

Coexistence of Hyper-IgE syndromes and Celiac Disease: a case report

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Abstract

A case of a 5 and a half year old male is described whose clinical and laboratory features included characteristic facial appearance, eczema, recurrent pneumonia and consistently increased serum IgE levels,. These are recognized as the main features of the hyper IgE syndrome. Apart from these features the patient has distended abdomen and hepatomegaly and splenomegaly. Laboratory studies revealed positive serum anti-endomysium and tissue transglutaminase antibodies. Small intestinal biopsy showed subtotal villous atrophy compatible with gluten-sensitive enteropathy. In conclusion we suggest that this case is the first with co-existence of hyper IgE syndrome and celiac disease.

INTRODUCTION

Hyperimmunoglobulin E syndrome (HIES) is a primary immune deficiency characterized by a high level of serum immunoglobulin E, chronic eczema, recurrent staphylococcal infections, pneumatocele, malfunctioning neutrophil chemotaxis and abnormalities in T-cell function. Abnormal neutrophil chemotaxis due to decreased production of interferon gamma (IFN- γ) is believed to be the underlying mechanism of the disease. Peripheral eosinophilia is also a common finding (1).

There are no clinical tools for diagnosis and definitive laboratory investigation. The diagnosis is based on clinical signs, elevated serum IgE levels and eosinophilia. Most patients with HIES are sporadic. However, there have been reports of autosomal dominant and recessive mode of inheritance. Although the gene for HIES has been mapped to chromosome 4, neither the fundamental host defect nor the defective gene has yet been identified (2).

Celiac disease (CD), is an immune mediated enteropathy that occurs in genetically susceptible individuals following the ingestion of gluten-containing storage proteins of wheat, barley and rye. CD is a complex genetic disease with multiple contributing genes. We suggest that this case is the first with co-existence of hyper IgE syndrome and celiac disease.

CLINICAL REPORT

A five and a half year old male patient presented at our

polyclinic with complaints of a cough, high temperature and shortness of breath. The patient was admitted to the clinic with an initial diagnosis of pneumonia. The patient history showed that at the age of eighteen months a children hospital had diagnosed HIES. One year previously at a university pediatric gastroenterology department, he had been diagnosed with CD from intestinal biopsy findings and positive anti-endomysial antibody (EMA) and tissue transglutaminase (t-TG) antibody and from liver biopsy results a diagnosis of cirrhosis of the liver. As a prophylactic he had been taking fluconazole, trimethoprim-sulphamethoxazole and ursodeoxycholic acid. Family history disclosed that the patient's parents were first cousins and his 10-year old brother had been diagnosed with celiac disease.

The patient's height was 99cm (3 -10 percentile) and weight 17kg (25 percentile). On physical examination his general condition was average, he was fully conscious, his face slightly puffy, dry skin and common eczematoid rashes. Examination of the respiratory system revealed fine rales in the lower right zone, the abdomen was distended, the liver and spleen 3cm palpable. Widespread decay and malocclusion were determined in the teeth (Figure 1 and 2).

Figure 1

Figure 1. 5.5 year-old HIES patient. A, Stereotypic facies include prominent forehead, broadened nasal bridge and atopic eczema like dermatitis. B, Widespread decay and malocclusion were determined in the teeth



The laboratory findings were determined as, eosinophil: 8.7%, IgA: 547 mg/dl (normal for the age), IgE: 14100 IU/ml (Normal: < 120 IU/ml), AST: 101 IU/l (normal 0–50 IU/l), ALT: 72.1 IU/l (normal 0–40 IU/l). All the other biochemical investigations were within the normal limits. The nitroblue tetrazolium test (-) and flow cytometric lymphocyte subpopulation analysis were normal. The thoracic computed tomography showed bilateral widespread bronchiectasis and consolidation in the right inferior lobe.

DISCUSSION

There have been reports of patients with hyperimmunoglobulin E syndrome together with different diseases (3,4). However, to the best of our knowledge there have been no reported cases to date of HIES together with a gastrointestinal system related pathology, particularly celiac disease.

In recent studies it has been determined that in celiac disease IgA antiactin antibodies (IgA-AAA) are circulating autoantibodies directed toward the intracellular cytoskeleton actin filaments. Moreover several immune factors play a role in celiac disease (5).

Grose et al. (6) investigated whether a deficiency in number and function of invariant natural killer cells (which produce IL-4 and interferon- γ , and hence suppress the T-helper-1 response) was present in celiac disease. Several immune defects are found in hyperimmunoglobulin E syndrome (7). These immune defects may be seen because of the 2 diseases together.

The genetics of these 2 diseases have to date not been fully explained. It has been reported that HIES has a relationship

with chromosome 4 and it is known that in the pathogenesis of celiac disease HLA genes play an important role (8). To define the gene areas apart from HLA which appear to play a role in CD research was carried out on chromosomes 3, 5, 6, 7, 11, 13, 15 and 22 and a relationship was found between gene areas and the disease (9). A recent study by Van Heel et al. (10) reported a relationship between chromosome 4 and celiac disease. As the genetics have not been fully explained, there may be a genetic relationship between these two diseases. The parents of our patient are first cousins and his brother has been diagnosed with celiac disease. This information indicates that genetic factors may play an important role in our case. It may be that there is a genetic relationship between the two diseases.

In conclusion HIES is a rarely seen primary immunodeficiency disease whose exact pathogenesis is not fully known. To the best of our knowledge, this is the first case report of celiac disease in a patient with hyper IgE syndrome. It is thought that being the first case as such in literature, this case can make a contribution to the understanding of the etiopathogenesis of these two diseases.

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