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Clinical Course of Eosinophilic Cellulitis

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The patient was a previously healthy 23-year-old woman who made an outpatient visit to our hospital's Department of General Internal Medicine after developing pain and edema of the lower legs a week earlier. The patient was diagnosed with eosinophilic cellulitis (EC) based on an increased eosinophil count of 5,418/mm^3 and the results of a skin biopsy of the lower leg that showed eosinophilic infiltration of the dermal tissue. Her condition improved after oral prednisone therapy.
EC presents clinically as edema and eosinophilia. Therefore, in many cases, patients make an outpatient visit to the internal medicine department. In the present study, the clinical course of nine patients diagnosed with EC as outpatients at our Department of General Internal Medicine over the past 10 years was examined.

Key words: Eosinophilic cellulitis, eosinophilia, Clinical course

INTRODUCTION

Eosinophilic cellulitis (EC) is a rare disease that is mainly characterized clinically by erythema nodosum and acute cellulitis-like infiltrative erythema, the hematological finding of eosinophilia, and histological findings of eosinophilic infiltration of the dermis and deposition of eosinophil granules in collagen fibers [1-3]. EC is classified as a dermatological disease, but it often presents as edema of the extremities and eosinophilia, etc., so that, in many cases, patients visit the internal medicine department. A patient who made an initial outpatient visit to our Department of Internal Medicine and was diagnosed with EC is presented. In the present study, we describe the clinical course of this patient along with those of eight other EC patients who were diagnosed and treated at the Tokai University Hospital over the past 10 years.

CASE REPORT

The patient was a previously healthy 23-year-old woman who visited our hospital with a chief complaint of edema of the lower extremities. The patient had engaged in strenuous exercise three to four weeks before her initial visit. She visited her local doctor after developing pain in both heels two weeks earlier and acute edema of the lower legs one week earlier. Since the edema and lower leg pain worsened, she was referred to our department. The patient was a nurse with no family or prior medical history of allergies and no other remarkable findings.

Patient's condition at admission: The patient was fully conscious with a blood pressure of 118/78 mmHg, normal heart rate of 72 beats per minute, respiratory rate of 12 breaths per minute, temperature of 36.3℃, and no anemia or jaundice. Superficial lymph nodes were not palpable, and there were no abnormal findings in the chest or abdomen. The patient had faint erythema and edema of the lower legs accompanied by a mild heat sensation.

The laboratory findings on admission are shown in Table 1. The white blood cell (WBC) count was increased at 12,600/mm^3, and the eosinophil count was also high at 5,418/mm^3, with eosinophils comprising 43% of the WBC differential count. The results of urine and stool parasite testing were normal, and plain chest X-ray findings were also normal. The magnetic response imaging (MRI) of lower legs are shown in Fig 1. Short tau inversion recovery images on MRI of the lower legs showed a high signal intensity centered on the adipose tissue of the subcutaneous ventral aspect of both lower legs. The T1-weighted images at these sites were slightly enhanced, suggesting inflammatory changes in the subcutaneous fat, and a skin biopsy was taken from the contrast-enhanced lower ventral subcutaneous tissue of the left lower leg. Significant eosinophilic infiltration was observed around the vessels from the dermis to subcutaneous tissue (Fig. 2).

The patient was diagnosed with EC since the absence of other organ dysfunction and the skin biopsy findings. Since the patient's edema and pain symptoms were severe, she was started on oral prednisone therapy at a dose of 20 mg. One week after this prednisone therapy, the lower extremity pain persisted, but the edema had largely subsided, and her eosinophil count had decreased to 975/μl. The prednisone dose was therefore tapered slowly by 2.5 mg per week, and after five weeks, the eosinophil count had returned to normal at 216/μl. The prednisone dose was reduced gradually because symptoms of edema of the lower extremities and calf pain persisting after she had finished her daily work. Twenty-four weeks later, the

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Table 1 Laboratory data on the first visit

WBC	12.600 /μl	Alb	4.5 g/dl
Neut	43.00%	AST	14 U/l
Lym	12.00%	ALT	8 U/l
Eos	43.0% (5.418 /μl)	LDH	275 U/L
Mono	2.00%	ALP	187 U/L
RBC	479×10^4 /μl	BUN	7 mg/dl
Hb	13.6 g/dl	Cr	0.62 mg/dl
Hct	41.40%	Na	144 mEq/L
PLT	21.7×10^4 /μl	K	3.8 mEq/L
		Cl	107 mEq/L
ESR (1hour)	5 mm		
CRP	0.20 mg/dl		

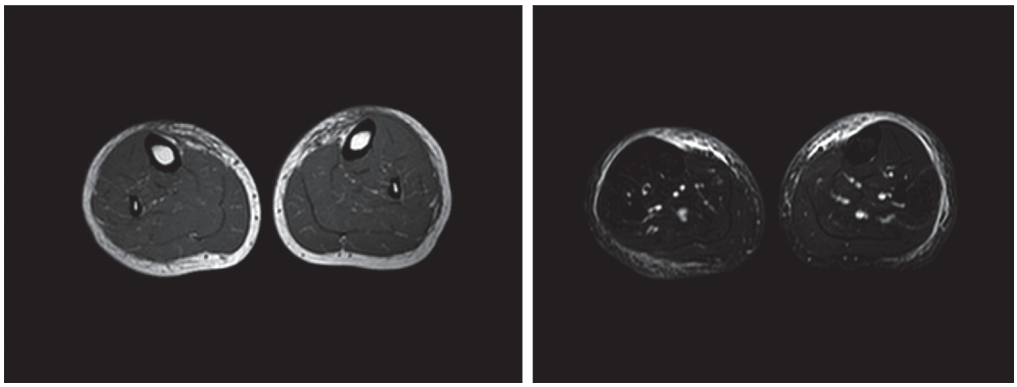

Fig. 1 Magnetic response imaging (MRI) of lower legs.
Left: T1-weight image on MRI . Right: Short tau inversion recovery images on MRI .
The T1-weighted images and Short tau inversion recovery images on MRI of the lower legs showed a high signal intensity centered on the adipose tissue of the subcutaneous ventral Aspect of both lower legs.

patient's symptoms had resolved completely, and the prednisone therapy was completed. The patient subsequently made good progress without any recurrence of EC or new onset of organ dysfunction.

DISCUSSION

EC was first described by Wells *et al*. in 1971 in a report of four cases as recurrent granulomatous dermatitis with eosinophilia [1], and it was again introduced by Wells and Smith *et al*. in 1979 along with eight similar cases [2]. EC is characterized clinically by edema and erythema of the extremities, peripheral blood eosinophilia, and the histopathological finding of eosinophilic infiltration [3]. The disease typically manifests as cellulitis-like redness and edema of the upper and lower extremities and eosinophilia, so that, in many cases, patients make an outpatient visit to the internal medicine department. Table 2 shows the clinical course of nine patients with EC who made an outpatient visit to our Department of General Internal Medicine over the 10-year period from 2007 to 2016.

EC is classified as either episodic angioedema associated with eosinophilia (EAE) or non-episodic angioedema associated with eosinophilia (NEAE). EAE often appears as extensive wheals and erythema on the back of the hands, face, and trunk. It is a serious, recurrent condition that mainly affects people in Europe and the U.S. [4, 5]. On the other hand, NEAE is a relatively mild condition with a low recurrence rate that is localized to the upper and lower extremities that mainly affects females in Japan and other parts of Asia. Approximately 90% of NEAE cases were reported to occur between summer and autumn [6, 7]. Similarly, all our cases were females, including Case No. 8, which occurred in a woman who was nine weeks pregnant. The mean age at onset was relatively young, at 27.4 years, with an age range of 23 to 40 years. All of the patients visited our hospital with a chief complaint of edema, four of which were limited to the lower extremities, and five of which affected the upper and lower extremities. All nine cases occurred between the start of summer and autumn, and none of the cases relapsed after treatment. EC is reportedly triggered by insect bites [8], tinea pedis, parasitic diseases, viral infections [9], cancer [10], surgery, and antibiotics such as beta-lactams, macrolides, and tetracyclines [11]. Among the nine female patients described in the present study, some patients developed EC after strenuous exercise, while two other patients developed EC after oral therapy with non-steroidal anti-inflammatory drugs, and one patient developed EC after oral therapy with cephem antibiotics. The maximum eosinophil count during the course in each patient ranged from 3,132 μ/l to 26,300 μ/l, with a mean value of 9,137 μ/l. EC is typically diagnosed on the basis of the following: (1) edema and erythema accompanied by peripheral

Table 2 Clinical data and therapeutic response of 9 patents of eosinophilic cellulitis

No	Age	Gender	Associated symptom	Initial location	season of onset	Eosinophil count (/μl)	Treatment	Significant improvement (W)
1	23	F	Edema & tenderness	Lower limbs	August	5418	prednisone	24
2	25	F	Edema	Upper & lower Limbs	October	3496	olopatadine	12
3	29	F	Edema	Lower limbs	October	8340	prednisone	20
4	40	F	Edema & tenderness	Lower limbs	May	3726	fexofenadine	3
5	25	F	Edema	Upper & lower Limbs	July	17296	prednisone	2
6	30	F	Edema	Upper & lower Limbs	July	4910	fexofenadine	2
7	25	F	Edema & tenderness	Upper & lower Limbs	August	3132	acetaminophen	4
8	27	F	Edema	Upper & lower Limbs	September	9167		6
9	23	F	Edema & tenderness	Lower limbs	September	26300	prednisone	12

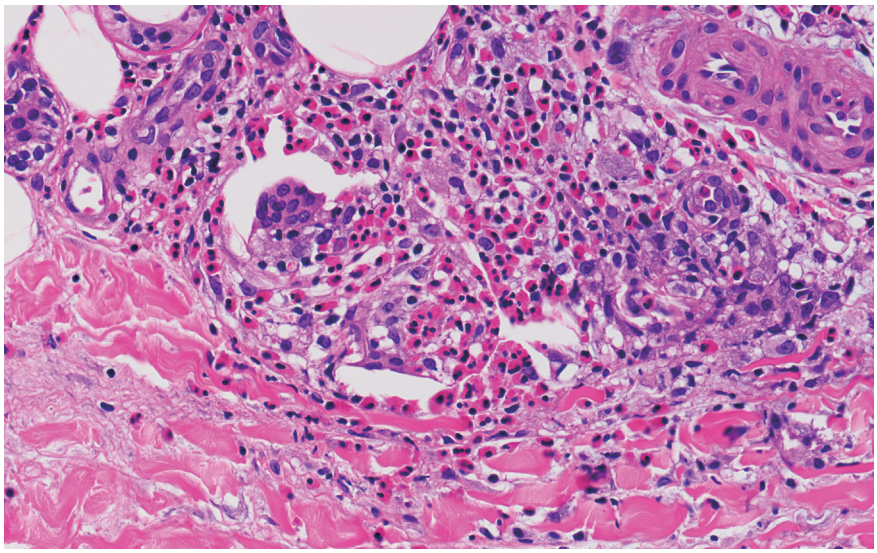

Fig. 2 Histologic findings in skin biopsy of left lower leg.
Significant eosinophilic infiltration was observed around the vessels and collagen fibers from the dermis to subcutaneous tissue.
(Hematoxylin and Eosin staining, x200).

blood eosinophilia; (2) no organ dysfunction and no other plausible reason for eosinophilia; and (3) skin biopsy showing inflammatory cell infiltration of the dermis including eosinophils [4]. Skin biopsy was also performed on eight of the nine EC cases treated at our hospital; the only exception being Case No. 8, which was diagnosed solely on the basis of the clinical course because she was pregnant.

Mild cases of EC are typically treated with antihistamines and antiallergic drugs, but some cases resolve after a follow-up period without any intervention. EC cases with severe symptoms such as the one described in the present study are typically treated with systemic corticosteroids [12, 13]. Four of the nine EC cases at our hospital were treated with corticosteroids, four were treated with antiallergic drugs, and one was followed up without any intervention. Corticosteroid therapy is usually administered for two to 24 weeks, but long-term oral therapy with adrenocortical hormones may be required in the event of repeated relapse of pain and edema [14, 15], as in the present case.

CONCLUSION

In Japan, EC occurs mainly in young women between summer and autumn in the form of localized edema and erythema of the upper and lower extremities, and recurrence is rare. Although EC is a less-frequently occurring dermatological disease, it presents clinically as edema, erythema, and eosinophilia. Therefore, in many cases, patients make an outpatient visit to the internal medicine department. It is important for primary care physicians to have an awareness of EC in their routine clinical practice.

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