An unusual association of hyperIgE syndrome with celiac disease: A case report

Abstract

Hyper IgE syndrome is a primary immune deficiency characterized by eczema, cold abscesses, lung infections, eosinophilia and very high serum IgE concentration. Its association with celiac disease is rare. We report the case of a 3-year-old child with psychomotor retardation and a history of recurrent infections, in whom the clinical examination revealed generalized eczema, delayed growth and weight, abdominal distension with hepatomegaly and splenomegaly. The patient was put on a monthly intravenous immunoglobulin infusion and a gluten-free diet with marked improvement. Immune deficiency and autoimmunity are two manifestations of immune system dysfunction that may be associated, with common pathophysiological links.

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

Introduction

The hyperIgE syndrome or job buckley 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 (mainly staphylococcal), a chronic eczematous dermatosis. This clinical triad is associated with biological signs: hyperimmunoglobulinemia E (>2000 IU/mL) associated with normal serum levels of other immunoglobulins and moderate eosinophilia [2, 3].

In our study we report a rare case of a child with hyperIgE syndrome and celiac disease.

Case Observation

3 year old child, 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 age of 5 months and 7 months respectively) and chronic glairy diarrhea.Admitted for respiratory distress, and in whom the clinical examination finds a child with a dysmorphic face (prominent forehead, hypertelorism, flattening of the base of the nose), a staturo-ponderal delay with a weight at 10 kg (-2DS) and height at 80 cm (-3DS),She was malnourished with spindly limbs, polypneic at 50 cycles/min, pale, febrile at 38°c, with generalized eczema with abdominal distension and hepatosplenomegaly (figures 1-2).

Chest X-ray showed a left paracardiac opacity (Figure 2).

the NFS had shown a hypereosinophilia at 1900 elements /mm3 and a bicytopenia with a microcytic hypochromic anemia (hemoglobin 6.1g/dl, VGM 66.2 µm3 , CCMH 31.2 g/dl) and a thrombocytopenia at 80,000 elements /mm3 .

CRP was 23.2 mg/L with ferritin at 8 mg/L. The IgA assay was 4.4 U/ml and the IgE assay was 7407 U/ml. The medullogram 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 oesogastroduodenal fibroscopy was performed with jejunal biopsy showing stage IIIa villous atrophy.

Abdominal ultrasound showed homogeneous hepatomegaly of 11 cm and splenomegaly of 9.5 cm . Echocardiography of the heart was normal.

The child was transfused with packed red blood cells, treated intravenously with ganciclovir, and given a gluten-free diet and cotrimoxazole prophylaxis. The evolution was marked by the appearance of a pre-septal orbital cellulitis of the left eye with sinusitis (Figure 3), the child was put on protected amoxicillin IV for 10 days with a good response to treatment.

A monthly intravenous infusion of immunoglobulin was performed in this child with a marked clinical improvement.

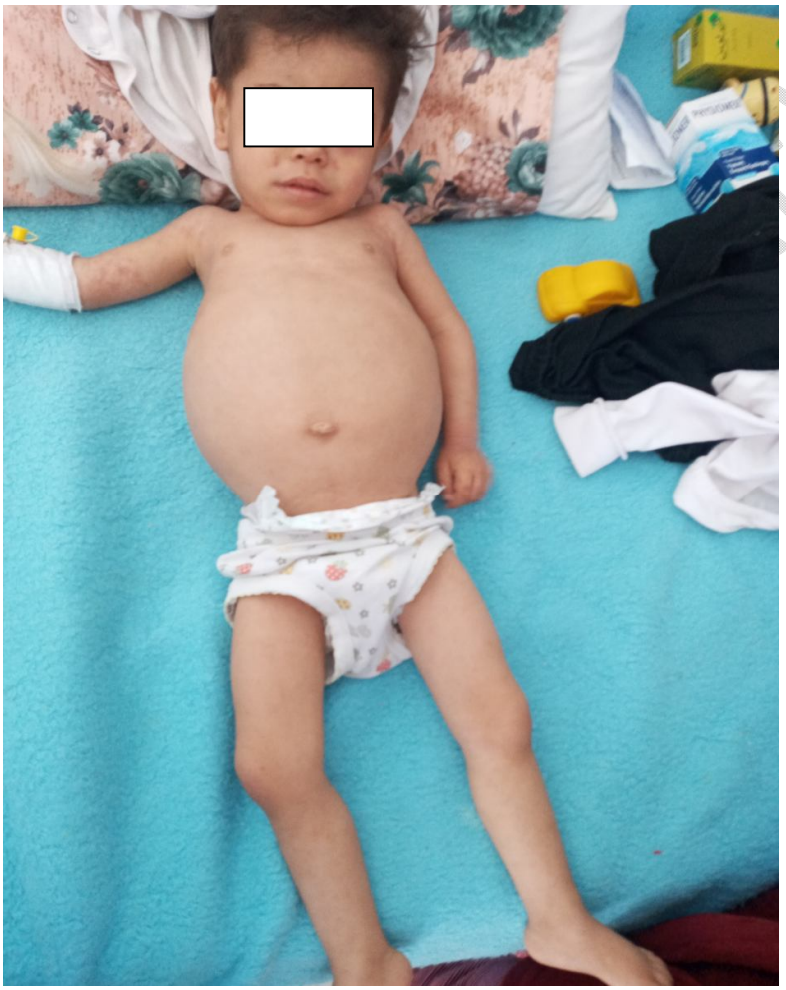

Figure 1: Image of the child with hyperIgE syndrome

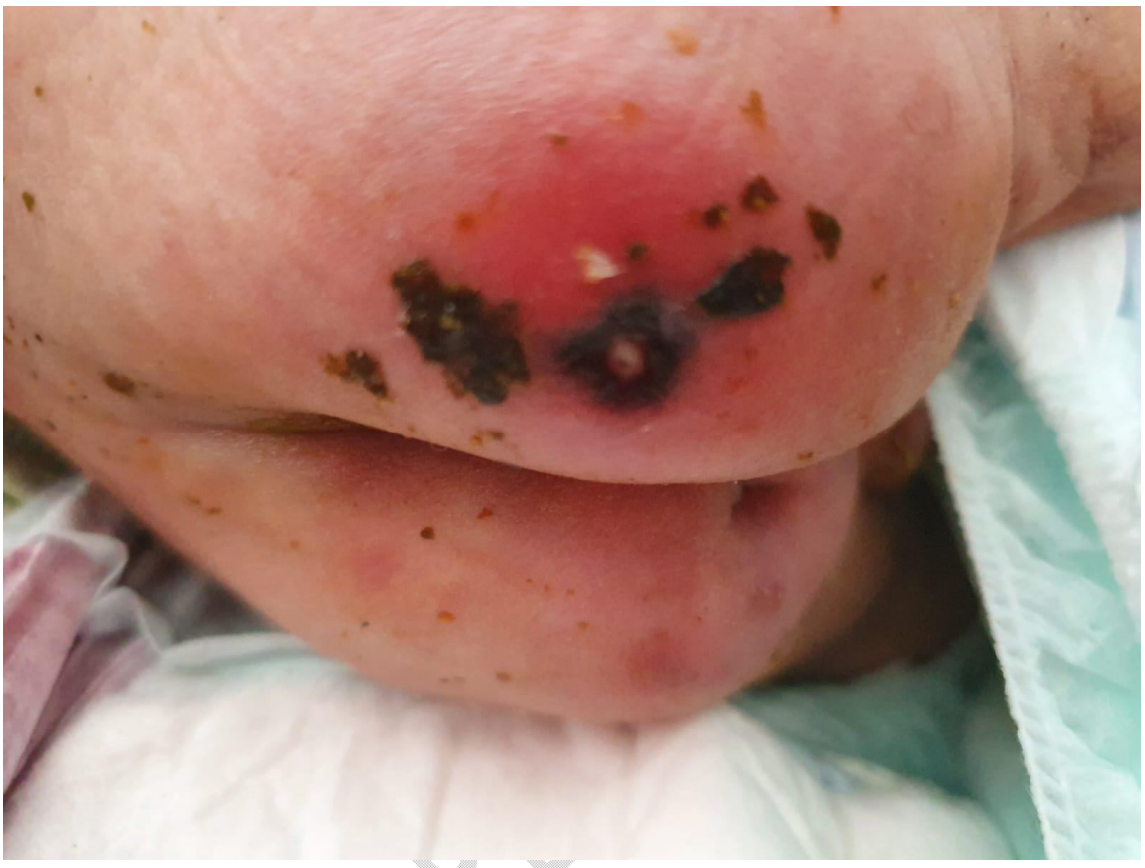

Figure 2: Image of a gluteal abscess

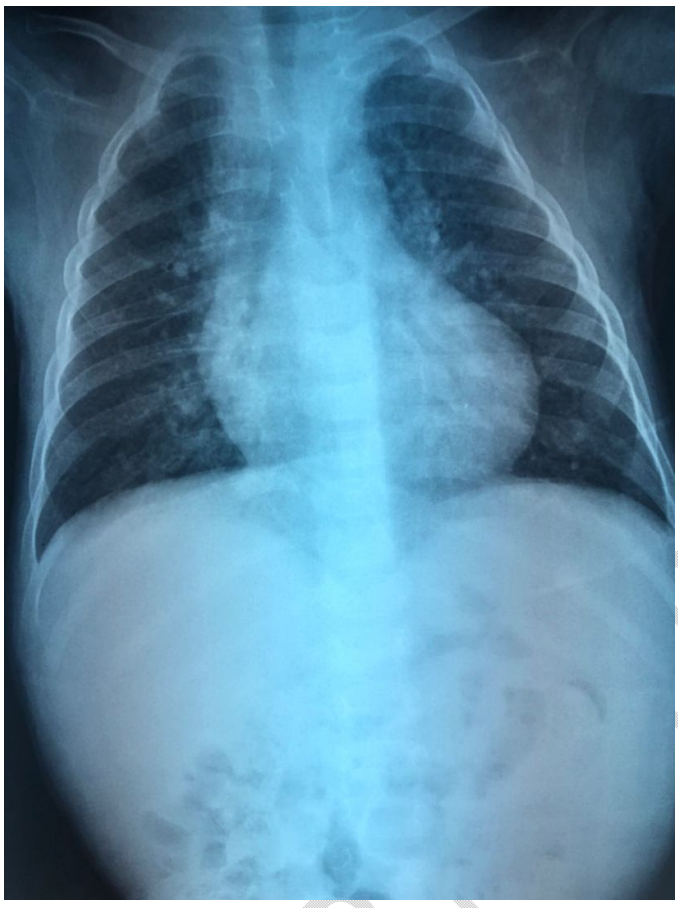

Figure 3 : Chest X-ray showing a left paracardiac opacity

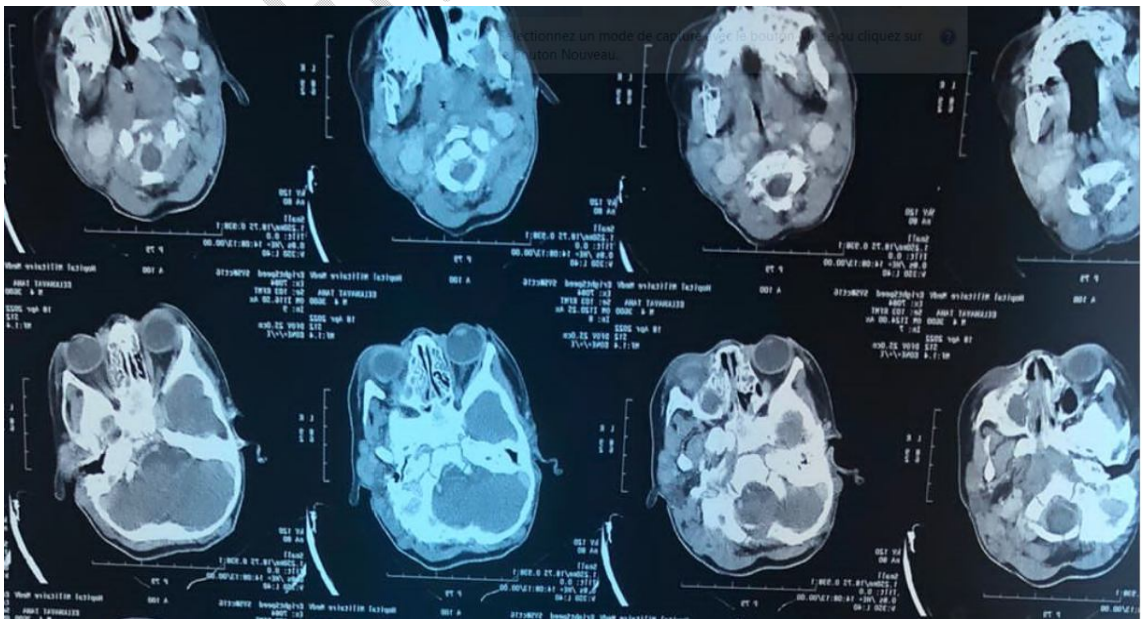

Figure 4: Cerebral-orbital CT scan with contrast injection showing pre-septal orbital cellulitis with sinusitis.

Discussion:

Initially described in females, both sexes are affected, without ethnic factors. Familial character has been rarely described [2, 3]. The first symptoms appear during the first weeks of life but may be delayed during adolescence or adulthood [4, 5].

This syndrome has specific clinical features.

Morphologically, the manifestations are mainly facial with facial asymmetry, hemihypertrophy, flattening of the base of the nose, 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 its many extra-immunological features such as osteopenia, hyperextensibility, scoliosis and degenerative joint disease, and vascular anomalies such as stenosis and aneurysm formation.

Dermatologically, this syndrome usually presents in the first few weeks of life with a rash in the newborn. This pustular rash is located on the face and scalp, suggesting neonatal acne or eosinophilic dermatitis [9, 10].

Recurrent staphylococcal skin boils and bacterial pneumonia usually occur in the early years of life.

Pneumatoceles and bronchiectasis often result from aberrant healing of pneumonia, which 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 occur sporadically; however, two types of HIES, the autosomal dominant form (AD-HIES) and the autosomal recessive form (AR-HIES), have also been reported.

- 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.

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

In the case of our patient, we can suggest that it is a recessive type since there is no similar case in the family, and in front of the presence of allergic manifestations such as eczema as well as the association with an autoimmune disease such as celiac disease. However, the genetic study could not be carried out due to lack of means (15,16).

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.

The diagnosis of celiac disease was retained in our patient due to the positivity of IgA-type anti-transglutaminase antibodies at a level of less than 10 times normal with stage IIIa villous atrophy. However, in our patient, celiac disease was associated with an immune deficit "job buckley syndrome" rather than an autoimmune disease (17,18).

Conclusion:

The reported case shows the specific clinical features of hyperimmunoglobulinemia E syndrome which are early diagnostic features of this syndrome.

The coexistence of celiac disease and hyperIgE syndrome remains rare.

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