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In Practice

Nasal
Polyps

Infectious

Allergic
Fungal
Sinusitis



Cystic
Fibrosis

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Other
Phenotypes



Chronic Rhinosinusitis Phenotypes

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First fatalities from tick bite anaphylaxis

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Clinical Implications

- This report details the first 4 fatalities of tick-induced anaphylaxis in the world (in eastern Australia). These reactions occurred only after the tick was removed, reinforces the need for prompt treatment, and displays the limited diagnostics within arthropod anaphylaxis.

TO THE EDITOR:

It has been 75 years since anaphylaxis, secondary to tick allergy, was first described in Australia.¹ Although now recognized as a complication of the bite of both hard- and soft-bodied tick species in the United States² and Europe,³ this problem remains most prominent in Australia.^{4,5} Historically, tick bite-related fatalities have only been reported in association with toxin-induced paralysis and vector-borne diseases.⁶ However, there has been increasing concern about the potential for serious morbidity and mortality from tick bite allergy, either mediated directly by tick salivary antigen-specific immunoglobulin E (IgE) antibodies^{2,3,5} or secondary to the induction of mammalian meat allergy through IgE antibodies directed to a mammalian oligosaccharide epitope.⁷ We now report the first fatalities from tick bite-induced anaphylaxis.

We identified 4 fatalities between January 1, 1979, and December 31, 2013, where a coronial cause of death certificate attributed death due to anaphylaxis after a tick bite. One record from 1979 to 2000 was obtained from the Australian Bureau of Statistics (ABS) Mortality Data Set; Registrar of Births, Deaths, and Marriages; State Coroner; and a hospital patient file record. The National Coronial Information System (NCIS) was used from 2000 to 2013. This project was approved by the University of Melbourne Human Research Ethics Committee, the NCIS ethics committee, and ABS (data 1979-2000). All cases, including 3 males and 1 female, were adults below the age of 50 years who lived in Queensland (1 person) or New South Wales (3 individuals). All cases occurred from late winter into summer (August, September, October, and February).

The first fatality was of a male who had a history of severe prior allergy to both ticks and bees, including requiring adrenaline for a reaction to a bee sting and, 4 and 5 years later, after tick bites. He was referred to an allergist after the second tick bite. This patient had marked bee venom sensitivity on intradermal testing at 0.01 mg/L. He had been given an adrenaline spray and an epinephrine autoinjector device for delivering 0.3 mg of injectable adrenaline. He was advised to kill further ticks *in situ* and to consider moving to a nonendemic area. He successfully completed 1 year of bee venom immunotherapy with

Apis mellifera venom (Bayer Albany). The fatal event began as he dislodged a small tick from his neck. He rapidly developed a rash, became severely dyspneic, and lost consciousness. The spouse injected adrenaline via the autoinjector. An ambulance was contacted, and cardiopulmonary resuscitation (CPR) was commenced by his neighbors.

When the local doctor arrived after 15 minutes, the patient was in asystole. The patient was intubated, given multiple boluses of intravenous adrenaline, and transferred to hospital. He developed progressive circulatory failure with arrhythmias and disseminated intravascular coagulation (investigations are listed in Table I) with bleeding from all venepuncture sites.

He was transfused various products in an effort to counter thrombocytopenia, coagulopathy, and anemia. A computerized tomogram scan was consistent with hypoxic brain injury. He was pronounced brain dead the day after admission. The postmortem noted extensive bruising to the skin, gross cerebral edema, and cardiac petechial hemorrhages with normal coronary vasculature.

The second death that occurred late one evening was of a male with a history of pneumothorax and mild asthma. This patient collapsed with difficulty breathing soon after a tick was removed from his posterior scalp. Despite CPR by family and ambulance staff, as well as prehospital adrenaline administration, he could not be revived and was declared dead at a nearby hospital. Postmortem revealed minimal patchy coronary atheroma and no occlusions; however, serum tryptase levels were significantly elevated (>200 mg/L) (normal range 0.0-15.0). There was no clear prior tick allergy history.

The third fatality collapsed and died within an hour of a tick being removed from his hand. He had been outdoors earlier that day and had difficulty breathing on witnessed tick removal. Unfortunately, despite adrenaline injections and resuscitation by paramedics, he could not be revived. He had a history of severe reaction to a tick bite 12 months previously. Postmortem reported no underlying lung or vascular disease but acute pulmonary edema and congestion as well as evidence of aspirated gastric contents.

The final case was a female with a history of tick bite allergy, Takayasu's arteritis, hypertension, depression, asthma, chronic airways disease, and smoking. She told her next of kin that she was unwell and discovered a tick at the back of her head, which was allegedly removed. She then collapsed and an ambulance was called. Although CPR was conducted and she was conveyed to hospital, where a CT scan showed global hypoxic ischemic brain damage, she could not be resuscitated. Of relevance, the postmortem revealed a tick in her scalp, severe coronary atherosclerosis, severe peripheral vascular disease, renal artery and celiac axis stenosis, pulmonary anthracosis, and mild emphysema. No information was available on her prior tick allergy management.

The majority of medically significant ticks found in Australia belong to the genus *Ixodes* of which the most dangerous species is *Ixodes holocyclus* (the paralysis tick), which is confined to the eastern coastline.⁶ These cases are most likely, therefore, attributable to *I. holocyclus* and represent the first documented fatalities from tick bite-related anaphylaxis. The first case also provides the first report of a potential cross-reaction between bee and tick allergens, as well as the first instance of disseminated intravascular

TABLE 1. Laboratory results indicative of disseminated intravascular coagulation in case 1

Investigation	Reference range	0 h	2 h	6 h	10 h
Hemoglobin	130-180 g/L	156	106	54	95
Platelets	150-400 × 10 ⁹ /L	191	122	67	91
Prothrombin time (PT)	11-16 s	30.6	28.3	>200	59.4
PT ratio	0.8-1.2	2.3	2.1	e	4.4
Activated partial thromboplastin time	30-40 s	>200	>200	>200	>200
Fibrinogen	1.5-4 g/L	1.3	1.0	e	0.7

coagulation complicating tick bite anaphylaxis. If this was a cross-reaction (tick anaphylaxis in a bee allergic patient), this has only been previously reported for the European hard-bodied tick *Rhipicephalus bursa*.⁸ Nevertheless, further investigations would be required to confirm this possibility.

The first case is also one of an apparent failure of an epinephrine autoinjector device to prevent fatal anaphylaxis. However, whether this was due to device or operator failure, a delay in administration or an epinephrine-resistant anaphylaxis^{9,10} is not apparent. This was also the only case where the patient had previously seen an allergist, despite all cases occurring within an area with accessible health care. Crucially, these cases suffered an anaphylactic reaction to a tick bite only when the tick was disturbed, prompting the reminder for public and patient counseling and first aid for tick-induced anaphylaxis in addition to tick avoidance for primary prevention. The lack of specific immunotherapy increases the importance of anaphylaxis emergency kits and patient (and family) education for those with life-threatening allergy to tick bites. Given the lack of recent fatal tick paralysis cases, and the temporal and spatial clustering of these events, tick-induced anaphylaxis seems as important, if not potentially more significant than tick toxicity.

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