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Letter to the Editor

A rare cause of severe superficial herpetic skin infection in a 13-month-old female patient: Autosomal recessive HIES

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Dear Editor,

Hyper Ig E syndrome (HIES) is a rare primary immunodeficiency characterised by high IgE (> 2000 IU/ml) level, eosinophilia, staphylococcus skin abscess, recurrent lung infections, eczema, scoliosis, joint deformities, pathological fractures, typical face appearance, craniosynostosis and impaired T cell function (1).

Most of the HIES cases are sporadic. HIES has two other types as autosomal dominant and autosomal recessive. Autosomal dominant HIES courses with eczema, recurrent skin abscess, pneumonia attacks with pneumatocel, recurrent bone fractures, mucocutaneous candidiasis, coarse facial appearance, high serum Ig E levels, eosinophilia and STAT3 gene mutation (2). Autosomal recessive HIES courses with recurrent severe herpes virus infections, molluscum contagiosum, eosinophilia, high serum Ig E level, recurrent pneumonia, chronic eczema and low DOCK 8 expression (3).

In this case, we aim to emphasize that autosomal recessive HIES should be kept in mind when patient is diagnosed with severe superficial herpetic skin infection.

A 13-month-old female patient referred with vesical lesion and papules around the mouth and on the distal of both extremities. The vital findings of the patient were as follows: fever was 36,3 ˚C, systolic blood pressure was 90 mmHg, heart rate was 124/min pulse, respiratory rate was 28 /min. Physical examination findings were as follows: weight was 7,8 kg (3-10 percentile), height was 73 cm (10-25 P). There were swollen, erythematous papulovesicular lesions on the right hand dorsum of bilateral perioral region (figure 1a). Other systemic examinations were normal. The patient's history revealed that she had lung infection at 7 and 12-months old and she was diagnosed with atopic eczema and food allergy at 2 months old. Her parents were second degree relatives. Her siblings were healthy. Clinical superficial herpes infection was considered in the patient. Laboratory findings were as follows: 9760/mm3 leukocyte, 10,9 g/dl haemoglobin, 547.000/mm3 thrombocyte, 25% leukocyte with polymorphic nuclei in peripheral blood smear, 50% lymphocyte, 17% eosinophile, biochemical parameters and electrolytes were within normal range. Since the skin lesions were severe, blood immunoglobulin levels were investigated. The results were as: blood Ig G level was 638 mg/dl (605-1430 mg/dl), IgA level was 53 mg/dl (30-107 mg/dl), IgM level was 63 mg/dl (60-328 mg/dl) and total IgE level was 7283 IU/ml. Autosomal recessive HIES was considered since the patient had atopic eczema, severe superficial herpetic skin infections and total Ig E level was higher than 2000 IU/ml. IV acyclovir treatment was given to patient due to severe superficial herpetic skin infections. DOCK8 expression analysed in Marmara University laboratory was found to be low. IVIG therapy was started. The patient's follow-up showed that her lesions had regressed (figure 1b).

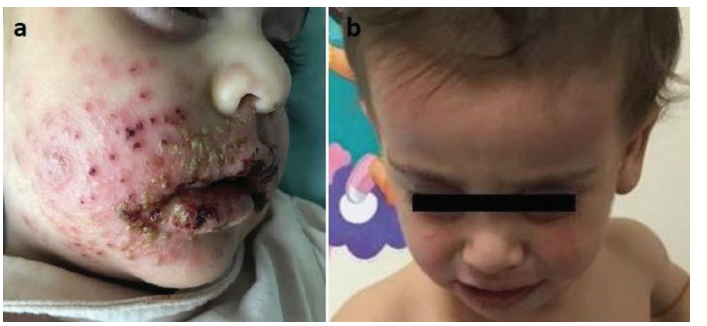

Figure 1a. The swollen, erythematous papulovesicular lesions on the perioral region. **b.**The regressed lession on the perioral region after treatment

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Hyper Ig E syndrome is a primary immunodeficiency syndrome and it can course with eczema, recurrent staphylococcal infections and pneumonia attacks, pneumatocele formation and mucocutaneous candidiasis (1,4). Non-immunological characteristics of HIES are characteristic coarse facial appearance, scoliosis, dental anomalies (delays in the exfoliation of baby teeth, malocclusion in permanent teeth), ophthalmic problems such as xanthelesma, eye lid tumours, strabismus and bone problems such as hyper extensibility in joints, bone fractures which occur with small traumas and which have a high probability of recurrence, osteoporosis and craniosynostosis (5). While HIES pathogenesis is still not clear, T and B cell function disorders, defective interferon-gamma production, impaired neutrophil chemotaxis and Th1/Th2 cytokine imbalance are considered to be responsible (6).

Most of the HIES cases are observed as sporadic and autosomal dominant and more rarely autosomal recessive inheritance. Autosomal recessive inherited HIES patients are differentiated from autosomal dominant HIES with frequent different infection types such as molluscum contagiosum and herpes virus infections, rare occurrence of pneumatocele formation when compared with autosomal dominant form and frequent comorbidity of central nervous system complications (3,4). Our case was considered to have autosomal recessive inherited HIES as pre-diagnosis.

Signal convertor and transcription activator 3 (STAT3) mutations are seen in autosomal dominant HIES and they are localized at 17q21 (3,7). In vitro immune responses of the peripheral blood cells of these patients to cytokines such as IL-6 and IL-10 are insufficient. STAT3 is a signal transmission molecule activated as a response to many cytokines, growth factors and hormones (7). DOCK8 mutation is a gene mutation which results in dendritic cell migration to lymph nodes and CD4 T cell interaction, it is localized at chromosome 4 and it is found in most of the patients with autosomal recessive HIES. In patients with DOCK8 deficiency, clinical findings are similar to that of patients with autosomal dominant HIES. Cases with DOCK8 deficiency are mostly seen in populations with a high rate of relative marriage, as in our country, and they result from high IgE level, eosinophilia, lymphopenia, severe atopic dermatitis, eczema and recurrent skin infections and being exposed to viral infections such as herpes simplex virus, molluscum contagiosum and varicella zoster, and weak CD4 + and CD8 + T cell proliferative response (8,9). Our case had symptoms of atopic eczema, vesicular papules around the mouth (herpes simplex virus infection) and recurrent lung infections in addition to low DOCK 8 expression.

Patients with HIES have normal serum Ig G, Ig M, Ig A levels and serum total complement activity. High Serum Ig E levels and peripheral eosinophile are the most frequent laboratory finding of the disease. Serum Ig E levels and total eosinophile count are higher in autosomal recessive form when compared with the other form. In early childhood, serum Ig E level is 2500 IU/ml or above (10). Our case had Ig E 7283 IU/ml and eosinophile.

As a conclusion, HIES is a primary immunodeficiency and it can show sporadic, autosomal recessive and dominant inheritance. Autosomal recessive form can appear with severe superficial viral skin infection at early period of life. Thus, autosomal recessive HIES should be kept in mind in patients who refer with severe superficial herpetic skin infection.

Competing interests: The authors declare that they have no competing interest.

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