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Tick anaphylaxis in Japan

Dear Editor,

Because of the spread of ticks related to global warming, it is not surprising that the prevalence of tick-borne diseases is increasing worldwide. Recently, alphagal syndrome, a delayed immediate hypersensitivity to red meat and drugs containing galactose-alpha-1,3-galactose (alphagal), has gained increasing attention because of its relationship with infestation by ticks harboring alphagal.[1,2] However, few studies have been done on immediate-type hypersensitivity induced by tick bites, termed tick anaphylaxis, in Japan. Recently, 133 patients visited our hospital in Japan with new tick bites and were interviewed about their clinical features and tick bite histories. Of these, 12 patients experienced tick anaphylaxis and eight patients had alphagal syndrome. To characterize the features of tick anaphylaxis, we compared the clinical features and laboratory data of patients with alphagal syndrome. This is the first report of tick anaphylaxis cases in Japan.

The characteristics of patients with tick anaphylaxis and alphagal syndrome are summarized in Tables 1 and 2, respectively. The former comprised eight males and four females aged 70.4 ± 7.74 years (mean ± SD). The number of anaphylactic episodes that required medication at the emergency room was 1.3 ± 0.49 in the patients. Importantly, in 41.7% (5/12) of cases, anaphylaxis occurred when patients removed ticks themselves. The serum total IgE level was 622.4 ± 507.8 U/mL, which was comparable to that of alphagal syndrome. Anti-alphagal IgE was positive (>0.35 IU/mL) in 83.3% (10/12) of patients (range, 0.4-16.7 IU/mL; mean 3.45 ± 5.22 IU/mL) although the levels were lower than those of alphagal syndrome ($P = 0.0054$, Mann-Whitney U test) and they had no history of red meat allergy except for one patient (case 3). The historical frequency of tick bites was ≥3 times. Most (91.7%) were non-B type by blood type, as reported for alphagal syndrome.[3] Case 1 with tick anaphylaxis was found dead in a field where she worked, suggesting a fatal case of tick anaphylaxis although it was not confirmed.

Tick anaphylaxis as well as alphagal syndrome, frequently seen in Australia,[4,5] is a life-threatening disorder; however, it has been underestimated in Japan. In Australia, alphagal syndrome developed following strong local reactions to tick bites, raising the

TABLE 1 Characteristics of 12 cases with tick anaphylaxis in Japan

Case #	Sex	Age (y)	Bite history[a]	Timing of anaphylaxis[b]	Anaphylaxis episodes[c]	α-gal (U/mL)[d]	Total IgE (U/mL)
1	F	78	4	Removal	2	0.00	7.1
2	M	64	4	In situ	1	0.00	177
3	M	73	7	In situ	1	0.40	309
4	M	69	>10	In situ	1	0.48	63
5	F	53	>3	In situ	2	0.64	410
6	M	67	3	Removal	1	0.88	533
7	M	70	>5	Removal	2	1.48	556
8	M	78	5	In situ	1	1.72	678
9	M	65	3	Removal	2	1.96	788
10	F	82	>10	In situ	1	6.68	890.6
11	M	72	2	Removal	1	10.40	1681
12	F	74	3	In situ	1	16.70	1376
Mean±SD		70.4 ± 7.7			1.3 ± 0.5	3.4 ± 5.2	622.4 ± 507.8

[a]Historical frequencies of tick bites are shown.
[b]Timing of anaphylaxis: removal, when ticks were being removed by the patients; in situ, when ticks were sucking blood from the skin.
[c]Times anaphylaxis was experienced.
[d]α-gal, anti-alphagal IgE antibody levels.

TABLE 2 Characteristics of eight cases of alphagal syndrome

Case #	Sex	Age (y)	Bite history[a]	Symptoms	α-gal (U/mL)[b]	Total IgE (U/mL)
1	M	69	>3	Wheal	2	212
2	M	85	>3	Wheal	2.44	82.2
3	M	65	4	Wheal	3.11	170.2
4	M	69	>20	Anaphylaxis	7.61	511.4
5	M	80	5	Wheal	8.09	57
6	F	75	3	Wheal	51.4	284
7	M	62	>3	Anaphylaxis	95.8	616
8	M	77	>10	Wheal	100	2024
Mean±SD		72.8 ± 7.8			33.8 ± 42.8	494.6 ± 648.6

[a]Historical frequencies of tick bites are shown.
[b]α-gal, anti-alphagal IgE antibody levels.

possibility that pathogenic antigens may overlap between tick anaphylaxis and alphagal syndrome.[5] Nevertheless, the tick-derived, IgE-reactive proteins from tick anaphylaxis patients having no history of red meat allergy did not necessarily include alphagal.[6] Indeed, the severity of clinical manifestations in this study did not correlate with the presence of anti-alphagal IgE antibody, suggesting that other antigens responsible for tick anaphylaxis may exist. Therefore, future studies on the potential antigens involved in anaphylaxis are required for the diagnosis and treatment. Our study demonstrates that tick bites are an important cause of anaphylaxis, even in Japan.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DECLARATIONS

Approval of the research protocol: The study was performed according to the Declaration of Helsinki, and the study protocol was approved by the Shimada Municipal Hospital Ethical Committee.

Informed Consent: Patients were enrolled after oral informed consent was provided.

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