In vitro detection of cytotoxic T and NK cells in peripheral blood of patients with various drug-induced skin diseases

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Background: Cytotoxic cells are involved in most forms of drug-induced skin diseases. Till now, no in vitro test addressed this aspect of drug-allergic responses. Our report evaluates whether drug-induced cytotoxic cells can be detected in peripheral blood of nonacute patients with different forms of drug hypersensitivity, and also whether in vitro detection of these cells could be helpful in drug-allergy diagnosis.

Methods: GranzymeB enzyme-linked immunosorbent spot-forming (ELISPOT) and cell surface expression of the degranulation marker CD107a were evaluated on peripheral blood mononuclear cells from 12 drug-allergic patients in remission state and 16 drug-exposed healthy controls.

Results: In 10/12 allergic patients culprit but not irrelevant drug elicited granzymeB release after 48-72 h stimulation. It was clearly positive in patients with high proliferative response to the drug, measured in lymphocyte transformation tests. In patients, who showed moderate or low proliferation and low drug-response in granzymeB ELISPOT, overnight preincubation with interleukin (IL)-7/IL-15 enhanced drug-specific granzymeB release and allowed to clearly identify the offending agent. CD107a staining was positive on CD4+/CD3+, CD8+/CD3+ T cells as well as CD56+/CD3- natural killer cells. None of the drug-exposed healthy donors reacted to the tested drugs and allergic patients reacted only to the offending, but not to tolerated drugs.

Conclusion: GranzymeB ELISPOT is a highly specific in vitro method to detect drug-reacting cytotoxic cells in peripheral blood of drug-allergic patients even several years after disease manifestation. Together with IL-7/IL-15 preincubation, it may be helpful in indentifying the offending drug even in some patients with weak proliferative drug-response.

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