

Serological and Genetic Evidence of Celiac Disease in Juvenile Arthritis and Rheumatoid Arthritis

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Abstract Is celiac disease associated with arthritis? We will try to answer to this question by studying the last news in serological and genetic testing of celiac disease in juvenile arthritis and rheumatoid arthritis.

Keywords: serological markers, genetic typing, celiac disease, arthritis, child, adult

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1. Introduction

Celiac disease is an autoimmune condition [1]. Autoimmune rheumatologic diseases with juvenile onset are intensively studied in recent years [2]. Is there a connection between celiac disease and arthritis? The presence of celiac disease (CD) in patients with juvenile arthritis was revealed in 2008 [3]. So the question was, if juvenile arthritis could be associated with other autoimmune diseases with similar genetic background [4]. There was a 5-10 increased risk of CD coexistence with other autoimmune diseases, such as type I diabetes mellitus (T1DM), juvenile arthritis or autoimmune thyroiditis [5]. A patient with rare association of juvenile arthritis with CD was reported later in 2011. So, again the question was, if juvenile arthritis could be associated with other autoimmune diseases [6]. But association of CD with juvenile arthritis was for a long time an enigma [7]. The clinical data about CD association with juvenile arthritis were few. We will analyze in this article the evidence given by serological and genetic testing related to CD association with juvenile arthritis and rheumatoid arthritis.

2. Serological Testing

Mayouf et al. revealed that positive anti-endomysium antibodies (EmA) needed further investigations for CD diagnosis among children with juvenile arthritis [8]. Koehne et al. concluded that positive anti-gliadin (AGA) IgA, AGA IgG or EmA results are probably nonspecific for the CD presence among rheumatologic disease patients [9]. AGA were more often detected in rheumatoid arthritis patients and primary Sjögren's syndrome patients than in the general population [10]. Anti-tissular transglutaminase

antibodies (tTG) were a useful screening test to find asymptomatic CD associated with active juvenile arthritis [11]. However, other study concluded that high levels of tTG IgA in patients with juvenile arthritis reflected increased polyclonal IgA production, not a specific intestinal inflammatory process. [12]. Therefore, the patients with juvenile arthritis needed a screening protocols for CD [13]. The screening of CD showed many associations of CD. But the evidence provided by the screening of CD in juvenile arthritis were also few.

3. Genetic Testing

3.1. Juvenile Arthritis

The 4q27 locus was related with susceptibility to juvenile arthritis. This locus was also associated with rheumatoid arthritis, T1DM, CD, and psoriatic arthritis [14]. One SNP in the LPP gene, rs1464510 and a second SNP, rs653178 in ATXN2, showed association with juvenile arthritis. Association at the SH2B3/ATXN2 locus, also supported this region to JIA susceptibility [15]. PTPN22 gene was also related to susceptibility to some autoimmune diseases [16]. The pattern diseases are important for managing the entryway diseases [17].

3.2. Rheumatoid Arthritis

Human leukocyte antigen (HLA) testing contributed to understanding CD pathogenesis compared to T1DM, multiple sclerosis, and rheumatoid arthritis [18]. Gluten-specific T cells utilises T cell repertoire (TCR) in HLA-DQ2(+) and HLA-DQ8(+) patients. Similar mechanisms are likely to play a role in rheumatoid arthritis [19]. But association of specific HLA molecules in rheumatoid arthritis remains poorly defined and an immune response against post-translationally modified protein antigens is a hallmark of each disease [20]. The diseases also share

multiple non-HLA loci that are crucial for activation and regulation of adaptive and innate immunity [21]. Gutierrez-Achury et al. discovered five new non-HLA loci shared by CD and rheumatoid arthritis. They also found that in nine of 24 shared loci the associated variants are distinct in the two diseases [22].

4. Conclusions

Serological testing have not helped too much in the diagnosis of CD in juvenile arthritis but genetic testing are important for monitoring of CD genetic risk in rheumatoid arthritis and juvenile arthritis.

References

- [1] Samasca G, Sur G, Lupan I, Tilinca M, Deleanu D. Celiac disease as an autoimmune condition. *Cent Eur J Immunol* 2014; 39: 396-399.
- [2] Sparchez M, Lupan I, Delean D, Bizo A, Damian L, Tamas MM, Muntean L, Simionescu B, Bolba C, Lazar C, Felea I, Rednic S. Primary immunodeficiency disorders and autoimmune rheumatologic diseases with juvenile onset: a Romanian multicenter clinical study. *Eur J Clin Invest* 2015; 45: 63.
- [3] Alpigliani MG, Haupt R, Parodi S, Calcagno A, Poggi E, Lorini R. Coeliac disease in 108 patients with juvenile idiopathic arthritis: a 13-year follow-up study. *Clin Exp Rheumatol*. 2008; 26: 162.
- [4] Pohjankoski H, Kautiainen H, Kotaniemi K, Korppi M, Savolainen A. Autoimmune diseases in children with juvenile idiopathic arthritis. *Scand J Rheumatol*. 2010; 39: 435-436.
- [5] Zwolińska-Wcisło M, Rozpondek P, Galicka-Latała D, Mach T. [Clinical symptoms variety in adults with celiac disease]. *Przegl Lek*. 2010; 67: 1325-1328.
- [6] Michelin CM1, Aikawa NE, Diniz JC, Jesus AA, Koda YK, Silva CA. Association of systemic-onset juvenile idiopathic arthritis and celiac disease - a case report. *Acta Reumatol Port*. 2011; 36: 404-407.
- [7] De Maddi F, Pellegrini F, Raffaele CG, Tarantino G, Rigante D. Celiac disease and juvenile idiopathic arthritis: a still enigmatic crossover. *Scand J Gastroenterol*. 2013; 48: 511-512.
- [8] Al-Mayouf SM1, Al-Mehaidib AI, Alkaff MA. The significance of elevated serologic markers of celiac disease in children with juvenile rheumatoid arthritis. *Saudi J Gastroenterol*. 2003; 9: 75-78.
- [9] Koehne Vde 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: 250-256.
- [10] Koszarny A, Majdan M, Suszek D, Dryglewska M, Tabarkiewicz J. Autoantibodies against gliadin in rheumatoid arthritis and primary Sjögren's syndrome patients. *Wiad Lek*. 2015;68:242-247.
- [11] Gheita TA, Fawzy SM, Nour El-Din AM, Gomaa HE. Asymptomatic celiac sprue in juvenile rheumatic diseases children. *Int J Rheum Dis*. 2012; 15: 220-226.
- [12] Stoll ML, Patel AS, Christadoss ML, Punaro M, Olsen NJ. IgA transglutaminase levels in children with Juvenile Idiopathic Arthritis. *Ann Paediatr Rheumatol*. 2012; 1: 31-35.
- [13] Robazzi TC, Adan LF, Pimentel K, Guimarães I, Magalhães Filho J, Toralles MB, Rolim AM. Autoimmune endocrine disorders and coeliac disease in children and adolescents with juvenile idiopathic arthritis and rheumatic fever. *Clin Exp Rheumatol*. 2013; 31: 310-317.
- [14] Albers HM, Kurreeman FA, Stoeken-Rijsbergen G, Brinkman DM, Kamphuis SS, van Rossum MA, Girschick HJ, Wouters C, Saurenmann RK, Hoppenreijns E, Slagboom P, Houwing-Duistermaat JJ, Verduijn W, Huizinga TW, Ten Cate R, Toes RE, Schilham MW. Association of the autoimmunity locus 4q27 with juvenile idiopathic arthritis. *Arthritis Rheum*. 2009; 60: 901-904.
- [15] Hinks A, Martin P, Flynn E, Eyre S, Packham J, Barton A; Childhood Arthritis Prospective Study (CAPS), UKRAG Consortium, BSPAR study group, Worthington J, Thomson W. Investigation of type 1 diabetes and coeliac disease susceptibility loci for association with juvenile idiopathic arthritis. *Ann Rheum Dis*. 2010; 69: 2169-2172.
- [16] Abbasi Z, Kazemi Nezhad SR, Pourmahdi-Broojeni M, Rajaei E. Association of PTPN22 rs2476601 Polymorphism with Rheumatoid Arthritis and Celiac Disease in Khuzestan Province, Southwestern Iran. *Iran Biomed J*. 2016: [Epub ahead of print]
- [17] Dietert RR, Zelikoff JT. Identifying patterns of immune-related disease: use in disease prevention and management. *World J Pediatr*. 2010; 6: 111-118.
- [18] Qiao SW, Iversen R, Ráki M, Sollid LM. The adaptive immune response in celiac disease. *Semin Immunopathol*. 2012; 34: 523-540.
- [19] Koning F. Recent insight in the pathophysiology of coeliac disease: relevance to rheumatoid arthritis. *Clin Exp Rheumatol*. 2015; 33: S8-10.
- [20] Koning F, Thomas R, Rossjohn J, Toes RE. Coeliac disease and rheumatoid arthritis: similar mechanisms, different antigens. *Nat Rev Rheumatol*. 2015; 11: 450-461.
- [21] Lerner A, Matthias T. Rheumatoid arthritis-celiac disease relationship: joints get that gut feeling. *Autoimmun Rev*. 2015; 14: 1038-1047.
- [22] Gutierrez-Achury J, Zorro MM1, Ricaño-Ponce I, Zernakova DV; Coeliac Disease ImmunoChip Consortium, RACI Consortium, Diogo D, Raychaudhuri S, Franke L, Trynka G, Wijmenga C, Zernakova A. Functional implications of disease-specific variants in loci jointly associated with coeliac disease and rheumatoid arthritis. *Hum Mol Genet*. 2016; 25: 180-190.