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Common Risk Allele in Aromatic Antiepileptic-Drug Induced Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis in Han Chinese

Shuen-Iu Hung, Wen-Hung Chung, Zhi-Sheng Liu, Chien-Hsiun Chen, Mo-Song Hsieh, Rosaline Chung-yee Hui, ...show all

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Abstract

Aims: Compared with other categories of drugs, such as antibiotics and NSAIDs, antiepileptic therapies are associated with a high incidence of Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). We previously reported that carbamazepine (CBZ)–SJS/TEN is strongly associated with the *HLA-B*1502* in Han Chinese, which has been confirmed in other Southeast Asian countries where the allele is prevalent. Here, we extend the study of HLA susceptibility to three different antiepileptic drugs, phenytoin (PHT), lamotrigine (LTG) and oxcarbazepine (OXC), which have structure similarity to CBZ. **Materials & methods:** We carried out a case–control association study. We enrolled 26 PHT-, six LTG- and three OXC-induced SJS/TEN patients, 113 PHT-tolerant and 67 LTG-tolerant subjects who were on the drug, respectively, for more than 3 months without the adverse reactions, and 93 normal subjects from the general population. The *HLA-A*, *B*, *C* and *DRB1* genotypes were determined. **Results:** We found that *HLA-B*1502* was present in eight out of 26 (30.8%) PHT–SJS/TEN (OR: 5.1; 95% CI: 1.8–15.1; $p = 0.0041$), two out of six (33%) LTG–SJS (odds ratio [OR]: 5.1; 95% CI: 0.8–33.8; $p = 0.1266$) and three out of three (100%) OXC–SJS (OR: 80.7; 95% CI: 3.8–1714.4; $p = 8.4 \times 10^{-4}$) patients. In addition, *HLA-B*1301*, *Cw*0801* and *DRB1*1602* also showed an association with PHT–SJS/TEN ($p = 0.0128$ – 0.0281 ; OR: 3.0–4.3). **Conclusion:** Our results indicate that OXC, PHT and LTG, which possess an aromatic ring just as CBZ does, when causing SJS/TEN, share a common risk allele. Aromatic antiepileptic drugs causing SJS/TEN in *HLA-B*1502* carriers may act on a similar pathogenetic mechanism, although other genetic/nongenetic factor(s) may also contribute to the pathomechanism of the disease. We suggest that aromatic antiepileptic drugs, including CBZ, OXC and PHT, should be avoided in the *B*1502* carrier and caution should also be exercised for LTG.

KEYWORDS: antiepileptic drugs, cutaneous adverse drug reaction, HLA susceptibility, lamotrigine, oxcarbazepine, phenytoin, Stevens–Johnson syndrome, toxic epidermal necrolysis

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Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed

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the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Additional information

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