Clinical Characteristics and Genetic HLA Marker for Patients with Oxaliplatin-Induced Adverse Drug Reactions

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Abstract:

Background: Oxaliplatin is commonly used to treat gastrointestinal malignancies. However, its applications are limited due to potential adverse drug reactions (ADRs), particularly severe anaphylactic shock. There is no method to predict or prevent ADRs caused by oxaliplatin. Therefore, we aimed to investigate the genetic HLA predisposition and immune mechanism of oxaliplatin-induced ADRs.

Methods: A retrospective review was performed for 154 patients with ADRs induced by oxaliplatin during 2016-2021 recorded in our ADR notification system. HLA genotyping was conducted for 47 patients with oxaliplatin-induced ADRs, 1100 general population controls, and 34 oxaliplatin-tolerant controls in 2019-2023. The in vitro basophil activation test (BAT) was performed and oxaliplatin-specific IgE levels were determined.

Results: The incidence of oxaliplatin-induced ADRs and anaphylactic shock in our cohort was 7.1% and 0.15%, respectively. Of the 154 patients, 67.5% suffered rash/eruption; 26.0% of the patients who could not undergo oxaliplatin rechallenge were considered to show oxaliplatin-induced immune-mediated hypersensitivity reactions (HRs). The genetic study found that the HLA-DRB∗12:01 allele was associated with oxaliplatin-induced HRs compared to the general population controls (sensitivity = 42.9%; odds ratio [OR] = 3.4; 95% CI = 1.4-8.2; P = 0.008) and tolerant controls (OR = 12; 95% CI = 2.3-63.7; P = 0.001). The in vitro BAT showed higher activation of $CD63^+$ basophils in patients with oxaliplatin-induced HRs compared to the tolerant controls ($P < 0.05$). Only four patients (8.5%) with oxaliplatin-induced ADRs were positive for oxaliplatin-specific IgE.

Conclusions: This study found that 26.0% of patients with oxaliplatin-induced ADRs could not undergo oxaliplatin rechallenge. HLA-DRB∗12:01 is regarded as a genetic marker for oxaliplatin-induced hypersensitivity.

Keywords:

Adverse drug reactions, Anaphylaxis, Biomarker, Drug hypersensitivity, HLA.