

Anticyclic Citrullinated Peptide Antibody: A Predictor of Juvenile Idiopathic Arthritis Progression Toward Rheumatoid Arthritis

Fariborz Ghaffaripasand*

Health Policy Research Center, Shiraz University of Medical Sciences, School of Medicine, Zand Avenue, Shiraz, Iran

Abstract

Rheumatoid Arthritis (RA) has been associated with several autoantibodies, including antiperinuclear factor, anti-keratin antibodies, anti-flaggrin antibodies, and anti-Cyclic Citrullinated Peptide (anti-CCP) antibodies. Most studies found that anti-CCP antibodies are only detected in Juvenile Rheumatoid Arthritis (JRA) patients with positive Rheumatoid Factor (RF). In our center we experimentally observed that children with Juvenile Idiopathic Arthritis (JIA) that tested positive for anti-CCP Abs were also tested positive for RF. In seven years of follow-up of these 86 patients, 63 (73.2%) developed RA. It can be hypothesized that the antibodies against CCP plays an important role in progression of the JIA towards RA. On the other hand anti-CCP Abs may play a role in the pathogenesis of RA. Further studies are needed to clarify this association.

Juvenile idiopathic arthritis (JIA) is a systemic autoimmune disease of unknown origin, which is characterized by chronic inflammation of the joints similar to RA. It is one of the most common chronic illnesses of childhood. Patients with JIA are divided into seven subgroups, which include oligoarthritis, RF-positive polyarthritis, RF-negative polyarthritis, extended oligoarthritis, systemic arthritis, psoriatic arthritis, and Entesitis-Related Arthritis (ERA) [1]. The diagnosis of JIA depends primarily on clinical manifestations of the disease [2]. Rheumatoid factor (RF) and Antinuclear Antibodies (ANA) are established tests. RA has been associated with several other autoantibodies, including antiperinuclear factor, anti-keratin antibodies, anti-flaggrin antibodies, and anti-cyclic citrullinated peptide (anti-CCP) antibodies. These autoantibodies bind antigenic determinants that contain the unusual amino acid citrulline. Citrulline is a posttranslational modification of the amino acid arginine by the enzyme peptidyl arginine deiminase [2]. There has been increasing interest in these antibodies as diagnostic and prognostic markers of JIA. Antinuclear antibodies are considered to be a marker for early onset oligoarticular disease with uveitis [2,3]. However, their presence is not related to the disease course or to the severity of the joint involvement [2]. Anti-CCP Abs have been studied in children a few times [3-7]. Reviewing the literature, Low et al. [7] found anti-CCP Abs in 77% (51/66) patients with JIA, including 15/18 (83%) RF-negative polyarthritis, 12/16 (75%) RF-positive polyarthritis, 16/19 (84%) oligoarthritis, 8/13 (62%) systemic arthritis. Noteworthy is that these results are unique. In contrast, Avcin et al. [4] found positive anti-CCP values in sera of 1.8% (2/109) patients with JIA. Both of them were relatively low. One of 25 (4%) patients with polyarticular onset, 1/64 (1.6%) with oligoarticular onset, and none of the 20 patients with systemic onset type were anti-CCP positive. The patient with polyarticular onset was RF-negative. In another study, Hromadnikova et al. [5] scrutinized the presence of anti-CCP Abs in sera of 140 patients with JIA aged 2-47 years. Overall, anti-CCP Abs were found in 5% (7/140) patients including 3/52 RF-negative polyarthritis, 2/18 RF-positive polyarthritis, 1/15 ERA, and 1/5 unclassifiable arthritis. Kasapçopur et al. [6] detected anti-CCP Abs in 2% (3/122) of children with JIA. Twelve of them had RF-positive polyarticular JIA. In the sera of 25% (3/12) of the patients with RF-positive polyarticular JIA, anti-CCP Abs were verifiable. Anti-CCP values of patients with JIA subtypes other than RF-positive polyarticular JIA were not found to be significantly different.

Most of the authors believe that anti-CCP Abs are not of prognostic

value. But in the study by Brunner and Sitzmann [8] it was shown that these antibodies are only detected in patients with positive RF. This means that the pattern of JIA in patients with positive anti-CCP Abs resembles the RA.

In our center we experimentally observed that children with JIA that tested positive for anti-CCP Abs were also tested positive for RF. In seven years of follow-up of these 86 patients, 63 (73.2%) developed RA according to the 1987 American College of Rheumatology (ACR) revised criteria for the RA classification. In a retrospective review of the clinical features of these 63 patients, we found that the clinical manifestations of JIA in these patients mostly resembled the RA.

According to the above preliminary data and the results of the previous studies, it can be hypothesized the antibodies against CCP plays an important role in progression of the JIA towards RA. On the other hand anti-CCP Abs may play a role in the pathogenesis of RA. Further studies are needed to clarify this association.

References

1. Petty RE, Southwood TR, Baum J, Bhettag E, Glass DN, et al. (1998) Revision of the proposed classification criteria for juvenile idiopathic arthritis: Durban, 1997. *J Rheumatol* 25: 1991-1994.
2. Woo P, Wedderburn LR (1998) Juvenile chronic arthritis. *Lancet* 351: 969-973.
3. Lawrence JM 3rd, Moore TL, Osborn TG, Neshor G, Madson KL, et al. (1993) Autoantibody studies in juvenile rheumatoid arthritis. *Semin Arthritis Rheum* 22: 265-274.
4. Avcin T, Cimaz R, Falcini F, Zulian F, Martini G, et al. (2002) Prevalence and clinical significance of anti-cyclic citrullinated peptide antibodies in juvenile idiopathic arthritis. *Ann Rheum Dis* 61: 608-611.

*Corresponding author: Fariborz Ghaffaripasand, Health Policy Research Center, Shiraz University of Medical Sciences, School of Medicine, Zand Avenue, Shiraz, Iran, Tel: 00989173095214; Fax: 00987112309615; E-mail: fariborz_ghaffaripasand@yahoo.com, ghafarf@sums.ac.ir

Received April 17, 2012; Accepted April 18, 2012; Published April 21, 2012

Citation: Ghaffaripasand F (2012) Anticyclic Citrullinated Peptide Antibody: A Predictor of Juvenile Idiopathic Arthritis Progression Toward Rheumatoid Arthritis. *J Med Diagn Meth* 1:e102. doi:10.4172/2168-9784.1000e102

Copyright: © 2012 Ghaffaripasand F. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

5. Hromadnikova I, Stechova K, Pavla V, Hridelova D, Houbova B, et al. (2002) Anti-cyclic citrullinated peptide antibodies in patients with juvenile idiopathic arthritis. *Autoimmunity* 35: 397-401.
6. Kasapçopur O, Altun S, Aslan M, Karaarslan S, Kamburoglu-Goksel A, et al. (2004) Diagnostic accuracy of anti-cyclic citrullinated peptide antibodies in juvenile idiopathic arthritis. *Ann Rheum Dis* 63: 1687-1689.
7. Low JM, Chauhan AK, Kietz DA, Daud U, Pepmueller PH, et al. (2004) Determination of anti-cyclic citrullinated peptide antibodies in the sera of patients with juvenile idiopathic arthritis. *J Rheumatol* 31: 1829-1833.
8. Brunner JK, Sitzmann FC (2006) Anticyclic citrullinated peptide antibodies in juvenile idiopathic arthritis. *Mod Rheumatol* 16: 372-375.

Submit your next manuscript and get advantages of OMICS Group submissions

Unique features:

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

Special features:

- 200 Open Access Journals
- 15,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, DOAJ, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: <http://www.omicsonline.org/submission>

