomyolysis and multiple organ dysfunction were diagnosed.

Specific IgE for wasp venom and skin prick test were negative. Renal replacement therapy was initiated due to severe oliguria and pulmonary edema. She received continuous renal replacement therapy (CRRT) for 10 days and peritoneal dialysis for another 10 days. She also recieved steroid, antihistamine, fresh frozen plasma, vitamin K and intravenous antibiotics. Upon discharge on the 30th day of admission, she was well with normal blood chemistries and renal function.

Case 2

A previously healthy 4-year-old girl was admitted due to generalized urticaria immediately after multiple wasp stings. She was seen by a general physician who prescribed chlorpheniramine, dexamethasone, and adrenaline. Twenty four hours later, she developed acute upper gastrointestinal tract bleeding and was admitted. The investigations showed acute kidney injury, pulmonary edema and acute liver injury. Her clinical conditions deteriorated despite treatment and she was transferred to Siriraj Hospital five days after the stings.

Physical examination at our hospital revealed a body temperature of 38.4^{o}C, pulse rate 138/min, respiratory rate 52/min and blood pressure 110/60 mmHg. She appeared

TABLE 2. Clinical manifestations in this study compared with the previous studies.

Clinical manifestations and final outcome	This study n=9 n (%)	onset	Visitsunthorn N and Poranwong N [unpublished data] n=7 n (%)	Onset	Watana D et al.[4] n=20	Vachvanich sanong P and Dissaneewate P[6] n=49
Anaphylaxis	4 (44.4)	15 min-2 hr	2 (28.6)	10 min-2 hr	NA	19 (38.8)
Anaphylactoid	1 (11.1)	25 hr	0	-	NA	NA
Shock	3 (33.3)	1-25 hr	2 (28.6)	10 min-2 hr	3 (15)	NA
Urticaria	4 (44.4)	10-30 min	1 (14.3)	30 min	NA	7 (14.3)
Angioedema	2 (22.2)	30 min-3 hr	1 (14.3)	16 hr	NA	8 (16.3)
Acute kidney injury	2 (22.2)	25-48 hr	2 (28.6)	10 min-2 hr	12 (60)	7 (14.3)
Acute liver injury	2 (22.2)	25-48 hr	2 (28.6)	10 min-2 hr	NA	3 (6.1)
Jaundice	2 (22.2)	25-48 hr	3 (42.9)	NA	7 (35)	3 (6.1)
Coagulopathy	1 (11.1)	25 hr	NA	NA	NA	NA
Rhabdomyolysis	2 (22.2)	25-48 hr	1 (14.3)	4 hr	5 (25)	NA
Neurological Involvement	2 (22.2)	NA	2 (28.6)	40 min-1 hr	17 (85)	NA
Respiratory Involvement	2 (22.2)	1-25 hr	2 (28.6)	2-3 hr	7 (35)	NA
Death	1 (11.1)	39th day	2 (28.6)	17 hr and 41th day	7 (35)	1 (2.0)

NA- not available

drowsy with generalized edema. tachypnea, dyspnea and crepitations on both lower lungs were noted. Twenty sting marks were recorded.

She was immediately intubated and artificially ventilated. Blood chemistries revealed urea nitrogen of 164 mg/dl, creatinine of 9.4 mg/dl, wide anion gap metabolic acidosis, hyponatremia, hyperuricemia and hyperphosphatemia (Na^+ 127 mmol/L, K^+ 4.4 mmol/L, Cl^- 97 mmol/L, HCO_3^- 14 mmol/L, uric acid 19.8 mg/dl and phosphate 7.6 mmol/L). Complete blood count showed leukocytosis with adequate platelets and no features of hemolysis. Urinary examination showed blood 3+ with RBC 30-50 / HPF. Liver function test revealed SGOT 89 U/L, SGPT 450 U/L, total bilirubin 1.1 mg/dl and direct bilirubin 0.7 mg/dl. Prothrombine time and partial thromboplastin time were normal. Lactate dehydrogenase levels were markedly elevated. A chest radiograph showed bilateral pulmonary edema. Rhabdomyolysis and multiple organ dysfunction were diagnosed.

She received steroids, antihistamines intravenous fluid and intravenous antibiotics. Acute peritoneal dialysis was initiated. She was on peritoneal dialysis for 29 days, developed sepsis and died on the 34th day of admission despite intensive broad spectrum antibiotics.

DISCUSSION

Wasp toxins can cause multisystem involvement. The most important substance in wasp toxins is the enzyme phospholipase A2 and its product lysolecithin which may affect the phospholipids of the cell membrane, mitochondria and lysosomes of any organ.[1-4]

The prevalence of systemic allergic reaction is 3.3 and 26.5% of patients had IgE antibodies to venom demonstrated by skin test or radioallergosorbent test.[7] Anaphylaxis from IgE mediated reaction is estimated to occur in 3% of adults and 1% of children.[8] Ennik F et al., reported that anaphylactic shock was the immediate cause of death from wasp stings.[9] The onset range of anaphylaxis was 1-4 hours.[9] Allergic reactions may be characterized by urticaria, angioedema, bronchospasm, edema of the large airway, and hypotension. The most serious anaphylactic reactions involve the cardiovascular and respiratory systems.[10] Patients with severe systemic allergic reaction should be tested for specific IgE antibodies to stinging insects and should be considered for venom immunotherapy if test results are positive. Medical identification of stinging insect hypersensitivity should also be considered.[10]

Anaphylactoid or non IgE mediated reaction after Hymenoptera stings was also reported. The clinical features were similar to those occurring in patients with IgE mediated reaction, but did not have detectable serum specific IgE or gave a negative skin prick test.[11,12] Clayton WF et al.,[11] reported 25 patients who had systemic reactions due to insect stings, but did not have detectable serum specific IgE. In our study, non IgE mediated reaction was confirmed in one patient (case 1) who had anaphylaxis like symptoms and a negative result of specific IgE for wasp venom and a negative skin prick test. Non IgE mediated reaction may not be diagnosed in other patients because a specific IgE or skin prick test were not routinely performed. Anaphylaxis and anaphylactoid reaction were found to be as high as 55.5% of our patients comparing with 28.6% and 38.8% in another study.[6, unpublished data] No death from immediate allergic reaction was found in our study.

Neurological involvements included cerebral infarction, hemorrhage, necrosis and degeneration (due to cerebral vasoconstriction, platelet aggregation and direct toxicity of venom to brain cells).[13,14] The onset of neurological symptoms varies up to 96 hours. Clinical manifestations include consciousness change, facial palsy, convulsion, hemiparesis, quadriparesis, myasthenia gravis, myeloradiculopathy and optic neuropathy.[13-17] Watana D et al.,[4] reported 85% of patients with consciousness change, facial palsy and convulsion. Neurological abnormalities were noted in 2 patients (22.2%) in this study (and in 2 patients (28.6%) from another study [unpublished data]).

Cardiac involvement is characterized both by a ische-mic type and arrhythmic type of coronary damage including atrial fibrillation and ventricular fibrillation.[18,19] Kogias JS et al.,[20] described an acute coronary syndrome with mast cell activation induced by allergic or hypersensitivity and anaphylactic or anaphylactoid reaction. In this study, no cardiac involvement was demonstrated.

Respiratory involvement was reported in 35% of cases in one study[4] (28.6% in another [unpublished data)] and 22.2% in this study. Respiratory manifestations included laryngeal edema, pulmonary edema and pneumonia. Respiratory failure was the cause of death in 1 boy [unpublished data].

Hematologic involvement included intravascular hemolysis, neutrophil leukocytosis, thrombocytopenia and coagulopathy.[4,21-23] Coagulopathy was noted in one of our patients.

Hepatic damage has frequently been reported as part of the multi-organ failure. Elevated liver enzymes were often the only evidence for hepatic damage.[4,24-27] Weizman Z et al., reported a Reye-like syndrome following multiple stings.[28] In this study, the first patient had marked elevated liver enzymes levels.

Direct toxicity of the venom to muscles is considered the main cause of rhabdomyolysis due to wasp stings. Rhabdomyolysis and subsequent myoglobinuria may be an important cause of acute kidney injury. A CPK level greater than 5,000 U/L is associated with acute kidney injury. Early recognition is essential in the prevention of kidney injury.[29-32]

Acute kidney injury due to multiple wasp stings is an uncommon, but serious complication. Renal damage may be caused by direct toxin nephrotoxicity, hypotension leading to ischemic tubular necrosis and nephropathy due to hemoglobinemia and myoglobinemia. Renal pathology has mainly shown acute tubular necrosis and acute interstitial nephritis.[4,24,25,27,33,34] Renal recovery in acute interstitial nephritis was much longer than in acute tubular necrosis (66.5 versus 35.6 days) and may result in interstitial fibrosis and irreversible renal failure.[34] Renal biopsy should be encouraged for patients with delayed recovery of renal function. Vetter RS et al.,[3] suggested a higher risk of renal failure and death in patients with 20 or more stings mark, but Watana D et al.,[4] reported a 6-year- old patient with only 5 sting marks who had multiple organ dysfunction. Renal function in most patients who survived was normal within 3 months.[4,24,25,27,33,34] Renal tubular acidosis, a rare complication, has also been reported.[35]

Wasp stings can result in multiple organ dysfunction and death. The complications may occur after the first 24 hours as in our study. High risk patients, including older children with more than 20 stings marks or younger children with more than 5 sting marks, should be hospitalized for close observation even if they appear to be well initially. Monitoring of renal function test, serum electrolytes and complete blood count at least once daily for three days

are recommended. Hemolysis or rhabdomyolysis should be treated promptly with adequate hydration, diuretics, urine alkalinization and proper supportive care. Patients with multiple organ dysfunction should be referred to a tertiary hospital for proper management. The treatment of choice for severe acute kidney injury is renal replacement therapy.

Before discharge, patients with a history of systemic reactions to wasp stings should be educated to avoid wasp stings, carry epinephrine for emergency treatment, and undergo specific IgE testing for stinging wasp sensitivity and be considered for immunotherapy.[10]

CONCLUSION

We suggest that clinicians should be aware that children with wasp stings may be at risk of delayed serious complications. These patients should be hospitalized for close observation, early detection of complications and proper management.

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