PATHOLOGIC ANTIBODY RESPONSES IN CELIAC DISEASE: SPECIFICITY AND IMMUNOLOGICAL CORRELATIONS

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SUMMARY

Celiac disease (CD) which affects at least one percent of the population in Europe is one of the most frequent autoimmune diseases. The main tools for diagnosing the disease are specific serological tests followed by confirmatory small intestinal histology in positive cases. Celiac specific autoantibodies target the enzyme tissue transglutaminase (TG2).

In our studies, we showed that CD can be detected by a rapid method based on the use of TG2 antigen in the patients' own red blood cells, which does not need either laboratory equipment or skills. The CD rapid test enables the doctor to get the results more quickly. Furthermore, it can be done by the patient himself at home. Whole blood fingertip sampling requires less blood and it is less stressful for small children than traditional venous blood sampling for serum examinations. Screening by the onsite rapid test and biopsy intervention following a positive result need less time and diminish the number of other invasive tests. Rapid antibody determinations also improve the dietary compliance and the status of the patients. Family members and the population can also be screened by a minimally invasive method in this way.

HLA-DR3:DQ2 haplotypes that are specific to CD affect the activation of T lymphocytes and practically all aspects of the immune response related to cytokine production. In our study, we examined whether production of protective antibodies to the protein-like HBsAg is diminished in CD. We found that HLA-DR3:DQ2 carriers do not necessarily have insufficient humoral immune response to hepatitis B immunization. Specific antibody production was lower in undiagnosed and therefore untreated CD patients. However, patients prospectively immunized on a gluten-free diet showed normal immune response. We concluded that the non-responder status is not permanent in CD, so revaccination is indicated after gluten elimination. No correlation was found between the immune response to the hepatitis B vaccination and haptoglobin polymorphism of the patients.

The use of serological tests that are non-specific to CD has long been disputed. Our study also evaluated the diagnostic value of non-organ specific autoantibodies and anti-glycan antibodies as well as how they are affected by the gluten free diet. We found that their presence depends on the activity of CD. That is partly due to tissue damage and partly to the loss of tolerance to microbial antigens. The above antibodies seem to be secondary, and in the absence of other autoimmune diseases, they disappear from blood when gluten is eliminated. When they are present or found accidentally during other examinations, CD should be suspected, however use of these tests is not sensitive enough to find all CD patients. The prevalence of anti-CMV antibodies was also studied in patients with chronic diarrhoea, but their presence was not found to be related to CD.

The aim of my thesis was to present the different ways how disease specific TG2-targeted antibody tests and other serologic tests can be applied in clinical settings and how are they immunologically interrelated. They are useful to facilitate the diagnosis of CD and the monitoring of the dietary intervention, as well as the prevention of contagious diseases. The role they play in the pathomechanism of CD needs further studies.

KEYWORDS

celiac disease, transglutaminase antibody, endomysium antibody, gluten-free diet, rapid test, hepatitis B immunization, haptoglobin, cytomegalovirus, anti-glycan antibody