Kapitány Anikó, DEOEC, Belgyógyászati Intézet, III.sz. Belgyógyászati Klinika, Regionális Immunológiai Laboratórium
Klinikai Orvostudományok doktori iskola, vezető: Prof. Dr. Berta András**,** az MTA doktora
Immunológia doktori program, programvezető: Prof. Dr. Zeher Margit**,** az MTA doktora
Témavezető: Prof. Dr. Sipka Sándor, az MTA doktora

Summary

Coeliac disease (CD) is strongly associated with HLA-DQ2 or DQ8 genotypes. The diagnosis of CD nowadays is based on demonstrating crypt hyperplastic villous atrophy, endomysial (EMA) or transglutaminase antibodies (anti-TG) and correlation of disease activity with gluten intake. Our aim was to evaluate the clinical utility of HLA-DQ typing when coeliac disease diagnosis had previously been established solely by histology. HLA-DQ alleles, EMA and anti-TG were investigated and histology slides reviewed in 70 patients diagnosed 2-25 years earlier by small-intestinal biopsy but without measuring EMA or anti-TG. Patients without DQ2 or DQ8 or without unequivocal villous atrophy were followed up on free diet by using serology and biopsies. We have found that all EMA/anti-TG positive patients carried DQ2 or DQ8, and had severe villous atrophy. Only 56% of patients without EMA or anti-TG positivity had DQ2 or DQ8 ($p<0.001$). Seropositivity and relapse developed in 4 of 11 DQ2 positive but in none of 15 DQ2 and DQ8 negative patients on long-term gluten exposure. As a conclusion we can say that coeliac disease diagnosis based solely on histology is not always reliable. HLA-DQ testing is important in identifying DQ2 and DQ8 negative subjects who need revision of their diagnosis, but it does not have additive diagnostic value if EMA positivity is already known.

Certain HLA-DR1 (DRB1*01) and HLA-DR4 (HLA-DRB1*04*)* alleles, also known as "shared epitope"(SE), are associated with increased susceptibility to rheumatoid arthritis (RA), and may also have relevance for disease outcome. Anti-CCP antibody positivity is thought to associate with the presence of HLA-DR4 alleles in patients with RA. However, there is little information available regarding any relationship between serum anti-CCP concentrations and the SE. Therefore our aim was to determine the frequency of HLA-DR1 and -DR4 subtypes in our patients with RA in comparison to healthy control subjects, and to determine the association between anti-CCP antibody production and various HLA-DRB1 alleles. We have found, that among the HLA-DR4 subtypes, DRB1*0401 and DRB1*0404, among DR1 subtypes DRB1*0101 were the most common alleles in both groups, but there

were no significant differences in their frequencies between the two examined groups. In contrast, HLA-DRB1*0405 and DRB1*0408 were significantly more common among RA patients in comparison to control subjects. Our data suggest, that in our patients, HLA-DR4, as well as its subtypes DRB1*0405 and DRB1*0408, may be involved in the susceptibility to RA, but HLA-DR1 may not. Furthermore we have found that not only the presence, but the serum concentration of anti-CCP antibody is in association with HLA-DRB1*04 alleles.

I also investigated the HLA-DRB1 and HLA-DQB1 alleles in patients with systemic lupus erythematosus (SLE only), SLE with secondary antiphospholipid syndrome (SLE+SAPS) and in those, whose clinical course began as primary APS and subsequently progressed to SLE (PAPS+SLE), searching explanation behind phenotypical differences: patients with primary or secondary APS present more thrombotic and less inflammatory activity, while fetal wastage was the highest in the PAPS+SLE group. Our results confirmed that the HLA-DRB1 and DQB1 profile of PAPS and SAPS is different, therefore it is unlikely that they are responsible for the partly similar phenotype of the two groups.

Keywords: HLA, coeliac disease, rheumatoid arthritis, SLE, APS, polymorphism
Kulcsszavak: HLA, coeliakia, rheumatoid arthritis, SLE, APS, polimorfizmus