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Hyperimmunoglobulin E-Recurrent Infection Syndrome In A Patient With Juvenile Dermatomyositis

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A 13-year-old girl presented with multiple skin abscesses. She was diagnosed as having juvenile dermatomyositis (DM) at the age of 7 years. She had suffered from recurrent skin infections, atypical pruritic dermatitis and pneumonia since the age of 8 years. Bacteriologic and fungal cultures for skin abscesses and oral mucosa were positive S. aureus and C. albicans, respectively. Chemotactic defect in peripheral blood neutrophils was observed. The level of serum IgE was markedly elevated, and anti-S.aureus specific IgE was found. A diagnosis of hyperimmunoglobulin E-recurrent infection syndrome (HIE) was made and she was successfully treated with surgical drainage and antibiotics. To our knowledge, this is the first case report of HIE in a patient with juvenile dermatomyositis.

Key Words : *Juvenile dermatomyositis, hyperimmunoglobulin E-recurrent infection syndrome (HIE)*

INTRODUCTION

Juvenile dermatomyositis (DM) is a multisystem disease characterized by nonsuppurative inflammation of striated muscle, skin and the gastrointestinal tract, and also characterized early in its course by an immune complex vasculitis and, later, the development of calcinosis[1]. Although the etiology of juvenile DM remains unclear, it is suggested that IgE can be associated with autoimmune diseases, such as systemic lupus erythematosus (SLE) and juvenile DM, by mediating the release of chemical mediators and by faciliating the local deposition of immune complexes[2]. Intercurrent infections with elevated serum IgE level during the course of the disease give rise to problems in patients with juvenile DM. Atopic dermatitis, or development of calcinosis, may contribute to this problem[3, 4]. HIE also has the characteristic findings of recurrent infections of the skin and sinopulmonary tract and high serum IgE level. Other findings of HIE include eosinophilia, presence of anti-*S.aureus* specific IgE, defect of neutrophil chemotaxis, poor delayed hypersensitivity responses and eczematoid dermatitis[5]. Herein, we describe a patient with juvenile DM complicating HIE.

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CASE REPORT

A 13-year-old girl was admitted to the hospital because of multiple skin abscesses. Six years before admission, juvenile dermatomyositis was diagnosed at another hospital on the basis of symptoms of proximal muscle weakness, abnormal findings of muscle biopsy, elevated serum muscle enzyme and skin rash on her face. She had not been managed with regular follow-up. There was a history of recurrent skin infections,

pneumonia and eczematous dermatitis over the whole body after the diagnosis of juvenile dermatomyositis. She denied any history of allergic diseases. There was no family history of specific diseases. The temperature was 38.0℃, the pulse was 116 and the respirations were 24. The blood pressure was 90/50 mmHg. On physical examination, the skin of her entire body showed multiple hyperpigmented lesions, lichenoid patches and eczemaoid confluent plaques. Oral thrush and subcutaneous cold abscesses of the left upper eye lid, back and right lower quadrant abdomen were found (Fig. 1). No lymphadenopathy was observed. The lungs were clear. Both knee joints had flexion contractures with muscle atrophy. The following laboratory findings were recorded: hemoglobin 10.5 gm/dl, white blood cell count 15,000/㎣ (88.3 % neutrophils, 6.6 % lymphocytes, 3.5 % monocytes, 0.2 % eosinophils, 1.4 % basophils), platelet count 288,000/㎣, erythrocyte sedimentaion rate 68mm/hour (Westergren method), The protein was 6.7 g/dl (albumin 3.2 g/dl; globulin 3.5 g/dl). The values for glucose, urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, creatine kinase, lactic dehydrogenase, aldolase, alkaline phosphatase, bilirubin, calcium, phosphorus, sodium, potasium, chloride and magnesium were normal. Urine analysis was normal except for proteinuria(+). Levels of C3, C4 and CH50 were normal. The tests for antinuclear antibody, rheumatoid factor, VDRL, hepatitis surface antigen, hepatitis C virus antibody and C-reactive protein were negative. Antibodies to Sm, RNP, Ro, La, Jo-1 and ds DNA were not detected. Serum immunoglobulin examination revealed normal IgG (1,970 mg/dl; normal 800-1,500 mg/dl), IgM (111 mg/dl; normal 45-150 mg/dl), elevated IgA (455 mg/dl; normal 90-325 mg/dl) and IgE (6,650 mg/dl; normal <200 mg/dl).

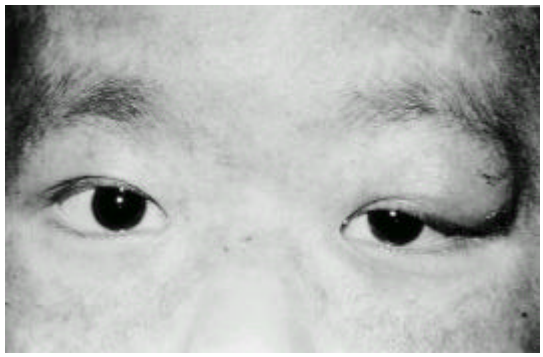

Fig. 1. Cold abscess in left upper eye-lid. *S.aureus* was isolated by bacterial culture.

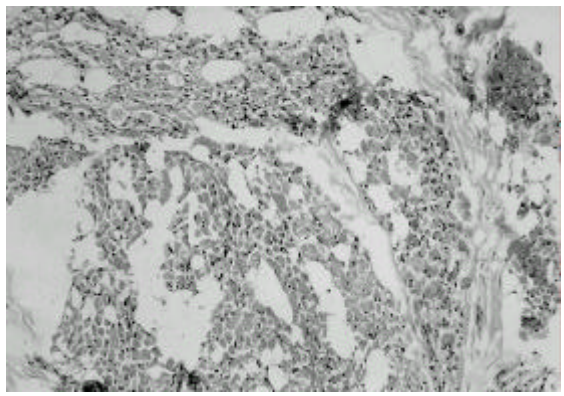

Fig. 2. Muscle biopsy specimen showed various-sized muscle fibers and moderately increased adipose tissue due to extensive necrosis and degeneration of muscle fibers (× 100).

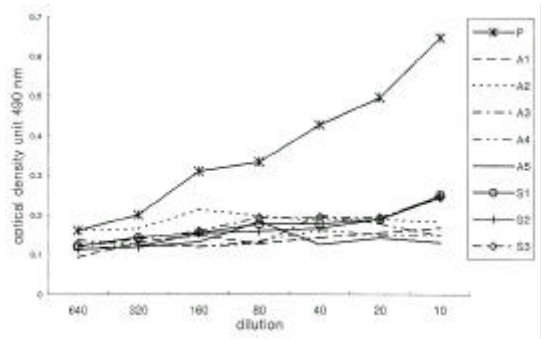

Fig. 3. IgE binding to *S. aureus*. Anti-*S. aureus* specific serum IgE was measured with *S. aureus* Wood 46 strain (Sigma) in our patient (P), five patients with bronchial asthma (A) and three bacteremic patients with *S. aureus* (S) by direct ELISA as Dreskin's method with some modifications. All samples were assayed in duplicate.

Follow-up serum IgE levels decreased with the treatment of *S. aureus* infection, but still remained high (3,180 mg/dl, 3,120 mg/dl). Immunoelectrophoresis of serum revealed no evidence of paraproteinemia. Radiographs of the abdomen and both lower extremities showed multiple soft tissue calcifications. EMG and muscle biopsy findings were compatible with inflammatory myopathy (Fig. 2). Antibodies to *S. aureus* of the IgE class were detected by direct ELISA method, as previously described, with some modifications[6] (Fig. 3). The result of a delayed hypersensitivity skin test to purified protein derivative, tetanus, diphteria, streptococcus, candidia, trichophyton

and proteus was negative. Radioallergosorbent tests to common allergens were negative except for Penicillium notatum. Bacteriologic cultures from skin abscesses were positive for *S. aureus*. Cultures from oral mucous lesion grew *Candida albicans*. The total numbers of T cells, T cell subpopulations (CD4+/CD8+) were within normal limits. The Nitroblue-Tetrazolium-test was normal. In vitro lymphocyte proliferation was normal exposure to nonspecific antigens (phytohemagglutinin, phorbol myristate acetate plus ionomycin). The polymorphonuclear leukocyte motility, assessed in a reversible Boyden chamber with fmet-leu-phe and patient's serum as chemo-attractants, as prevoiusly described[5], was impaired. She was successfully managed with surgical drainage and antibiotics.

DISCUSSION

Some diseases, including chronic granulomatous disease, Wiskott-Aldrich syndrome, icthyosis vulgaris, severe combined immunodeficiency and HIE, have similiar clinical findings of recurrent skin infections[7]. This patient was diagnosed as having HIE on the basis of recurrent infections of skin and pulmonary, extremely elevated levels of serum IgE and presence of anti-*S.aureus* specific IgE, chemotactic defect of neutrophile, eczematoid dermatitis and normal nitroblue tetrazolium test. The late onset of her recurrent infection and normal eosinophil count were atypical. But these have been observed in other reports[5]. *S.aureus* and *C. ablicans* were isolated from skin cold abscesses and oral cavity, respectively, in this case. These organisms are known to be most predominant pathogens in recurrent infections of HIE[5]. *S. aureus* infection with elevated serum IgE is rarely observed in juvenile DM, and this can be partially explained by the previous two reports. First, atopic dermatitis, which is frequently accompanied by *S. aureus*, has a higher tendency for developing juvenile DM[1]. Second, the development of calcinosis and granulocyte chemotactic defect in juvenile DM is associated with staphylococcal infections[4]. The causes of recurrent skin infections of *S. aureus* in this patient are presumed to have a somewhat different mechanism from those two. Hochreutener et al suggested that increased *S. aureus* specific IgE level, decreased *S. aureus* specific IgA level, diminished chemotaxis and soft tissue abscesses can be differential points between atopic dermatitis and HIE, but chemotactic defect and anti-*S.aureus* specific IgE were found to be not only HIE but also atopic dermatitis[8, 9]. So, sometimes, it may be hard to differentiate HIE from atopic dermatitis in a patient with juvenile DM who has elevated IgE level and *S.aureus* infection. Differential diagnosis is important because treatment and prognosis is different. Atopic dermatitis does not have recurrent infections of the sinopulmonary tracts and peculiar cold abscesses and has a dermatitis that differs in character and distribution from lesions of HIE[5]. This patient denied any history of allergy, and RAST(radioallergosorbent test) to common allergens, except for Penicillium notatum, were negative. Moore et al emphasized the relationship between the development of calcinosis and recurrent staphylococcal infections with raised IgE in juvenile DM[1]. Although the level of serum IgE in Moore's cases are elevated, most of them do not meet the definition of HIE ($\geq$2,000 IU/ml). But this patient had extremely elevated IgE level (6,600 IU/ml) during infection and had constantly raised serum IgE levels ($\geq$3,000 IU/ml) during follow-up. Anti-*S.aureus* specific IgE was detected only during *S. aureus* infection in this case. Calcinosis occurs commonly with scleroderma, as well as dermatomyositis, and rarely in association with SLE[10]. HIE has been rarely reported in patients with SLE[11-13], but these cases had no association with calcinosis. Calcinosis develops in up to half the patients with juvenile dermatomyositis[1]. It must be clarified whether recurrent skin infection with elevated IgE occurs in most juvenile DM patients with calcinosis or not. Although the immunologic basis of elevated serum IgE in patients with HIE has not been defined, a deficiency of suppressor T cell to inhibit IgE production[5], imbalances between IL-4 producing and IFN-γ producing helper T cells[14] and decreased metabolism of IgE[15] seem to be responsible for elevated levels of IgE. There were reports that $CD8^+$ to $CD4^+$ ratio was reduced in a patient with juvenile DM[16]. But this was not found in our case. The causes of susceptibility to infections have not been documented. Schopfer et al suggest that histamine is released on crosslinkng of mast cell-bound antistaphylococcal IgE by staphylococcal antigens and interferes with the activity of polymorphonuclear leukocytes, resulting in the failure of effective *S. aureus* clearing[17]. It is known that there is variability in both HIE and juvenile DM patient's neutrophil and monocyte chemotaxis[5]. Whether the neutrophils were intrinsically abnormal or not was inconclusive in a patient with HIE, but chemotactic defect of neutrophil to fmet-leu-phe and

patient's serum as chemo-attractants was observed in this case. HIE has significantly lower proportions of circulating T cells that can produce IFN-γ and TNF-α, in comparison with normal controls, which also may contribute to recurrent infections[14]. In conclusion, similar findings, including elevated serum IgE, anti-*S.aureus* IgE and chemotactic defect of neutrophil, can be found in patients with HIE, juvenile DM and atopic dermatitis. HIE must be considered in the differential diagnosis of a patient with juvenile DM who has an elevated level of IgE and staphylococcus aureus skin infection. It will be interesting to define whether the underlying mechanism is the same or not in these diseases.

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