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Association between polymorphisms in the TSHR gene and Graves' orbitopathy.

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Abstract

BACKGROUND:

Graves' orbitopathy (GO) as well as Graves' disease (GD) hyperthyroidism originate from an autoimmune reaction against the common auto-antigen, thyroid-stimulating hormone receptor (TSHR). GO phenotype is associated with environmental risk factors, mainly nicotinism, as well as genetic risk factors which initiate an immunologic reaction. In some patients GO is observed before diagnosis of GD hyperthyroidism, while it can also be observed far after diagnosis. The intensity of GO symptoms varies greatly in these patients. Thus, the pathogenesis of GD and GO may correlate with different genetic backgrounds, which has been confirmed by studies of correlations between GO and polymorphisms in cytokines involved in orbit inflammation. The aim of our analysis was to assess genetic predisposition to GO in young patients (age of diagnosis ≤30 years of age), for whom environmental effects had less time to influence outcomes than in adults.

METHODS:

768 GD patients were included in the study. 359 of them had clinically evident orbitopathy (NOSPECS ≥2). Patients were stratified by age at diagnosis. Association analyses were performed for genes with a known influence on development of GD - TSHR, HLA-DRB1, cytotoxic T-lymphocyte antigen 4 (CTLA4) and lymphoid protein tyrosine phosphatase (PTPN22).

RESULTS:

The rs179247 TSHR polymorphism was associated with GO in young patients only. In young GO-free patients, allele A was statistically more frequent and homozygous carriers had a considerable lower risk of disease incidence than patients with AG or GG genotypes. Those differences were not found in either elderly patients or the group analyzed as a whole.

CONCLUSIONS:

Allele A of the rs179247 polymorphism in the TSHR gene is associated with lower risk of GO in young GD patients.