Hypereosinophilic Syndrome Accompanied with Necrosis of Finger Tips

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We report a case of hypereosinophilic syndrome (HES) with marked eosinophilia (59.7%) and mononeuritis multiplex (upper limbs and buttocks). Necrosis of the finger tips was the primary manifestation which simultaneously occurred on both sides. These clinical manifestations were improved dramatically by subsequent steroid therapy. Interestingly, an elevation of serum tumor necrosis factor (TNF) was observed. These findings suggest that TNF may play a role in the etiology of necrosis of the finger tips.

Key words: Churg-Strauss syndrome, eosinophilia, collagen disease, steroid therapy, TNF

Introduction

Hypereosinophilic syndrome (HES) and allergic granulomatous angiitis (AGA; Churg-Strauss syndrome) are diseases presenting characteristic clinical pictures resulting from eosinophilia in the peripheral blood and infiltration of eosinophils into systemic organs. Recently, attention has been focused on the homology of these two diseases with regard to their pathogenesis and clinical diagnosis.

This paper reports a recent case of HES accompanied by massive necrosis in the tips of the fingers. Although histological analysis did not show distinct vasculitis, clinical pictures of this patient seem to be derived from necrotizing vasculitis.

Case Report

The patient, a 31-year-old man, who had a family history of bronchial asthma, began to feel coldness in the right fifth finger in October 1988. He suffered from coughing attacks accompanied by wheezing and nocturnal perspiration about one year later. An attending physician suspected bronchial asthma and performed spirography, which revealed no abnormalities (%VC, 131%; FEV1.0%, 79%). These symptoms persisted until about April 1990 and improved thereafter. At that time, the patient noted a cold sensation, pain and swelling in the fingers of the right hand and itchy papules over the limbs and lower abdomen. In the middle of March, the distal areas of the first and third fingers of the right hand became necrotic, accompanied by severe pain. By the end of the same month, the distal parts of the left hand second and third fingers had also become necrotic. Because of these symptoms, the patient visited our department on June 21, 1990.

The patient was 175 cm in height and 78.0 kg in weight. There had been a weight loss of about 5 kg during the previous month. On admission, his blood pressure was 110/70 mmHg, pulse rate 76/min, and body temperature 37.1°C. No lymph-node was palpable, and there was no abnormality in the heart, lung or abdomen. Subjective symptoms were radiating pain in the upper limbs and numbness in the buttocks while walking. There were many red to brown solid itchy papules with clear borders over the limbs and lower abdomen. Incrustation was noted on the top of some of these papules. Histological findings of a purpuric papule on the right lower leg (Fig. 1) showed a slight hyperkeratosis and mild superficial and deep perivascular infiltration of lymphocytes, histiocytes, neutrophils and scattered eosinophils. Extravasation of erythrocytes and nuclear dust were present in the perivascular area. The small blood vessels showed thickening, obliterative changes, and disruption of the walls with lymphocytes, neutrophils and a few eosinophils. There was general rubor and swelling in the right first and third, and left second, third and fourth fingers, the distal parts being necrotic and ulcerated (Fig. 2).
except for the right third finger healed, showing dermal regeneration. The patient is now on prednisolone at a decreased dose of 15 mg/day, and has shown no aggravation of symptoms.

Discussion

Löffler syndrome, pulmonary infiltration with eosinophilia syndrome (PIE syndrome), disseminated eosinophilic collagen disease (DECD), and eosinophilic leukemia are cited as diseases associated with marked eosinophilia of unknown etiology and with damage to multiple organs. In 1968, Hardy and Anderson (1) proposed the name hypereosinophilic syndrome for this series of diseases. In 1975, Chusid et al (2) introduced the following diagnostic criteria for HES; 1) eosinophilia in peripheral blood (15,000 or more/mm³) persisting for 6 months or more; 2) absence of conditions that might cause eosinophilia (verminosis or allergy); 3) signs and symptoms suggestive of damage to multiple organs due to eosinophilic infiltration (hepatosplenomegaly, cardiac failure or central nervous disorder). The present case was diagnosed as HES because it satisfied all three of these criteria. The elevation of serum vitamin B₁₂ level and a decreased NAP score which are frequently observed in HES, and sweating, weight loss, skin lesions and respiratory symptoms, typical clinical pictures of HES, were present in this case. Shulman syndrome and eosinophilia-myalgia syndrome were ruled out due to the lack of sclerotic skin, fasciitis, and no history of having taken tryptophan.

According to Spry et al (3), cardiac disorder associated with HES occurred in 79 (75%) of 106 patients. The characteristic lesion is eosinophilic endomyocardial fibrosis. It has been speculated that damage to the myocardium due to eosinophilic infiltration into the endocardium, embolism and endocardial fibrosis result in secondary restrictive cardiomyopathy. However, the present patient exhibited no cardiac disorder typical of HES such as embolism in the endocardium (i.e. no abnormal uptake in this patient was found by scintigraphy for embolism, and no mural embolism was found by UCG). It is noteworthy that he had extensive pericarditis with pericardial effusion (Fig. 3), which is typical of a clinical feature due to vasculitis.

On admission, we tried skin biopsies from the finger necrosis lesions, however these sections were not diagnostic due to necrosis. During the withdrawal of the steroid therapy, the skin eruption transiently appeared. The histological analysis of the eruption showed mild vasculitis with extravasation of RBC, accompanied with mild eosinophilia. Thus, the necrosis in the distal fingers was most likely due to necrotizing vasculitis. Improvement of the necrotic lesions of fingers (Fig. 2) by steroid therapy also support the diagnosis of necrotizing vasculitis.

With regard to the mechanism of vasculitis due to eosinophils, Slungaard et al (4) have recently reported that TNF-stimulated eosinophils affect vascular endothelial cells via superoxide, and thus may result in vasculitis. Actually the serum TNF level detected by enzyme-immunoassay was elevated in the present patient. According to their report, the biological effect derived from eosinophils is strongly suppressed by methyl-prednisolone.

It is presumed that cytokines such as TNF play a role in the etiological difference between HES and AGA, which are both associated with eosinophilia, but are present in various clinical pictures.

To our knowledge, only four patients with HES have been reported to reveal necrotizing vasculitis as main clinical manifestations (5–8, Table 2). Thus, it is noteworthy that the involved blood vessels in those cases are mainly observed within internal organs. There has been no report of lesions on the distal fingers as seen in the present case.

Kashiwazaki (9), Hayakawa and their coworkers (10) have suggested that HES and AGA partially overlap each other. The present rare case of HES accompanied with necrotizing vasculitis may be closely related in some form.

References

3) Spry CJF. The hypereosinophilic syndrome; Clinical features, laboratory findings and treatment. Allergy 37: 539, 1982.

Table 2. HES Cases with Necrotizing Vasculitis in the Literature

<table>
<thead>
<tr>
<th>Reported case</th>
<th>Age</th>
<th>Sex</th>
<th>Sites</th>
<th>Reference</th>
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<td>Systemic organ</td>
<td>(5)</td>
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<tr>
<td>Case 2</td>
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<td>F</td>
<td>Mesenteric artery</td>
<td>(6)</td>
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<td>81</td>
<td>F</td>
<td>Renal artery</td>
<td>(7)</td>
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<tr>
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<td>M</td>
<td>Temporal artery</td>
<td>(8)</td>
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<td>Our case</td>
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