



POSTER PRESENTATION

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Evidence of fibrinogen as a target of citrullination in IgM rheumatoid factor-positive polyarticular juvenile idiopathic arthritis

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From 2011 Pediatric Rheumatology Symposium sponsored by the American College of Rheumatology Miami, FL, USA. 2-5 June 2011

Purpose

The role of anti-cyclic citrullinated peptide (anti-CCP) antibodies in juvenile idiopathic arthritis (JIA) has become better understood; however, the identity of the target proteins of this modification remains elusive. We evaluated serum from patients with various subtypes of JIA to investigate the presence of anti-citrullinated fibrinogen and anti-citrullinated α -enolase antibodies, and their association with rheumatoid factor (RF) and anti-CCP antibodies.

Methods

Sera were obtained from 96 JIA patients, 19 systemic lupus erythematosus (SLE) patients, and 10 healthy children. All sera were measured for antibodies against citrullinated and native fibrinogen and α -enolase by enzyme-linked immunosorbent assay. All results were correlated with clinical and laboratory parameters.

Results

Thirty-one (32%) JIA patients demonstrated reactivity to citrullinated fibrinogen and 9 (9%) to citrullinated α -enolase. Reactivity to citrullinated fibrinogen and α -enolase was predominantly found in IgM RF-positive polyarthritis patients (81% and 18%, respectively). Anti-citrullinated fibrinogen antibodies were significantly elevated in JIA patients when compared to the healthy and SLE control groups ($p < 0.05$). Antibody reactivity patterns showed that the largest group of JIA patients reacted only with fibrinogen (17%). Ninety-three percent of JIA patients positive for IgG anti-CCP antibodies also reacted with citrullinated fibrinogen, making up 10% of the JIA population. Anti-citrullinated fibrinogen antibodies correlated significantly

with IgG and IgA anti-CCP antibodies and IgA and IgM RF ($p < 0.05$). Significantly elevated levels of IgG, IgM, and IgA anti-CCP antibodies, and IgA and IgM RF were noted in JIA patients who were also positive for anti-citrullinated fibrinogen antibodies. IgM RF and anti-citrullinated fibrinogen antibodies demonstrated the highest sensitivity for IgM RF-positive polyarthritis (100% and 81.3%, respectively) and JIA overall (43.4% and 32.3% respectively). IgG and IgA anti-CCP antibodies and anti-citrullinated fibrinogen antibodies exhibited the highest specificity for JIA (96.6%, 86.2%, and 86.2%, respectively).

Conclusion

Of the antibodies measured in this study, anti-citrullinated fibrinogen antibodies showed the strongest association with JIA when compared to healthy and SLE control groups. Additionally, anti-citrullinated fibrinogen antibodies demonstrated high sensitivity and specificity for IgM RF-positive polyarthritis patients, along with IgG anti-CCP antibodies and IgM RF. Our data would suggest that measuring anti-citrullinated fibrinogen antibodies, in addition to anti-CCP antibody isotypes and IgM RF, may be beneficial in identifying patients that will develop more aggressive disease. For the first time, we have identified fibrinogen as a potential target for citrullination in JIA, particularly in patients with IgM RF-positive polyarticular JIA.

Disclosure

Brooke E. Gilliam: None; Melinda R. Reed: None; Anil K. Chauhan: None; Amanda Dehlendorf: None; Peri H. Pepmueller: None; Terry L. Moore: None.

Published: 13 July 2012

doi:10.1186/1546-0096-10-S1-A119

Cite this article as: Gilliam *et al.*: Evidence of fibrinogen as a target of citrullination in IgM rheumatoid factor-positive polyarticular juvenile idiopathic arthritis. *Pediatric Rheumatology* 2012 **10**(Suppl 1):A119.

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