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Eosinophilic Cellulitis (Wells' Syndrome) Associated with Ascariasis

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A case of eosinophilic cellulitis (Wells' syndrome) in association with ascariasis is described. The clinical and histopathologic features of the patient responded well to an oral anthelminthic drug. According to our search, this association has not previously been reported. ***Key words: eosinophilia; skin disease; parasitic infection; degranulation; electron microscopy.***

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Recurrent granulomatous dermatitis with eosinophilia was described by Wells in 1971 (1). This uncommon cutaneous disorder was later denominated eosinophilic cellulitis or Wells' syndrome in 1979 (2, 3).

Although there are well-documented cases in the literature (4, 5), the etiology and pathogenesis of eosinophilic cellulitis remains unknown. It is probably an idiopathic skin disorder that appears to be a hypersensitivity response to various antigens. Parasitic infections have been presented as the cause of this disease (6, 7).

In this report we describe an additional case of eosinophilic cellulitis in association with ascariasis.

CASE REPORT

A 38-year-old Japanese woman was referred to the Dermatology Clinic of the Kurume University Hospital, for evaluation of recurrent, pruritic, infiltrated, erythematous plaques on the upper extremities (Fig. 1) and lower abdomen. The disorder had begun abruptly a month earlier as localized edematous eruption with prodromal burning sensations. The patient did not have fever, chills, swelling of lymph nodes, or epigastric distress. She had no remarkable family or past history, and did not have a history suggestive of atopy. She had not been taking any medications prior to her disease onset.

Pertinent laboratory data included the following: white blood cell count, 10600/mm^3 with 22% neutrophils, 47% eosinophils, 2% basophils, 26% lymphocytes and 3% monocytes; hemoglobin level, 13.3 g/dl; hematocrit reading, 40% and platelet count, 21.7×10^4/mm^3. Bone marrow aspiration and biopsy showed an increase of eosinophils (25.3%). No significant infiltration of blast cells was observed in peripheral circulation or in bone marrow. Serum immunoglobulin determinations showed an IgG of 1997 mg/dl (normal range, 1080 ~ 2050 mg/dl), IgA of 168 mg/ml (124 ~ 493 mg/ml), IgM of 197 mg/ml (60 ~ 330 mg/ml), and an IgE of 1200 U/ml (normal maximum, 250 U/ml). Stool samples were positive for *Ascaris lumbricoides* eggs and the adult worms.

A biopsy was taken from an erythematous lesion with slight induration on the right forearm. The excised specimen was fixed in 10% buffered formalin, and conventional hematoxylin and eosin sections of paraffin-embedded tissue were prepared in the usual manner for light microscopy. In the skin biopsy, dense inflammatory infiltrates, composed of eosinophils, macrophages and a few lymphocytes, were located in the deep dermis and adjacent subcutaneous tissue. "Flame figures" were present, together with necrobiotic foci in the collagen, which showed accumulation of histiocytic cells and eosinophils (Fig. 2). The upper dermis showed mild edema, but no abnormality of the epidermis was seen. The vessel walls showed no sign of necrosis and there was no leukocytoclastic vasculitis.

The excised skin specimens, fixed by perfusion with 2.5% glutaraldehyde in 0.1% cacodylate buffer, were prepared for observation with transmission electron microscopy, as previously described (8). Ultrastructurally, large numbers of degranulated eosinophils with the appearance of Charcot-Leyden crystals were present (Fig. 3). The cytoplasm of the eosinophils exhibited signs of cytolysis and disintegration.

Eosinophil cationic protein (ECP) concentration in serum was measured by a radioimmunosorbent assay kit for ECP (Pharmacia ECP RIA, Kabi Pharmacia Diagnostics AB, Uppsala, Sweden), as previously described (8). The mean level of serum ECP concentration was 36.6 μg/l, which was estimated in triplicate. In contrast, the mean value of ECP in serum from normal subjects ($n = 25$) was 5.6 μg/l (8).

In our patient, topical corticosteroids were of little benefit. A trial of short duration of oral administration of corticosteroid (Prednisolone 30 mg per day for 4 days, 15 mg for 3 days and 10 mg for 2 days) was not successful in clearing the lesions.

The patient was examined under suspicion of parasite infection. A great number of fertilized eggs of *Ascaris lumbricoides* were collected in stool samples by formalin-ether technique (9). After the diagnosis of ascariasis had been made, the patient was treated orally with an anthelminthic drug, Pyrantel pamoate (Combantrin®) 500 mg. On the day after medication, 3 adult worms (2 females and 1 male) of *Ascaris lumbricoides* were eliminated into the stool. No more worms and/or eggs were observed in the stool, when the patient was treated with the same dosage of Pyrantel pamoate a week later. The eruptions reduced approximately 2 weeks after the second medication. Clinical symptoms, such as pruritus and eosinophilia, completely disappeared. ECP concentration in the serum also became normal.

DISCUSSION

We have described a new case of eosinophilic cellulitis in association with parasitic infection. Treatment with anthelminthics was effective in eliminating not only the adult worms and eggs of *Ascaris lumbricoides* but also the dermatological symptoms. These results indicate that the symptoms must be regarded as a reaction to ascariasis.

There have been fewer than 50 cases of eosinophilic cellulitis

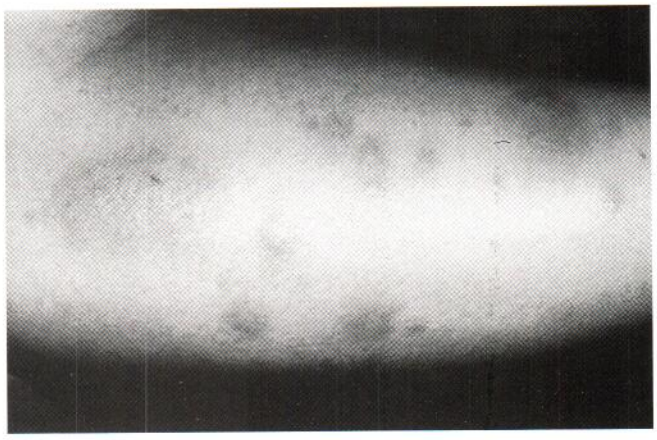

Fig. 1. Erythematous indurated plaques on the patient's right forearm.

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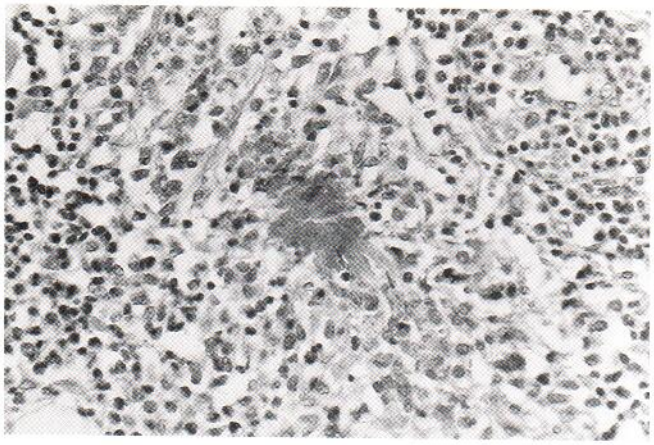

Fig. 2. Photomicrograph of "flame figure" showing a mass of necrobiotic collagen, surrounded by histiocytes and eosinophils. H&E (× 100).

reported in the dermatological literature until 1989 (4, 5). Several entities such as eosinophilic panniculitis (10), Churg-Strauss allergic granulomatosis (11), hypereosinophilic syndrome (12) and parasitic worm infections including toxocariasis (13) and gnathostomiasis (14) have been reported to be characterized by attraction of eosinophils to the cutaneous tissue. They partially share clinical features with eosinophilic cellulitis. When compared with these published cases, our patient has the typical features of eosinophilic cellulitis as regards clinical aspects – recurrent and persistent cutaneous swelling and erythema – and pathological aspects – eosinophilic infiltration and "flame figures" in the dermis.

Although the etiology is unknown, eosinophilic cellulitis appears to be a localized hypersensitivity reaction to various antigens. The well-known triggers that have been thought to precipitate the syndrome include drug reactions (2, 4, 15), insect bites (1, 2, 16), infections (1, 2, 17), hematologic disorders (18) and parasitic infections, such as toxocara (2) or onchocerciasis (5, 6). Therapeutically, systemic corticosteroids seem to be effective in controlling the lesions of eosinophilic cellulitis in most patients (16, 19). However, in some cases, treatment of the underlying disease(s) may be helpful in curing the disease.

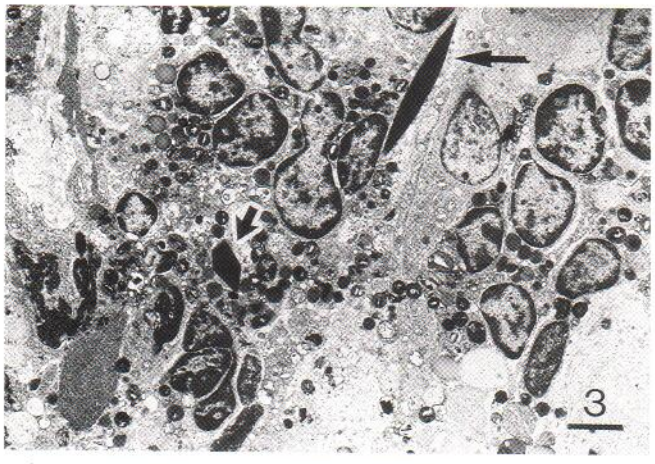

Fig. 3. Ultrastructure of numerous eosinophils in the dermis. Eosinophils are degranulated with loss of cytoplasmic membrane. *Arrows* indicate Charcot-Leyden crystals.

Ascariasis is one of the soil-transmitted helminthiases, and *Ascaris* eggs require a certain period of time to develop an infective stage larva (20). Infection is the result of swallowing fully embryonated eggs from contaminated soil. The mode of infection in our case is not clear, since ascariasis has been sufficiently eradicated in Japan. Imported vegetables or fruits from highly infected fields are often the cause.

The pathogenesis caused by *Ascaris* infections is attributed to the host's immune response, the effects of larval migration, the mechanical effects of the adult worms, and nutritional deficiencies due to the presence of the adult worms (20). Larvae migrate into the lungs from the intestine after hatching and cause Löffler's syndrome, which includes pneumonia, eosinophilia, and increase of radiological shadows. None of these visceral or systemic disorders occurred in our case, although eosinophilic cellulitis was elicited.

The pathogenesis of eosinophilic cellulitis is unknown. Recent evidence has indicated that "flame figures" contain the aggregated granules and nuclear fragments of eosinophils (21). When examined by immunofluorescence for major basic protein (MBP), the "flame figures" show bright extracellular staining, suggesting that extensive eosinophil degranulation has occurred and is associated with collagen breakdown (22). The localization of such large quantities of MBP in these lesions suggests that eosinophils may be involved in the pathogenesis of this disorder. The elevated concentration of ECP observed in our patient's serum also supports this possibility. Further support for the participation of eosinophils in the formation of "flame figures" is provided by electron microscopic observations of free eosinophil granule-coating collagen fibres in "flame figures" (23).

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