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The Utility of CCP Antibodies in Autoimmune Diseases

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Abstract Autoimmune diseases have a constellation of immunological changes that make possible the appearance of clinical manifestations. There are often similarities of clinical manifestations in these autoimmune diseases as possible associations of them during evolution.

Keywords: *autoimmune diseases, clinical manifestations, associations, child*

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1. Introduction

Autoimmune diseases are increasingly known and studied due to the multitude of clinical manifestations as well as due to their intricacy. The incidence of these autoimmune diseases has increased recently and due to the notified clinical manifestations as well as the possibility of a better laboratory diagnosis [1].

Celiac disease and juvenile idiopathic arthritis (JIA) are part of the category of autoimmune diseases. Often the intricate clinical manifestations can make the two diseases initially difficult to diagnose. Studies in our clinic have shown that rheumatic signs can be described in celiac disease. The most common of these are arthralgia, arthritis, early joint pain, enthesopathy. We also found that in JIA digestive manifestations can coexist such as: dysphagia, damage to the esophagus with reflux, temporomandibular arthritis, digestive vasculitis. Based on these, we found in the pathology of the clinic that some cases that had symptoms of celiac disease later turned out to be JIA [2,3].

Idiopathic juvenile arthritis among other diagnostic markers also benefit from anti-CCP antibodies. Unlike adult pathology, these anti-CCP antibodies are found in RF-positive forms of polyarticular arthritis that correspond to adult rheumatoid arthritis. For this reason, anti-CCP antibodies are less common in JIA.

2. Study Analysis

The diagnosis of this disease is often delayed by the lack of reliable markers and this predicts a child's prognosis difficult [4]. The diagnosis of JIA is based on the clinical manifestations and there are only a few serological markers that are used in clinical practice [5]. Anti-CCP antibodies have been recently studied. Citrullin is a post-translation modification of arginine residues. This aminoacid exists in high concentrations in the filaggrin peptide chain. Areas that are citrullin rich appear to become the main target of antifilaggrin antibodies. The prevalence of these autoantibodies in adults with rheumatoid arthritis (RA) has been intensively researched, but the number of studies in JIA is limited [6].

RA was definited as a severe, chronic inflammatory joint disease. Van Gaalen FA et al performed a prospective study in patients enrolled in a recent-onset arthritis cohort to investigate the value of anti-CCP antibodies in predicting the development of RA in patients with UA. This study showed that autoantibodies seen in RA can be detected years before clinical symptoms develop. Recently developed assays detecting anti-CCP antibodies in adults with RA have a specificity of 95-96% and a sensitivity of 53-71% [7].

Since 2002, several studies have assessed the diagnostic accuracy and efficacy of anti-CCP antibodies in JIA. Occurrence rates of anti-CCP in JIA patients were between 1.8% to 41.7%. Multiple studies have revealed that anti-CCP can be detected in a small number of JIA patients and less common than in adults with RA [6,8,9,10,11,12]. Previous studies [13,14], revealed that these anti-CCP antibodies are present in the polyarticular, immunoglobulin M (IgM) rheumatoid factor (RF)-positive subset of JIA patients but they cannot be used for the diagnosis of JIA [15]. In their prospective cohort study, van Gaalen FA et al showed that children with positive RF and onset of polyarthritis, anti-CCP levels are positively correlated with high disease activity [7]. Hammoda et al demonstrated that there is a strong correlation between the prevalence of anti-CCP antibodies and the degree of joint damage and bone erosions. JIA patients who are positive for the anti-CCP antibodies had radiological bone damage and a severe form of arthritis [6]. Yasui K et al reported both anti-CCP antibody positive and IgM-RF positive polyarticular JIA to a youngest child. They concluded that positivity for both antibodies (anti-CCP and RF) can forecast the severity of JIA (radiographic bone

destruction) [15]. Furthermore, the case-control study performed by Hamooda M et al showed that medication options and disease duration did not differ significantly between anti-CCP positive and negative patients. For the diagnosis of JIA, the specificity of anti-CCP is extremely high (>95%) but its sensitivity is extremely low, varying from 2% to 14% [6]. The low sensitivity of the anti-CCP test in JIA shows that is not valuable for the diagnosis of JIA and it cannot be used as a screening test, but because of its high specificity, it may become one of the most useful serological tests for the diagnosis of RF+PA [5]. In the presence of a positive anti-CCP antibody result in a child with specific clinical symptoms, a clinician should take appropriate measures. A negative test does not mean the absence of JIA and should be confirmed by other laboratory tests or clinical manifestations. Anti-CCP antibodies are rarely found in non-JIA patients or healthy subjects. Hence, these antibodies facilitate the differential diagnosis of early UA arthritis in children [5]. Most of the studies agreed that anti-CCP antibodies could be utilized as an important and valuable marker in the polyarticular form of JIA to detect early, and could point toward an aggressive therapeutic intervention [6].

Correlations can be made between the existence of uveitis in patients with JIA and the presence of RF and anti-CCP antibodies. A research study performed by Yasumura et al. published in Pediatric Rheumatology in 2019, shows that uveitis is relatively frequently diagnosed in patients with JIA (approx 6%). Therefore, uveitis has an increased prevalence in patients with early onset of JIA, OA and anti-nuclear antibodies. It has also been determined that uveitis has a significantly lower frequency in patients with positive RF and positive anti-CCP antibodies [16,17].

Key Messages

- anti-CCP positivity can be found in children with positive RF
- onset of polyarthritis but is less frequently present compared to adults with RA.
- anti-CCP antibodies in JIA are related to bone erosions and the degree of joint damage.
- anti-CCP antibodies have lower values in child pathology because they are correlated with the presence of RF in children with polyarticular JIA.

Author Contributions

All authors contributed equally to this work.

Conflict-of-interest Statement

The authors declare that they have no conflict of interest.

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