

Transient Coeliac Disease Specific Antibodies in Systemic Lupus Erythematosus: Case Report

Mihaela Spârchez^{1,*}, Alexandru Pîrvan^{1,2}, Nicolae Miu¹, Gabriel Samasca^{2,3}, Bianca Simionescu^{1,2}, Simona Rednic⁴

¹2nd Department of Pediatrics, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

²2nd Pediatric Clinic, Emergency Clinical Hospital for Children, Cluj-Napoca, Romania

³Department of Immunology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

⁴Department of Rheumatology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

*Corresponding author: spirchez.mihaela@umfcluj.ro

Received February 09, 2015; Revised February 10, 2015; Accepted February 12, 2015

Abstract The prevalence of coeliac disease (CD) in systemic lupus erythematosus (SLE) is unclear since evidence of this co-association is scarce. Furthermore, CD-specific antibodies have been described in patients with SLE without biopsy-confirmed CD. Here we describe the diagnostic challenges of CD in a patient suffering from SLE and secondary antiphospholipid syndrome, with transient positive serum levels of CD-specific antibodies, with an increased genetic risk for CD, demonstrated by HLA-DQ2 positivity. Guidance is still needed for the CD diagnosis in some atypical conditions.

Keywords: systemic lupus erythematosus, children, anti-tissue transglutaminase antibodies, antiendomysial antibodies

Cite This Article: Mihaela Spârchez, Alexandru Pîrvan, Nicolae Miu, Gabriel Samasca, Bianca Simionescu, and Simona Rednic, "Transient Coeliac Disease Specific Antibodies in Systemic Lupus Erythematosus: Case Report." *International Journal of Celiac Disease*, vol. 3, no. 1 (2015): 37-39. doi: 10.12691/ijcd-3-1-9.

1. Introduction

The association between coeliac disease (CD) and a wide spectrum of autoimmune diseases (AID) such as type 1 diabetes mellitus [1,2], autoimmune thyroid disease [3], juvenile idiopathic arthritis [4] or autoimmune liver disease [5] has been well documented in the medical literature before. The appearance of CD-specific antibodies has also been described in patients with other AID, like systemic lupus erythematosus (SLE), with much lower prevalence and controversial clinical relevance, since not all of them were diagnosed as coeliac following intestinal biopsy [6,7].

2. Case presentation

This boy was first referred to our Pediatric Clinic for evaluation at the age of 12 years old with a two years history of intermittent fever and right ankle arthritis, persistent anaemia, hepatosplenomegaly, one episode of pleural effusion accompanied by pericarditis with cardiac tamponade with emergency subxiphoid percutaneous drainage. The laboratory investigations, performed in another Hospital including an extended microbiological evaluation, antibody profile and clotting tests revealed increased inflammation parameters, micro- normocytic hypochromic anemia, positive antinuclear Abs with a peripheral and homogeneous immunofluorescence pattern, positive anti-dsDNA Abs, anticardiolipin Abs in low titers,

hyperimmunoglobulinemia G and M, low C3 concentration. He was diagnosed with SLE and treated with oral Prednisone. At the time of diagnosis, CD specific Abs was negative and histological analysis of duodenal biopsies was normal.

Moreover, at the age of 8 years old he was diagnosed with cryptogenic occipital lobe epilepsy based on sudden motor focal seizures with secondarily generalization, electroencephalogram pattern of epileptic activity within the occipital lobe, normal brain computed tomographic scan results and normal routine laboratory tests.

His family history included a second-degree relative with SLE (maternal aunt), and a first degree relative with spherocytosis (father).

On admission, physical examination was unremarkable, except for the moderate splenomegaly (4 cm below the left costal margin), short stature (< 3rd percentile for age) and a generalized anxiety disorder. Initial laboratory results showed moderately increased indicators of inflammation (erythrocyte sedimentation rate 36 mm/h, C reactive protein 56 mg/L, serum ferritin levels 393 ng/ml), microcytic hypochromic anaemia (haemoglobin of 8.7 g/dl, mean corpuscular volume 77 fL, mean corpuscular hemoglobin concentration 32.7 g/dl), hyposideremia (35 µg/dl), reticulocytosis (2.66 %), rare spherocytes on the peripheral blood smear, normobilirubinemia, normal results on the osmotic fragility test, no spectrin gene defects, leucocytes 8100/µL, platelet count 423×10³/µL, high serum concentrations of IgG and IgM, normal IgA levels, slightly decreased serum C3. There were no signs of infectious disease. The antibody profile showed

antinuclear Abs (titer of 1/640), high titers of anti-dsDNA Abs [1131 UI/ml; 5.6 times the upper limit of normal (ULN)], antihistone Abs, anti-nucleosome Abs, positive lupus anticoagulant, low titers of anti- β_2 glycoprotein I IgM Abs (2 times ULN), low anticardiolipin IgG Abs levels (1.2 times ULN), anti-thyroid peroxidase Abs (anti-TPO) in high concentration (153 UI/ml, 25 times ULN, with normal thyroid function tests). The investigation of

gastrointestinal –related Abs spectrum revealed IgA anti-tissue transglutaminase type 2 Abs (anti-TG2) in levels 3 times ULN, detected by an enzyme-linked immunosorbent INOVA assay (ELISA), positive IgA antiendomysial Abs (EMA) on indirect immunofluorescence (Figure 1), negative anti-smooth muscle Abs, anti-mitochondrial Abs, anti-liver kidney microsomal type 1 Abs.

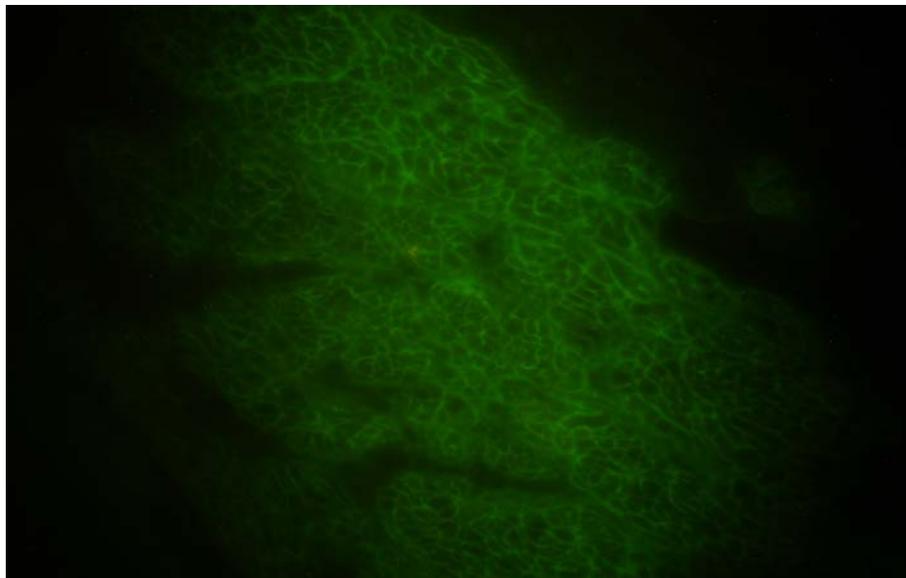


Figure 1. Positive IgA antiendomysial antibodies on indirect immunofluorescence

Even without specific symptoms, the positivity for anti-TG2 and EMA was highly suggestive of a possible associated CD. An evaluation by a paediatric gastroenterologist was recommended. In order to make a definitive diagnosis, an upper endoscopy with duodenal biopsies was suggested. Unfortunately the procedure was unsuccessful at that time and genetic testing for HLA-DQ2 and HLA-DQ8 was offered. The DNA testing was positive for HLA-DQ2 heterodimer, encoded by HLA-DQA1*05 and HLA-DQB1*02 (subtype HLA-DQ2.5). Ultimately, the decision of repeated serological testing on a normal gluten-containing diet in 3 to 6 monthly intervals was taken. During 2 years follow-up, on periodically assessments, using the same TG2 ELISA kit, anti-TG2 and EMA were always negative. He is now 14 years old. Somatic growth was on average developmental scores under low dose maintenance glucocorticoid therapy, normalization of hemoglobin occurred during the first 3 months of sustained disease suppression. No CD specific symptoms or significant SLE complications developed in the meantime. So far, parents refused to undergo another endoscopy for intestinal biopsy. On repeated testing, the anti-TPO were also negative. He is now considered at risk of developing CD as an associated condition to SLE. He is under the care of a pediatric gastroenterologist and pediatric rheumatologist, with periodically clinical and laboratory evaluation.

3. Discussion

Gluten sensitivity has been linked to many autoimmune pathologies, but the co-association of CD with SLE is mainly based on case reports. Patients with SLE appearing later in the clinical course of the CD have been reported [7,8] and even patients with gluten sensitivity masquerading

as systemic lupus erythematosus have been described [9]. Therefore, the real prevalence of CD in SLE is unclear [10].

The association of CD with the antiphospholipid syndrome (APLS) was even less studied. To our knowledge, there is one published article reporting a high prevalence of EMA in patients with APLS [11].

In our patient suffering from SLE and secondary APLS, the passing incidence of EMA and anti-TG2, on a continuous normal gluten-containing diet, in the condition of strong genetic predisposition to CD, made the diagnosis very challenging. According to the recent ESPGHAN diagnostic criteria of CD [12], in asymptomatic patients at genetic risk for CD with positive anti-TG2 at a low rate and positive EMA, the diagnostic workup should be extended to include duodenal biopsies. In our case, the definitive diagnosis was not accomplished at that time since the endoscopy was unsuccessful. And now after two years of persistent seronegativity for both IgA anti-TG2 and IgA EMA with normal serum total IgA on a normal gluten-containing diet and without any symptoms suggestive of CD, we are facing a dilemma. In such situations involving an imbalance between serological findings throughout the time, without any external interventions, gluten -free diet or new drugs, the ESPGHAN working group has deliberated no specific recommendation. We are aware that useful information for the diagnosis could be obtained from a duodenal histological examination. But unfortunately, the parents do not consent to the endoscopy for the moment. Therefore, for the time being, our patient is considered at risk of developing CD as an associated condition to SLE and he is investigated by serology every 6 months, on a normal diet.

Despite the evolving performances of the serologic testing and the new ESPGHAN guidelines for the

diagnosis of CD [12] there are still significant problems concerning the diagnosis approach in some atypical conditions, when not all criteria for diagnosis are satisfied. Before starting a lifelong restrictive and demanding diet, the diagnosis of CD must be accurate. Conversely, if the undiagnosed CD patients remain untreated, they are exposed to the risk of long-term complications, such as osteoporosis or osteopenia, low stature, infertility or intestinal malignancies [13,14].

4. Conclusion

Guidance is still needed for the CD diagnosis in some atypical conditions, such as patients with systemic autoimmune diseases, where the appearance of CD - specific antibodies has been documented before in the absence of the disease.

Conflict of Interest

None.

Acknowledgement

This paper was published under the frame of European Social Found, Human Resources Development Operational Programme 2007- 2013; project no. POSDRU159/1.5/S/138776.

References

- [1] Salardi S, Volta U, Zucchini S, Fiorini E, Maltoni G, Vaira B, et al. Prevalence of celiac disease in children with type 1 diabetes mellitus increased in the mid-1990 s: an 18-year longitudinal study based on anti-endomysial antibodies. *J Pediatr Gastroenterol Nutr* 2008; 46(5): 612-614.
- [2] Hansen D, Brock-Jacobsen B, Lund E, Bjørn C, Hansen LP, Nielsen C, et al. Clinical benefit of a gluten-free diet in type 1 diabetic children with screening-detected celiac disease: a population-based screening study with 2 years' follow-up. *Diabetes Care* 2006; 29(11): 2452-2456.
- [3] Valentino R, Savastano S, Tommaselli AP, Dorato M, Scarpitta MT, Gigante M, et al. Prevalence of coeliac disease in patients with thyroid autoimmunity. *Horm Res* 1999; 51(3): 124-127.
- [4] Lepore L, Martellosi S, Pennesi M, Falcini F, Ermini ML, Ferrari R, et al. Prevalence of celiac disease in patients with juvenile chronic arthritis. *J Pediatr* 1996; 129(2): 311-313.
- [5] Caprai S, Vajro P, Ventura A, Sciveres M, Maggiore G. Autoimmune liver disease associated with celiac disease in childhood: a multicenter study. *Clin Gastroenterol Hepatol* 2008; 6(7): 803-806.
- [6] Koehne V de B, Bahia M, Lanna CC, Pinto MR, Bambirra EA, Cunha AS. Prevalence of serological markers for celiac disease (IgA and IgG class antigliadin antibodies and IgA class antiendomysium antibodies) in patients with autoimmune rheumatologic diseases in Belo Horizonte, MG, Brazil. *Arq Gastroenterol* 2010; 47(3): 250-256.
- [7] Ludvigsson JF, Rubio-Tapia A, Chowdhary V, Murray JA, Simard JF. Increased risk of systemic lupus erythematosus in 29,000 patients with biopsy-verified celiac disease. *J Rheumatol* 2012; 39(10): 1964-1970.
- [8] Freeman HJ. Adult celiac disease followed by onset of systemic lupus erythematosus. *J Clin Gastroenterol* 2008; 42(3): 252-255.
- [9] Hadjivassiliou M, Sanders DS, Grünewald R a, Akil M. Gluten sensitivity masquerading as systemic lupus erythematosus. *Ann Rheum Dis* 2004; 63: 1501-1503.
- [10] Marai I, Shoenfeld Y, Bizzaro N, Villalta D, Doria A, Tonutti E, et al. IgA and IgG tissue transglutaminase antibodies in systemic lupus erythematosus. *Lupus* 2004; 13(4): 241-244.
- [11] Shamir R, Shoenfeld Y, Blank M, Eliakim R, Lahat N, Sobel E, et al. The prevalence of coeliac disease antibodies in patients with the antiphospholipid syndrome. *Lupus* 2003; 12(5): 394-399.
- [12] Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. *J Pediatr Gastroenterol Nutr* 2012; 54(1): 136-160.
- [13] Grainge MJ, West J, Solaymani-Dodaran M, Card TR, Logan RFA. The long-term risk of malignancy following a diagnosis of coeliac disease or dermatitis herpetiformis: a cohort study. *Aliment Pharmacol Ther* 2012; 35(6): 730-739.
- [14] Admou B, Essaoudouni L, Krati K, Zaher K, Sbihi M, Chabaa L, et al. Atypical celiac disease: from recognizing to managing. *Gastroenterol Res Pract* 2012; 2012: 637187.