Single Case

Facial Edema in an Elderly Man: An Unusual Presentation of Nonepisodic Angioedema with Eosinophilia

Takashi Hashimoto^{a, b} Kanako Muneta^a Ken Watanabe^a

^aDepartment of Dermatology, Yokohama City Minato Red Cross Hospital, Yokohama, Japan; ^bDepartment of Dermatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University, Tokyo, Japan

Keywords

Eosinophilia · Angioedema with eosinophilia · Nonepisodic angioedema with eosinophilia · Thymus- and activation-regulated chemokine

Abstract

Nonepisodic angioedema with eosinophilia (NEAE) is a rare allergic disease with a young Japanese and East Asian female predominance. NEAE features transient, nonrecurrent angioedema and peripheral blood eosinophilia without visceral organ involvement. Angioedema in NEAE occurs on the extremities, while the trunk and face are rarely involved. Here, we report a case of NEAE affecting only the face in an 80-year-old Japanese man. He was otherwise healthy and took no medication until the sudden development of angioedema on the face. The extremities and trunk were not involved. Skin biopsy examination revealed eosinophilic infiltration and degranulation between collagen bundles through the entire dermis, and perivascular and perifollicular infiltration of eosinophils and lymphocytes, but no evidence of vasculitis. Peripheral hypereosinophilia and high serum thymus- and activation-regulated chemokine (TARC) level were noted. Visceral organ involvement, parasite infection, and an allergic response were not detected in the patient. Administration of oral corticosteroid improved his symptoms rapidly and dramatically with improvements in the blood eosinophil count and serum TARC level. After the corticosteroid was discontinued, no recurrence was

observed for 3 years. Thus, he was diagnosed as having NEAE. It should be noted that angioedema with eosinophilia might occur with an unusual presentation and might develop in elderly patients.

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Introduction

Nonepisodic angioedema with eosinophilia (NEAE) is a rare allergic disease with a young Japanese and East Asian female predominance [1]. NEAE features transient, nonrecurrent angioedema and peripheral blood eosinophilia without visceral organ involvement [1, 2]. Angioedema in NEAE occurs on the extremities, while the trunk and face are rarely affected [1–4]. Here, we report a case of NEAE in an elderly man, who developed angioedema only on the face.

Case Report

An 80-year-old Japanese man presented with a 10-day history of facial edema. He was otherwise healthy. He denied dyspnea, oliguria, body weight gain, abdominal pain, diarrhea, or any exposure to a parasite or substance that could cause a hypersensitivity reaction. His medical history was unremarkable and he took no medication. Physical examination revealed brawny, nonpitting edema of the face with slight erythema (Fig. 1a). The extremities and trunks were not involved. Laboratory data showed a normal white blood cell count (9,500/ μ L) and C-reactive protein level (0.1 mg/dL), with a high eosinophil count (1,060/ μ L; reference, <500/ μ L). Flow cytometric analysis of white blood cells and T cell phenotypes was not conducted. Renal and liver functions, thyroid function test results, and serum levels of adrenocorticotrophic hormone and cortisol were normal. Serum levels of immunoglobulin (Ig)G, IgM, IgA, and IgE were normal. Hypocomplementemia was not observed. Antinuclear antibody and anti-neutrophil cytoplasmic antibodies were negative. Urine analysis showed no proteinuria. Echocardiography disclosed no cardiac involvement or congestive heart failure. Computed tomography detected no visceral organ involvement. An occlusion or thrombus was not detected in the jugular vein or superior vena cava. No evidence of parasite infection was detected. Skin biopsy specimens obtained from his cheek revealed eosinophilic infiltrate and degranulation between collagen bundles through the entire dermis with a slight subcutaneous involvement. Perivascular and perifollicular infiltration of eosinophils and lymphocytes was also noted (Fig. 1b, c). Sebaceous glands and hair follicles were not involved. Epidermal changes, a pustule, granulomatous formation, or vasculitis was not observed. Antihistamine and topical corticosteroid administration failed to improve the patient's symptoms. In 10 days, the blood eosinophil count increased (5400/ μ L), and the serum level of thymus- and activation-regulated chemokine (TARC) was markedly elevated (29,176 pg/mL; reference, <450 pg/mL). Thus, an oral corticosteroid (prednisolone, 20 mg/day) was administered, and the symptoms were dramatically improved in a week (Fig. 1d), with improvements in the blood eosinophil count (170/ μ L) and serum TARC level (3,592 pg/mL). After the corticosteroid was tapered over 3 weeks and discontinued, no recurrence was observed for 3 years.

Discussion

The differential diagnosis of this patient's symptoms includes angioedema with eosinophilia (AE), hypereosinophilic syndrome (HES), eosinophilic pustular folliculitis (EPF), and contact dermatitis (CD). The diagnosis of HES was less likely as the patient had no visceral organ involvement. EPF was excluded, as a pustule or involvement of follicles and/or sebaceous glands was not detected clinically and histopathologically. CD was excluded as histopathological examination revealed no epidermal changes, and the patients denied any exposure to contact allergens. Parasite infection-induced eosinophilia and drug-induced angioedema were also excluded, as the patient had no medication and showed no evidence of parasite infection. Thus, the diagnosis of AE was made. Interestingly, histopathological examination in the patient failed to reveal significant subcutaneous tissue involvement; but this finding is consistent with the previous report showing that involvement of subcutaneous tissue is sometimes absent or slight in NEAE [5].

AE includes the following 2 subtypes: episodic angioedema with eosinophilia (EAE, or Gleich syndrome, named after the proponent of this disease) and NEAE [1, 5]. EAE is characterized by recurrent angioedema, weight gain, pyrexia, peripheral eosinophilia, and increased polyclonal serum IgM levels [6]. Angioedema in EAE occurs on the limbs and face, and occasionally on the trunk. In contrast, patients with NEAE develop milder angioedema almost exclusively on the extremities and have normal IgM levels [1–4]. Our patient had only a single attack of angioedema and a normal serum IgM level. In this regard, the diagnosis of NEAE might be appropriate for our patient, although the affected site of angioedema and the age at onset were unusual. Of course, it is sometimes difficult to distinguish EAE from NEAE. In addition, some suggest that NEAE lacks reliable diagnostic criteria and is just merely the abortive type of real EAE, or that EAE and NEAE are on the same spectrum; this point is still a subject of controversy [2].

Serum TARC levels in the patient appeared to be in parallel with the disease activity, which is consistent with previous reports [7–9]. TARC/CCL17 is a chemoattractant for T-helper (Th)2 cells, and these cells express a TARC receptor called C-C chemokine receptor type 4 (CCR4) [10]. Eosinophil-activation by Th2 cell-derived cytokines, including IL-5, is considered to drive AE [11]. TARC may be implicated in the development of AE via the promotion of skin-homing of Th2 cells.

Accumulation of similar cases is needed to clarify the characteristics of this unusual presentation of NEAE in our patient. Nevertheless, it should be noted that NEAE might occur with an unusual presentation and might develop even in elderly patients.

Statement of Ethics

The patient has given informed consent for the publication of his case.

Disclosure Statement

The authors have no conflicts of interest associated with the present work.

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Fig. 1. **a** At initial presentation, nonpitting, brawny edema with slight erythema was observed on the face. **b, c** Histopathological findings of the cheek skin biopsy. **b** Cellular infiltration in the perivascular area, around hair follicles, and between collagen bundles through the dermis. No apparent change is observed at the epidermis, sebaceous glands, and follicles. Hematoxylin and eosin (HE) staining. Original magnification, ×4. **c** Interstitial infiltration of eosinophils in the deep dermis. HE staining, ×400. **d** Symptoms show improvement after corticosteroid administration.