

Unusual reactions to insect stings

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Purpose of review

A variety of unusual or unexpected reactions have occurred in a temporal relationship to insect stings. This review will summarize these case history reports in recent years. As these reactions are very infrequent, the review will also include prior reported unusual reactions attributed to insect stings.

Recent findings

Acute encephalopathy occurred 8 days after yellow jacket stings, without any other obvious cause. There have been prior reports of other neurological reactions, myasthenia gravis, peripheral neuritis and Guillain–Barré syndrome related to insect stings. Acute renal failure with tubular necrosis has occurred following massive numbers of stings from Africanized honeybees. Nephrotic syndrome has been reported in the past following single stings. Silent myocardial infarction has occurred, probably related to acute anaphylactic symptoms immediately following a sting. There are recent reports of other pathology, diffuse alveolar hemorrhage and rhabdomyolysis and prior reports of thrombocytopenic purpura and vasculitis. As the result of ocular stings, local reactions have occurred with corneal pathology leading to cataracts. Other prior reported reactions to ocular stings include conjunctivitis, corneal infiltration, lens subluxation, and optic neuropathy. There is scarce information regarding the pathogenesis of the majority of the unusual reactions and the subsequent allergic status or risk for sting anaphylaxis of people who have had these unusual reactions.

Summary

This review includes a variety of reactions, particularly involving neurological, renal and cardiovascular symptoms, related to insect stings. It is important that clinicians be aware of this relationship when assessing people with these reactions and address future prophylaxis.

Keywords

insect stings, venom reactions

Introduction

Unusual or unexpected reactions have occurred in a temporal relationship following insect stings. These reactions are very infrequent, usually described in isolated case reports, differ from typical allergic symptomatology, and often do not have an apparent cause. From a clinical viewpoint these sting reactions can be characterized by the organ system affected, cardiac, renal or neurologic; the local or systemic manifestations and the timing of symptoms in relationship to the sting. This review will specifically reference recently described unusual events attributed to venom exposure and comment on appropriate related prior reports referenced either in the current articles or prior reviews [1].

Neurologic reactions

One case report [2] describes a 46-year-old woman who developed symptoms of acute disseminated encephalomyelitis characterized by headache, memory dysfunction, and psychomotor dysfunction, starting 8 days after two yellow jacket stings. Local reactions did occur immediately at the sting sites, lasting 3 days. There were no systemic allergic symptoms. Extensive evaluation did not indicate any other obvious cause for these neurologic symptoms. The patient did respond to steroid therapy and the neurologic deficits resolved in about 3 months. The authors postulate potential cross reactivity between venom constituents and central nervous system myelin as the mechanism for the reaction. However, I believe this mechanism seems unlikely in view of only two insect stings and minimum venom exposure. There is no mention of venom testing or advice regarding future recommendations concerning insect venom exposure.

There is a multiplicity of other case reports describing neurologic reactions in a temporal relationship to insect stings, usually without immediate systemic reactions. These reactions summarized in this and other articles include Guillain–Barré syndrome, myasthenia gravis, peripheral neuritis, demyelinating disease, and cerebral infarction [1–9].

Studies in our own laboratory, reported previously, involve three people with neurologic reactions [1]. A 37-year-old man had Guillain–Barré syndrome. He had high titers of honeybee and yellow jacket venom specific IgE and honeybee venom specific IgG. A 9-year-old boy had an immediate anaphylactic reaction after an insect sting. Forty-eight hours later he developed fever and headache and was thought to have encephalopathy.

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His symptoms slowly resolved over a period of 1 week. Borderline titers of yellow jacket venom specific IgE were found 3 months after the sting. In view of the immediate allergic reaction, this finding would be expected. An 8-year-old boy developed ataxia, areflexia, and ophthalmoplegia about 72 h after four honeybee stings. The reaction slowly improved over several months. He was found to have anti-myelin antibodies.

Renal

Renal disease, primarily renal failure, has been reported following many, often massive, insect stings, particularly due to the Africanized honeybee and less commonly following single stings.

The African honeybee was introduced to South America many years ago for improving pollination. It interbred with the more docile native European honeybee and gradually spread northward reaching the southwestern United States in the late 1990s. The Africanized honeybee is highly aggressive, stinging in large and massive numbers without provocation, and usually causing reactions due to the toxic effects of bee venom. There are three recent reports of acute renal failure due to a massive number of stings. Daher *et al.* [10] reported acute renal failure in two children, ages 4 years and 17 years, who received an estimated 1700 and 600 stings, respectively. Immediate symptoms were characterized by hypotension with subsequent hemolysis, rhabdomyolysis, and coagulation abnormalities. The authors postulate, and I believe correctly so, that these reactions are due to the toxic effects of venom components such as hyaluronidase, phospholipase, mellitin, and apamin. The renal failure is due to hypotension and the vasoactive effect of these venom components. Both patients recovered after a prolonged period of time.

A second report by Zhang *et al.* [11] describes a 61-year-old man who developed acute renal failure after multiple wasp stings. Renal biopsies showed interstitial edema and tubular destruction. This article contains many references to prior similar reports.

Another case report by Chao *et al.* [12*] describes acute renal failure occurring in a 46-year-old man who had an estimated 40 to 50 stings. Renal biopsies were also done and again showed acute tubulointerstitial nephritis and acute tubular nephropathy.

None of these reports indicates whether the patient's allergic status was evaluated in regard to possible subsequent sensitivity and allergic reactions from single stings.

We previously reported two people who have developed renal disease in a temporal relationship to insect stings

[1]. A 33-year-old man developed nephrotic syndrome following two honeybee stings. He had renal failure and required dialysis. He was found to have elevated titers of yellow jacket and honeybee venom specific IgE. A 2-year-old girl developed edema, proteinuria, and decreased complement 48 h after an insect sting. These symptoms subsided over 1 week. Serum analysis 4 months later failed to detect any sign of venom specific IgE. There are several other published similar case reports [13,14].

Cardiac

The occurrence of 'silent' myocardial infarction following an insect sting was described in a 67-year-old man [15]. He was stung several times on his head and arms by wasps and had a brief episode of syncope followed by periorbital edema and glossopharyngeal paresthesia with respiratory discomfort. He had chronic obstructive lung disease. He was treated in an emergency room and an electrocardiogram showed signs of a myocardial infarction without any classic clinical symptoms. The authors postulated that venom constituents can cause endogenous amine release and vasodilatation leading to endothelial dysfunction. They also postulated that it was possible that adverse effects of therapeutic doses of epinephrine could be responsible for the reaction.

This case history does suggest that the episode of hypotension (syncope) could have been a major factor in the pathogenesis of the myocardial infarction. There was no mention of subsequent testing or venom immunotherapy. There are other case reports of myocardial infarction, some referenced in this and summary articles [1,15–21].

Pulmonary

A 20-year-old male developed diffuse alveolar hemorrhage following an insect sting [22]. He had two prior sting reactions characterized by urticaria. Immediately following this sting he developed urticaria followed by hypotension, wheezing, shortness of breath, and hemoptysis. He was treated with steroids, epinephrine, and antihistamines. He was mildly hypoxic. His chest radiograph showed infiltrates, which cleared in about 1 week. One similar reported case is referenced in this article [23]. The mechanism of the alveolar hemorrhage is unknown.

Muscle

A 41-year-old male developed rhabdomyolysis after an insect sting [24]. He was stung by a hornet and 8 h later developed a generalized erythematous rash. He was treated with antihistamines. The rash initially resolved and then recurred 24 h later with swelling of his right arm and 'numbness' in the extremities. At that time he was found to have generalized edema extending from the

sting site to the distal part of the right arm and involving the right side of his body and leg. He also had a small bulla on his right wrist. His creatinine, creatinine kinase, and myoglobin were elevated and his urine was noted to be dark. He was diagnosed with rhabdomyolysis. He was treated in the hospital with steroids, furosemide, and sodium bicarbonate, and the symptoms gradually resolved. He was discharged after one week. No follow-up information was presented.

Ocular

Arcieri *et al.* [25] described five people who developed ocular lesions, corneal decompensation, and cataracts after honeybee and wasp stings. The reactions were attributed to direct trauma and potential toxicity of venom components. The symptoms generally started immediately after the sting and gradually became worse over a period of time. Surgery was ultimately required for treatment of cataracts.

Other referenced reports in this article describe other reactions due to stings in the eye and include conjunctivitis, corneal infiltrates, lens subluxation, lens abscess, and optic neuropathy. None of these patients had more typical allergic reactions. No follow-up information was provided regarding reactions to subsequent stings.

Other reactions

Previously reported other reactions occurring in a temporal relationship to an insect sting include thrombocytopenic purpura, Henoch–Schönlein syndrome, and vasculitis [26–28].

Conclusion

The usual allergic reactions following insect stings are large local swelling extending from the sting site, often lasting up to 1 week, and immediate typical anaphylactic symptoms. These reactions usually have an allergic basis and the pathogenesis and subsequent treatment recommendations are well established. This paper describes a variety of unexpected or unusual reactions occurring in a temporal relationship to an insect sting without any other obvious cause (Table 1). These reactions are quite diverse and often have no known underlying pathogenesis.

The neurologic reactions in particular are difficult to understand. The reactions such as acute encephalomyelitis and Guillain–Barré syndrome have been described following one or two insect stings. The mechanisms are not apparent. Anti-myelin antibodies have been detected on several occasions, but the importance of their presence is unclear.

Acute renal failure following massive insect stings is mediated by the toxic properties of the venom constituents. The single sting induced reactions such as nephrotic

Table 1. Unusual reactions to insect stings

Organ system	Reaction
Neurologic	Acute disseminated encephalomyelitis Myasthenia gravis Peripheral neuritis Demyelinating disease Cerebral infarction
Renal	Acute renal failure Acute interstitial nephritis Acute tubular necrosis Nephrotic syndrome
Cardiac	Myocardial infarction (silent) Cardiac arrhythmia
Pulmonary	Alveolar hemorrhage
Ocular	Corneal decompensation: cataracts Conjunctivitis Corneal infiltrates Lens abscess Optic neuropathy
Others	Thrombocytopenic purpura Henoch–Schönlein syndrome Vasculitis

syndrome are not explainable. Similarly, the cause of vasculitis and purpura is unknown.

Silent myocardial infarctions or cardiac arrhythmias are most likely due to the effect of hypotension and other biochemical and physiologic consequences of acute anaphylaxis. I believe it is unlikely that the usual dose of epinephrine used to treat acute anaphylaxis will cause these reactions. The eye symptoms with cataract development are due to direct trauma to the eye and the effect of venom on these tissues.

As noted in the body of the paper, there is generally no follow-up of these patients who have had unusual reactions and specifically reports of the results of future stings or recommendations regarding any type of venom immunotherapy. I believe it is reasonable to do venom skin tests to determine whether patients who have had these unusual reactions are potentially at risk for subsequent single sting induced anaphylaxis. If venom skin tests are positive, patients who have had neurologic reactions should not receive venom immunotherapy, as the mechanism of their reaction is unknown and it is conceivable that the venom exposure could reproduce these symptoms. These patients should be instructed in measures to avoid stings and carry epinephrine.

People who have had renal disease as a result of massive stings may become sensitized. Venom is a highly sensitizing protein. If skin tests are positive, these people should receive venom immunotherapy. Those people who have had single sting reactions such as nephrotic syndrome should not receive immunotherapy.

People who have had cardiac pathology presumably as part of anaphylaxis and people who have had reactions from

direct effects of venom such as cataracts are certainly candidates for immunotherapy if their skin tests are positive.

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- of special interest
- of outstanding interest

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