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Case Report

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Emesis, terrors and multiple autoimmune syndrome: Coincidence or novel association?

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Abstract

We report a rare combination of coeliac disease, type 1 diabetes, eosinophilic esophagitis, alopecia areata, multiple food allergies, asthma, and atopy, that initially presented with recurrent episodes of vomiting and night terrors. This case demonstrates that atypical symptoms may be the first link to an autoimmune or inflammatory disease, especially if combined with a family history of autoimmunity. Continued research and an interdisciplinary approach are required to evaluate the genetic association between common autoimmune and inflammatory diseases.

Keywords: Night terrors; Coeliac disease; Diabetes; Alopecia areata; Eosinophilic esophagitis; Children.

Abbreviations: AA: Alopecia areata; CD: Coeliac disease; EoE: Eosinophilic esophagitis; GERD: Gastroesophageal reflux disease; GFD: Gluten-free diet; HbA1c: Hemoglobin A1c; HLA: Human leukocyte antigen; MRI: Magnetic resonance imaging; T1D: Type 1 diabetes.

Introduction

Sleep disorders have been associated with several chronic diseases, including gastrointestinal causes. Apart from gastroesophageal reflux (which remains a major cause of interrupted sleep), Coeliac Disease (CD) more recently has been linked with a spectrum of sleep disorders [1,2].

On the other hand, it is known that CD often coexists with Type 1 Diabetes (T1D), sharing common Human Leukocyte Antigen (HLA) variations [3]. In addition, Alopecia Areata (AA) is associated with various inflammatory and autoimmune diseases, including atopy or asthma and coeliac disease or T1D (4).

We report a case of multiple inflammatory and autoimmune diseases (a combination of CD, T1D, Eosinophilic Esophagitis (EoE), alopecia areata, multiple food allergies, asthma and atopy) in a pediatric patient, which initially presented with night terrors and emesis.

Case presentation

A 7-year-old male was admitted with recurrent episodes of vomiting and night terrors for the previous 12 months. The patient was an extreme preterm neonate, with a history of multiple food allergies, atopy, allergic rhinitis, asthma, and constipation. In addition, his past medical history was, also, indicative of Gastroesophageal Reflux Disease (GERD) in infancy and his family history was indicative for asthma, allergic rhinitis, and atopic dermatitis.

On admission, physical examination was unremarkable, apart from alopecia. However, due to concern for intracranial hypertension and idiopathic occipital lobe epilepsy, he underwent further investigation with fundoscopy, electroencephalogram and brain Magnetic Resonance Imaging (MRI). The only finding was mild cerebral atrophy on MRI, without clinical significance.

Laboratory tests revealed moderate eosinophilia (1,790/μl) and increased tissue transglutaminase IgA antibodies (>88.1 ug/g), that were indicative of coeliac disease. Further investigation with upper endoscopy showed erosive esophagitis and erythematous gastric mucosa, while coeliac disease (Marsh 3) was confirmed by microscopic evaluation. Pathology report was also indicative for eosinophilic esophagitis (esophageal eosinophil count of 20 per high-powered microscopic field).

During further history taking, the patient's mother reported that the child had polyuria, excessive thirst and 2 episodes of nocturnal enuresis. Laboratory tests set the diagnosis of diabetes mellitus type 1: Blood glucose levels over 200 mg/dl, hemoglobin A1C (HbA1C): 8.0% (normal for age <7.5%), insulin levels (2.79 mIU/L, normal: 2.6-24.9 uIU/ml) and c-peptide (0.73 ng/ml, normal 0.5-2.7 ng/ml). In addition, HLA typing showed positivity for HLA-DR3-DQ2 (DRB1*03-DQA1*05:01-DQB1*02) and HLA-DR4-DQ8 (DRB1*04-DQA1*03:01-DQB1*03:02) which are observed in T1D and coeliac disease patients [5].

The child started Gluten-Free Diet (GFD) and insulin therapy for coeliac disease and T1D accordingly. In the last follow-up (one year later), the patient remains asymptomatic, planning for a new upper endoscopy and biopsy, to evaluate the esophageal eosinophilic concentration and intestinal response to GFD.

Discussion

This case represents a rare combination of coeliac disease, T1D, EoE, AA, multiple FA, asthma, and atopy. Recent studies tried to evaluate the correlation between coeliac disease and sleep quality [1,2]. More specifically, data from case-control and cohort studies indicate that sleep disorders are common in untreated patients with coeliac disease. In addition, coeliac disease has been associated with other autoimmune and idiopathic disorders, such as AA, T1D, EoE, asthma, FA, and atopy [3,6,7].

Furthermore, AA has been related to other autoimmune conditions, including coeliac disease, T1D, atopy and allergies [4,8-10]. There are numerous data showing the coexistence of coeliac disease and T1D [3,11,12]. Predisposition to both diseases is due to the presence of common HLA class II alleles, with HLA-DR3-DQ2 and HLA-DR4-DQ8 haplotypes being considered the strongest genetic risk factors for T1D and coeliac disease. Our patient, who carries both HLA-DQ2/DQ8, has been reported to be associated with increased risk for coexistence of both diseases [3]. There are also previous data describing the association between EoE and coeliac disease in children [13,14]. This coexistence was first described in 2007 by *Verzegnassi et al*, that assumed the presence of a generalized defect of the immune regulatory system [13]. According to limited data, pediatric patients with EoE might have a positive response to a GFD, combined with a proton-pump inhibitor.

Finally, it is worth mentioning that gluten ataxia is a condition described in adult patients with gluten sensitivity. In a large cohort, the prevalence of antigliadin antibodies was significantly increased in patients with ataxia and 79% of them had cerebellar atrophy in brain MRI [14]. However, our patient had no symptoms related to ataxia, but he is under regular follow-up for the possible appearance of neurological symptoms.

Conclusion

In conclusion, atypical symptoms may be the first link to an autoimmune or inflammatory disease, especially if they are combined with a family history indicative of autoimmunity. Continued research and an interdisciplinary approach are required, in order to evaluate the genetic association between common autoimmune and inflammatory diseases.

Declarations

Conflicting interests: Authors declare no conflict of interest.

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