



PAEDIATRIC DERMATOLOGY

ASSOCIATION OF AROMATIC ANTIEPILEPTIC DRUGS INDUCED SEVERE CUTANEOUS ADVERSE REACTIONS AND HLA ALLELE OR A NEW SUSCEPTIBILITY GENE, CGREF1

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Background: Aromatic antiepileptic drugs (AEDs) induced Severe cutaneous adverse reactions (SCARs) refer to a group of life-threatening severe drug eruptions characterized by the skin and mucous membrane involvement which of the pathogenesis is unclear. It is considered that genetic susceptibility and innate immune response together contributed to it. Our aim is to identify the susceptibility loci for AEDs-related SCARs to provide the basis and proof for individualized and accurate medical care and genetic biomarkers for screening and prevention of AEDs-related SCARs.

Objective: To investigate the correlation between HLA-A, B, C and aromatic antiepileptic drugs induced-severe drug eruption in Han Chinese populations, and other candidate susceptibility genes.

Material and Methods: Using high resolution Sequencing-based typing (SBT) techniques, we analyzed the genotypes of HLA-A,B,C of 12 cases of aromatic anti-epileptic drugs (AEDs) induced SCARs and whole-exome sequencing and correlation analysis were performed on 6 patients suffering from AEDs-SCARs with specific HLA alleles to explore possible candidate susceptibility genes.

Results: The allele frequencies of HLA-A*03:01 (8.33% vs 0.79%, OR=11.465, $P<0.05$), HLA-B*13:01 (25% vs 7.78%, OR=3.951, $P<0.05$), HLA-B*52:01 (8.33% vs 0.61%, OR=14.766, $P<0.05$) were significantly higher in the patients with AEDs-SCARs than in the healthy controls; Initially CGREF1 (NM_006569) gene was locked, which may be associated with the pathogenesis of AEDs-SCARs. However, due to the limited number of samples, it is necessary to expand the sample size for further verifications.

Conclusions: In Han Chinese population, we studied the correlations between HLA alleles and AEDs-SCARs, and we found that allele frequencies of the three HLA alleles, HLA-A*03:01, -B*13:01, and -B*52:01 was significantly higher than that of the healthy controls; CGREF1 gene may be related to AEDs-SCARs.

