An unusual association of hyper-IgE syndrome with celiac disease: A case report

Abstract

Hyper-IgE syndrome (HIES) is a primary immunodeficiency disorder characterized by eczema, cold abscesses, pneumonia, eosinophilia, and a very high serum IgE concentration. An association with celiac disease is rare. Immunodeficiency and autoimmunity are two manifestations of immune system dysfunction that can be associated with common pathophysiological links. We present the case of a 3-year-old child with psychomotor retardation and a history of recurrent infections who had generalized eczema, failure to thrive, and abdominal distension with hepatosplenomegaly. The patient improved after receiving a monthly intravenous immunoglobulin infusion and a gluten-free diet.

Key words: hyperIgE syndrome, celiac disease, immune deficiency, infection.

Introduction

The hyperIgE syndrome, or Job's syndrome, was first described in 1966 by Davis (1). It is characterized by the association of severe and recurrent infections of the skin (cold abscesses) and the sinopulmonary tract (primarily staphylococcal), as well as chronic eczematous dermatitis. This clinical triad is associated with biological signs such as hyperimmunoglobulinemia E (>2000 IU/mL) with normal serum levels of other immunoglobulins and moderate eosinophilia [2, 3].

In this study, we present a rare case of a child with hyperIgE syndrome and celiac disease.

Case Observation

A 3-year-old female patient, of non-consanguineous parents, with a history of neonatal eczema that appeared at 7 days of age and repeated infections (post-vaccination thigh abscess and sub-lingual abscess at the age of 2 months; 2 episodes of pneumopathy requiring intravenous antibiotic therapy occurring at the ages of 5 months and 7 months, respectively; and chronic glairy diarrhea). admitted for respiratory distress and in whom clinical examination reveals a child with a dysmorphic face (forehead prominence, hypertelorism, increased interalar distance), a failure to thrive at a weight of 10 kg (-2DS) and a height of 80 cm (-3DS). She was malnourished with spindly limbs, polypneic at 50 cycles/min, pale, febrile at 38°C, with generalized eczema, and hepatosplenomegaly. (figures 1-2).

A chest X-ray was normal (Figure 2).

A complete blood count (CBC) revealed a hypereosinophilia of 1900 elements/mm3, bicytopenia with hypochromic microcytic anemia (hemoglobin 6.1 g/dl, MCV 66.2 m3, MCHC 31.2 g/dl), and thrombocytopenia of 80,000 elements/mm3.
CRP was 23.2 mg/L, with ferritin at 8 mg/L. The IgA and IgE levels were 4.4 U/ml and 7407 U/ml, respectively. The bone marrow aspiration was normal.

Viral serologies were performed showing cytomegalovirus (CMV) infection with positive IgM and IgG antibodies and PCR. Anti-transglutaminase IgA antibodies were positive at 38 U/mL. An esophagogastroduodenoscopy was performed with a jejunal biopsy revealing stage IIIa villous atrophy.
Abdominal ultrasound revealed homogeneous hepatomegaly of 11 cm and splenomegaly of 9.5 cm. The echocardiography was normal.

A blood transfusion was administered, as well as ganciclovir IV, a gluten-free diet, and cotrimoxazole prophylaxis. The appearance of a pre-septal orbital cellulitis of the left eye with sinusitis marked the progression (Figure 3). The child was given amoxicillin and clavulanic acid IV for 10 days and responded well to treatment.

This child's clinical condition improved significantly after receiving a monthly intravenous infusion of immunoglobulin.

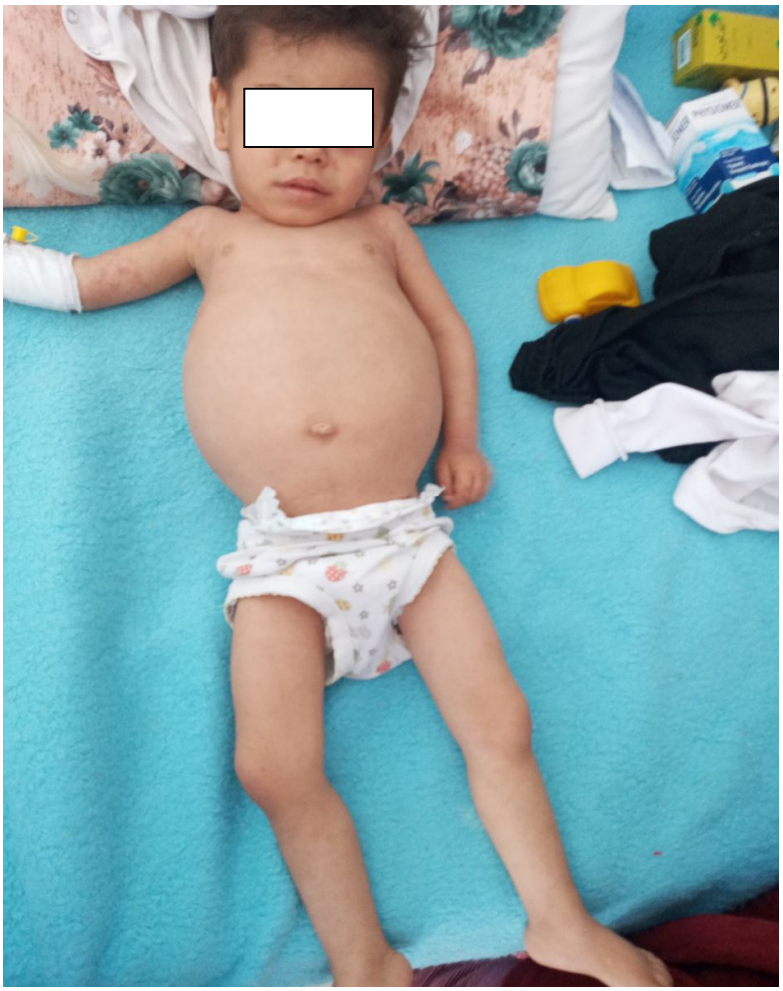

Figure 1: Image of the child with hyperIgE syndrome

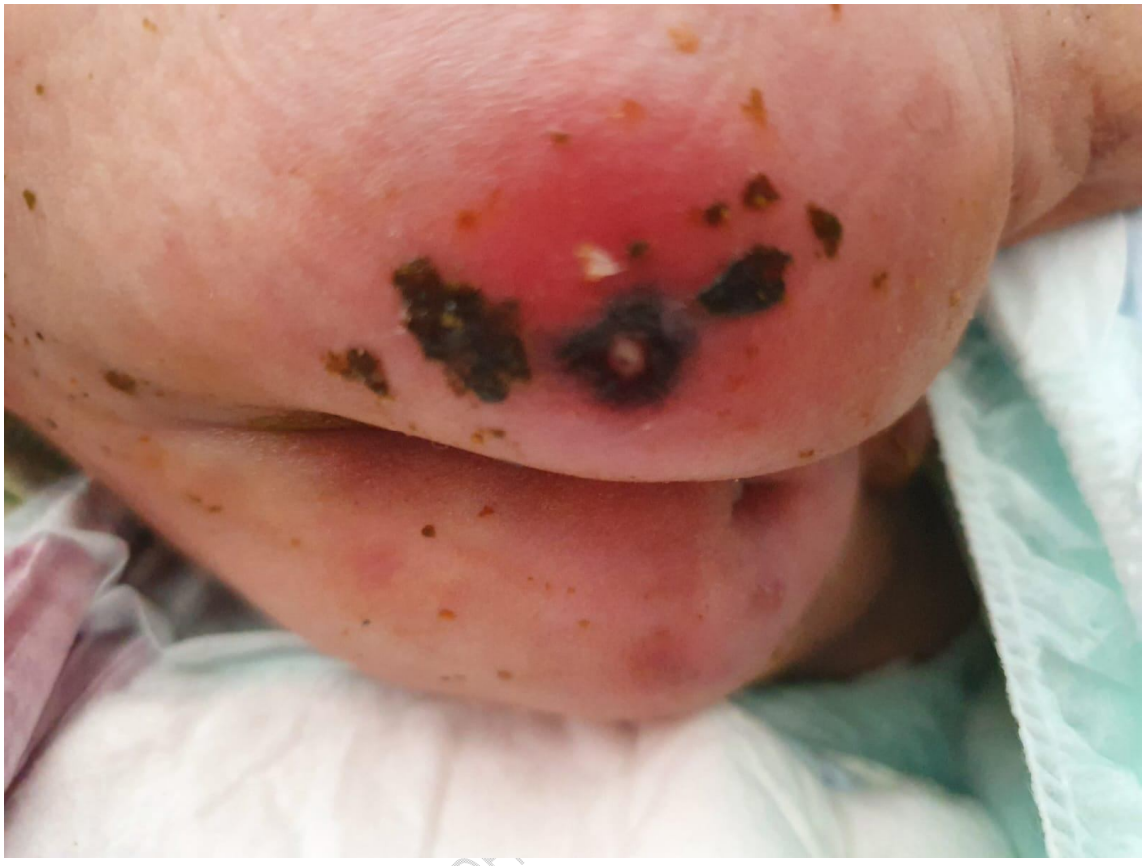

Figure 2: Image of a gluteal abscess

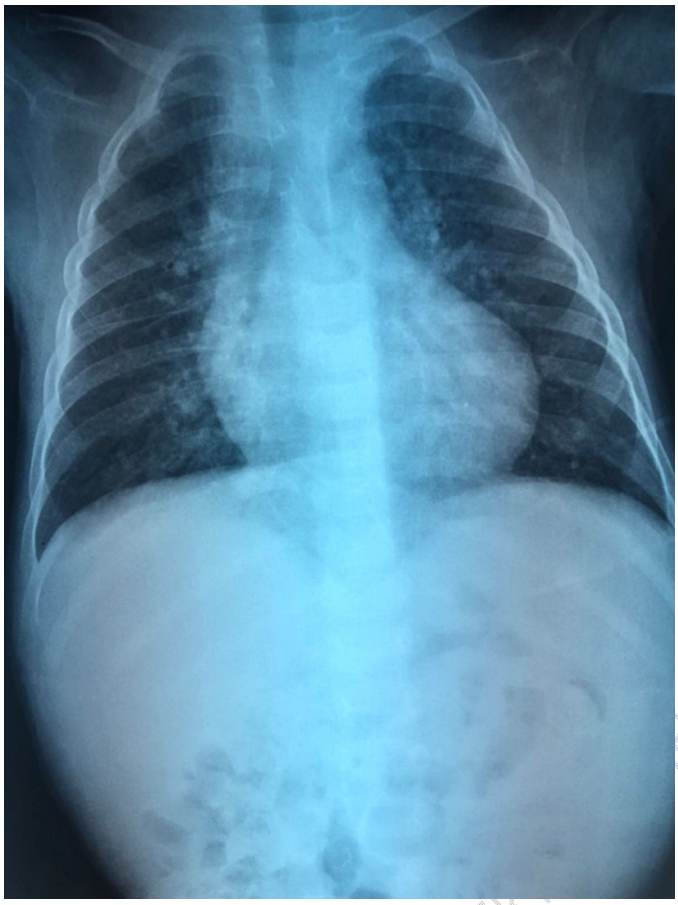

Figure 3 : Chest X-ray of the child

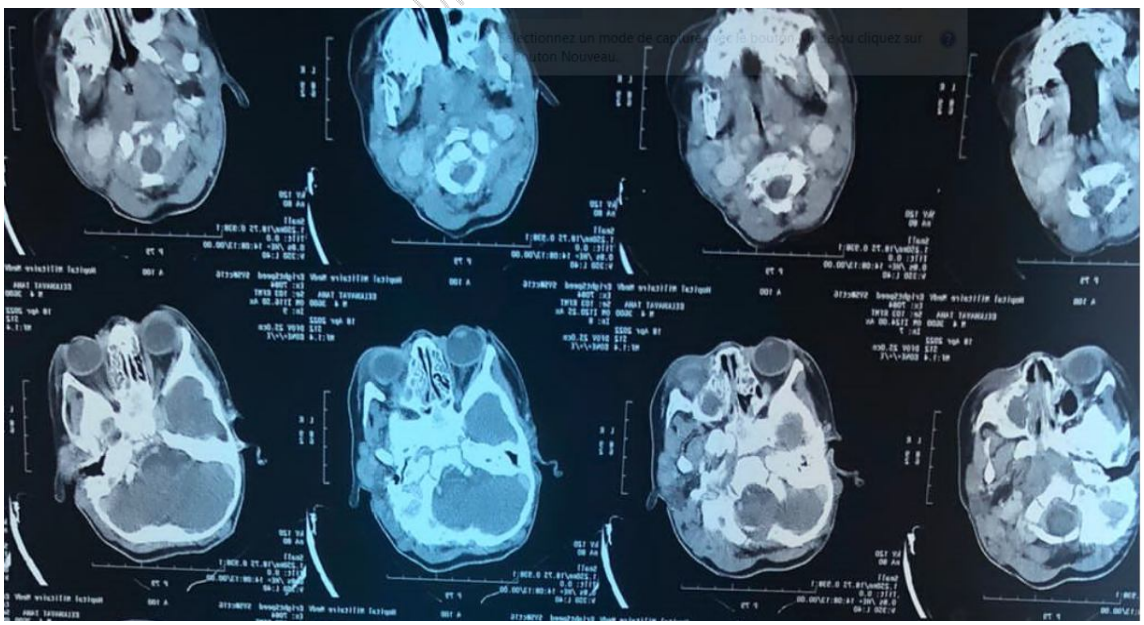

Figure 4: Cerebral-orbital CT scan with contrast injection showing pre-septal orbital cellulitis with sinusitis.

Discussion:

HyperIgE syndrome is a rare primary immunodeficiency disorder with an incidence of around 1/1,000,000 annually. Although it was first observed in females, the syndrome affects males and females equally, regardless of ethnicity. Familial character has been rarely described [2, 3]. The first symptoms appear during the first weeks of life, but they can appear later in adolescence or adulthood [4, 5]. This syndrome has specific clinical features:

Morphologically, the manifestations are mainly facial with facial asymmetry, hemihypertrophy, increased interalar distance, and a prominent forehead [6-8], as reported in our case. They develop early in childhood.

HIES is distinguished from many other primary immunodeficiencies by the presence of extra-immunological features, including osteopenia, hyperextensibility, scoliosis, degenerative joint disease, and vascular anomalies such as stenosis and aneurysm formation.

Dermatologically, this syndrome typically manifests in the newborn with a rash during the first few weeks of life. This pustular rash on the face and scalp could be caused by neonatal acne or eosinophilic dermatitis [9, 10].

Recurrent staphylococcal skin boils and bacterial pneumonia are most common in childhood.

Pneumatoceles and bronchiectasis are common complications of aberrant healing of pneumonia, and they are major causes of morbidity and mortality.

The bacterial species involved are Staphylococcus aureus in 60% of cases, Hemophilus influenzae in 10% of cases, and, rarely, Streptoccoccus pneumoniae, Cryptococcus neoformans, Aspergillus fumigatus, and chronic candidal infections, mainly related to Candida albicans, both in the skin and in the oropharynx, are also frequently reported in this syndrome [11, 12].

Biologically, there is hyperimmunoglobulinemia E (>2000 IU/mL) associated with normal serum levels of other immunoglobulins and moderate eosinophilia.

The majority of cases are sporadic; however, two types of HIES have been reported: the autosomal dominant form (AD-HIES) and the autosomal recessive form (AR-HIES).

Autosomal dominant hyper-IgE syndrome (AD-HIES) is characterized by eczema, recurrent skin and lung infections, elevated serum IgE, and various connective tissue, skeletal, and vascular abnormalities, and is caused by mutation of the signal transducer and activator of transcription 3 (STAT3) gene (13,14).

A distinct syndrome known as autosomal recessive HIES (AR-HIES) due to mutations in DOCK8 manifests as severe eczema, recurrent bacterial skin infections with particular susceptibility to viral infections by herpes simplex, herpes zoster, and Molluscum contagiosum associated with autoimmunity and allergic manifestations (14).

In contrast to STAT3-deficient HIES, AR-HIES lacks connective tissue and skeletal manifestations, but has increased neurological abnormalities (15).

In our patient's case, we can say that it is a recessive type due to the absence of a similar case in the family, the presence of allergic manifestations such as eczema, and the association with an autoimmune disease such as celiac disease. However, due to a lack of funds, the genetic study could not be carried out (16,17).

Celiac disease is a chronic enteropathy with villous atrophy secondary to an inappropriate immune response of the intestinal mucosa to gliadin from wheat, barley, and rye in genetically predisposed individuals (HLA DQ2 and/or DQ8 haplotypes). It may be associated with other autoimmune diseases, including type 1 diabetes and autoimmune thyroiditis.

Our patient's celiac disease diagnosis was maintained due to the presence of IgA-type anti-transglutaminase antibodies at a level less than 10 times normal in conjunction with stage IIIa villous atrophy. However, celiac disease was linked to an immune deficit called "job buckley syndrome" rather than an autoimmune disease in this case (18-20).

Conclusion:

The described case demonstrates the distinct clinical features of hyperimmunoglobulinemia E syndrome, which are early diagnostic features of this syndrome. His association is still uncommon.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard, parental written consent has been collected and preserved by the author(s).

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