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Letter to the Editor

Nonepisodic angioedema with eosinophilia: A case series from Thailand

Dear Editor,

Angioedema with eosinophilia (AE) is a rare form of idiopathic angioedema.¹ It can be classified into episodic AE (EAE) and non-episodic AE (NEAE). EAE was first described in 1984 by Gleich *et al.* in patients with recurrent angioedema, urticaria, fever, weight gain, eosinophilia and elevated immunoglobulin (Ig) M levels.² Subsequently, NEAE whose clinical features including non-recurrent, self-limiting peripheral angioedema, arthralgia, eosinophilia and normal IgM levels was observed mainly among young women from Japan and Korea.^{1,3–7} Until present, at least 100 patients with NEAE have been reported. Herein, a case series of 4 patients with NEAE from Thailand is described.

Patients presented with angioedema to the Allergy Clinic at the Samitivej Sukhumvit Hospital, Bangkok, Thailand were retrospectively reviewed. Among those, there were 4 patients who were diagnosed with NEAE during April 2014–August 2016. All but one patient were female. The mean age at the onset was 37 years (28–52). All patients presented with symmetrical swelling of the distal extremities. One patient had a history of asthma, nasal polyps and aspirin sensitivity requiring montelukast, salmeterol/fluticasone and salbutamol inhalers. Another patient reported a history of chronic hepatitis B virus infection and eczema, both of which were in remission at that time. One patient developed angioedema 1 week following an upper respiratory tract infection. Urticaria and/or arthralgia were observed in 3 patients. Fever and weight gain were not present. All laboratory tests including complete blood count, kidney and liver functions, stool examination for parasites, inflammatory markers (ESR and CRP), complement levels and

immunoglobulin levels were within normal range except eosinophilia was demonstrated in all patients. The mean highest eosinophil counts were 4,253/mm³ (1,006–9,420). Unfortunately, C1 inhibitor (C1-INH) level and activity could not be measured due to the unavailability in Thailand. However, sufficient complement levels would preclude the possibility of abnormal C1-INH level and function. Pathologic studies were not performed. Antihistamines were temporarily prescribed for 2 patients with co-existing urticaria. All patients had gradual complete resolution of angioedema along with the normalization of eosinophil counts within few months after the onset. Clinical presentation, laboratory results and outcome of the patients were summarized in Table 1.

The clinical characteristics of the patients in this study were in accordance with those in previous reports of NEAE from Japan and Korea.^{1,6,7} However, their mean age at the onset was higher (37 years vs 28.5 years)^{1,7} and the mean eosinophil counts at the initial presentation were lower (4,253/mm³ vs 8,432/mm³).⁶

Although both EAE and NEAE predominantly affect young women, the former has been mainly observed in Western countries while NEAE was exclusively found in Japan and Korea. In addition, NEAE was reported to develop following an infectious illness in some patients, including one in this report.⁸ Taken altogether, it is possible that NEAE is a result of an aberrant immune response to various exogenous stimuli, including infectious organisms and/or environmental factors, in genetic susceptible individuals under the influence of sex hormones.

In conclusion, NEAE should be included in the differential diagnosis of peripheral angioedema with eosinophilia in young Asian women, in particular those from Japan, Korea and Thailand.

Table 1

Clinical presentation, laboratory results and outcome of 4 patients with NEAE from Thailand.

Patient	Gender	Age (years)	Onset	Underlying disease(s)	Involved area	Associated symptoms	WBC counts (/mm ³)	Eosinophil counts (/mm ³)	Treatment	Time to resolution of angioedema and eosinophilia
1	Female	31	Apr 2014	None	Hands and feet	None	18,840	9,420 (50%)	None	3 months
2	Female	39	Oct 2014	Chronic HBV infection, eczema	Lower legs and feet	Arthralgia	5,610	1,823 (33%)	None	2 months
3	Male	28	Mar 2015	None	Hands and feet	Prior URI, urticaria	9,580	1,006 (11%)	Antihistamine	1 month
4	Female	52	Jun 2016	AERD	Lower legs and feet	Arthralgia, urticaria	10,590	4,765 (45%)	Antihistamine	2 months

Abbreviations: AERD, aspirin exacerbated respiratory disease; HBV, hepatitis B virus; URI, upper respiratory infection; WBC, white blood cell.

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Conflict of interest

The author has no conflict of interest to declare.

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