

Case Report

HYPERIMMUNOGLOBULIN E SYNDROME (JOB'S SYNDROME) IN A-22-MONTH OLD GIRL AND IVIG TREATMENT

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ABSTRACT

Hyperimmunoglobulin E syndrome is a rare disorder characterized by pruritic dermatitis, recurrent staphylococcal skin abscesses and extremely elevated concentrations of immunoglobulin E in serum.

We report a patient who has pruritic vesiculopapules, recurrent episodes of skin abscesses on the scalp and face, and respiratory problems from the age of ten days (severe cough, wheezing, acute otitis media, pneumonia). She was diagnosed as Hyper-IgE syndrome and treated with IVIG along with antibiotics.

Key Words: Hyperimmunoglobulin E syndrome, Job's syndrome

INTRODUCTION

Hyper-IgE syndrome is a multisystem disorder characterized by recurrent skin abscesses, pneumonia, with pneumatocele formation, and elevated serum immunoglobulin (Ig) E levels. The infectious complications includes abscesses and pneumonia, most commonly caused by *S. aureus*, long-term administration of a

penicillinase-resistant penicillin is indicated, with the addition of other antibiotics as required for specific infections. IVIG should be administered to patients, especially if clinical and laboratory abnormalities persist.

Only a few reports have mentioned the initial presentation in infancy or childhood as a papulopustular or vesicular eruption (1). We describe a distinctive papulopustular eruption and skin abscesses as the initial manifestation of disease in a 22-month-old girl with hyper-IgE syndrome.

CASE REPORT

A 22-month-old girl presented with folliculitis, skin abscesses and eczematous lesions on the scalp and face since ten days of age and a three day history of coughing and high fever. She had been hospitalized twice diagnosed with pneumonia at 10 and 18 months of age. Eczematous skin lesions on the scalp and face responded to local antibiotics but never disappeared. Her family history was unremarkable.

Physical examination revealed a rectal fever of 38.8°C, pulse rate of 148 beat per minute, respiratory rate of 46 per minute. On the scalp

and face, there were papulopustular eruptions and skin abscesses (Figs. I-II) and in the perineal region there were eczematous eruptions (Fig. III). Auscultation of lungs revealed reduction in bilateral respiratory sounds, and bibasilar crepitan rales were present. There were no dental or other abnormalities.

The white blood cell count was 24000/mm³. The ratio of immature to mature neutrophils was 1/4 and 8% of the white blood cells were eosinophils in the peripheric blood smear. Iron deficiency anemia was also noted. C-reactive protein concentration was 201 mg/dL. Serum immunoglobulin E concentrations were extremely high (11330 u/ml). Serum immunoglobulin E concentrations were checked for several times, but the results were consistently high. Other immunoglobulin concentrations were within normal limits. Urinary examination, serum electrolytes, hepatic and

renal function tests were all within normal limits. *S. aureus* was identified on the cultures of the scalp pustules.

A biopsy was performed from the vesiculopapular lesions of the scalp. The histopathology of this biopsy showed superficial dermatitis with abundant eosinophils, similar to hypersensitivity reactions. Nitroblue Tetrazolium Test (NBT) and neutrophil chemotaxis tests were normal. The ratio of CD4 and CD8 lymphocytes was 1.71 in the flowcytometry of peripheral blood. HIV test was negative.

A chest radiogram revealed pneumonic infiltration in the right-middle and lower lobes and pneumatocells were present in right upper zones.

The history of eczematous dermatitis, recurrent skin abscesses and pulmonary infections with high immunoglobulin E levels were compatible

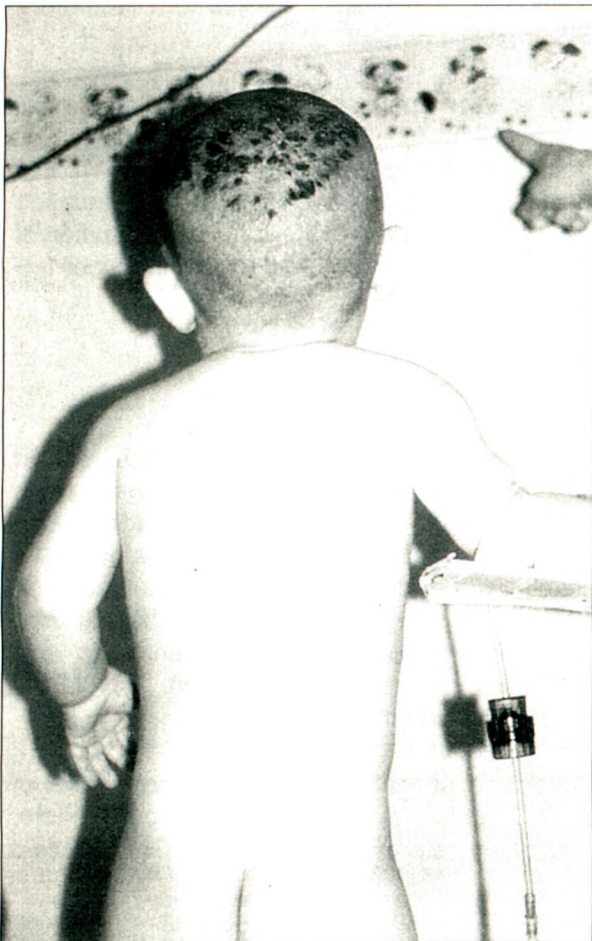


Fig. 1-2: Characteristic papulopustular eruptions and skin abscesses

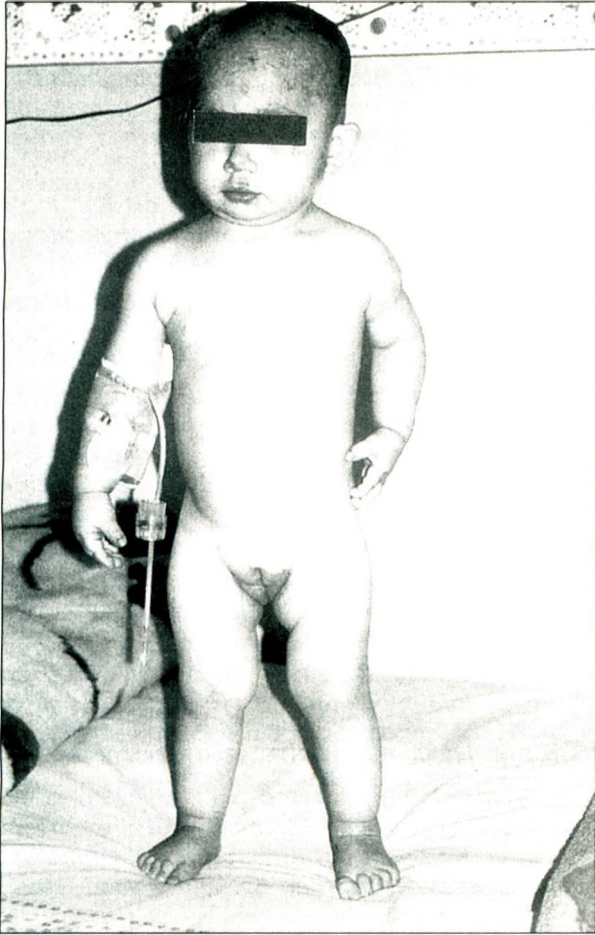


Fig.3: Eczematous eruptions on the perineum

with the diagnosis of hyperimmunoglobulin E syndrome.

After a course of vancomycin (40 mg/kg/day) and ampicillin (15 mg/kg/day) treatment, prophylaxis with ad sefalosporin and IVIG (0,4 g/kg month) was started.

Skin lesions and chest radiogram abnormalities improved. The patient is still followed by our clinic.

DISCUSSION

Davis in 1966 reported the association of infected eczematous dermatitis with sinusitis, acute pulmonary infections and recurrent 'cold' staphylococcal abscesses in two Caucasian red-haired girls and named it 'The Job's Syndrome', after biblical character Job (2). Job's syndrome, was later renamed as the Hyperimmunoglobulin

E Syndrome; a rare congenital immune-deficiency disorder.

Its characteristic findings are recurrent staphylococcal skin and pulmonary abscesses and markedly elevated levels of serum immunoglobulin E (3). Reports of over 200 cases have been published (4). There is no knowledge about the incidence of the syndrome.

Current pathogenic studies show dysregulation of TH1 and TH2 lymphocytes in favor of TH2 activation with depressed TH1 activation, leading to an imbalance in cytokine synthesis. Several reports have shown decreased interferon-gamma production by peripheral blood mononuclear cells of patients with hyperimmunoglobulin E syndrome (5,6).

A study including 30 patients with the hyperimmunoglobulin E syndrome and 70 of their relatives made by Grimbacher et al. suggested that 72% of patients had the previously unrecognized feature of failure or delay of shedding of the primary teeth owing to lack of root resorption, 57% of patients had recurrent fractures, 68% of them had hyperextensible joints and 76% of patients 16 year of age or older had scoliosis. They conclude that hyperimmunoglobulin E syndrome is a multisystem disorder that affects the dentition, the skeleton, connective tissue, and the immune system. The syndrome is inherited as a single-locus autosomal dominant trait with variable expressivity (7).

Pherwani et al. suggested in their study, including 6 cases of hyperimmunoglobulin E syndrome that 83% of patients had respiratory symptoms and 33.3% had diarrhea (8). In this study 80% of the cases were under 8 years old, and 3 cases in whom skin biopsies were done showed tissue eosinophilia. Two cases had retention of deciduous teeth. All patients in the study became symptomatic within few months after birth and 50% of the cases had normal NBT tests, as in our case had. Our case was also similar to patients reported by Pherwani.

Children with eruptions may erroneously be diagnosed as atopic dermatitis since differentiation may be difficult in this age group. In contrast to the morphology and distribution of

infantile atopic dermatitis, the initial eruption of hyper-IgE syndrome is primarily a papulopustular eruption. Although facial and scalp involvement are common in both atopic dermatitis and hyper-IgE syndrome, the skin lesions of atopic dermatitis typically have lichenification and scales, which are absent in hyper-IgE syndrome. Although axillae, anterior neck, groin perineum and trunk are not involved in atopic dermatitis, examatous eruptions were observed in these regions in our patient (1).

Wiskott-Aldrich syndrome is characterized by thrombocytopenia, draining ears and eczema. Usually children have splenomegaly, hepatomegaly and cervical lymphadenopathy. Serum IgA and IgE levels are elevated (9), but in our patient platelet count was normal so we moved away from this diagnosis.

Although treatment consists of antibiotic and profilactic therapy, some authors recommend IVIG treatment, added to this therapy especially if the clinical and laboratory abnormalities persist.

Waldfahrer et al. treated a 29-year-old woman with hyperimmunoglobulin E syndrome by intravenous immunoglobulin therapy and they showed that the symptoms markedly improved (10). Bilora et al. also treated a 38-year-old woman with hyperimmunoglobulin E syndrome and staphylococcal pneumonia by moderate-dose intravenous immunoglobulin therapy. They suggested that a moderate-dose intravenous immunoglobulin therapy resolved the clinical-radiological signs of the *S. aureus* bronchopneumonia and improved cytologic and biohumoral parameters (11). Gennery et al. reported a severely affected patient in whom successful bone marrow transplantation was followed by reappearance of the immunodeficiency. They concluded that bone marrow transplantation was not able to cure the immunological features of the hyperimmunoglobulin E syndrome (12).

Compatible with these authors, we have observed in our case that moderate-dose IVIG therapy is effective and useful in patients with hyper IgE syndrome.

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