Factors influencing production of anti-drug antibodies against biopharmaceuticals in rheumatoid arthritis patients

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[Background] Biopharmaceuticals including anti-TNF antibodies have exerted high therapeutic effects on rheumatoid arthritis (RA). However, they have potential to elicit immunogenicity inducing production of anti-drug antibody (ADA). The emergence of ADA in patients potentially causes loss of efficacy and/or adverse events. Therefore, measurement of ADA is one of the important issues for ensuring safety and efficacy of biopharmaceuticals. We previously developed ADA assay methods as a part of studies to elucidate the clinical factors that influence the ADA production against biopharmaceuticals. In this study, we measured ADA in sera of RA patients and analyzed the relationship between ADA production and concomitant medications or administration route.

[Methods] The ADA responses in RA patients' sera against anti-TNF antibody (infliximab, adalimumab, golimumab), and anti-IL-6 receptor antibody (tocilizumab) were determined with the previously established ADA assay methods using electrochemiluminescence (ECL) technique.

[Results] One hundred thirty-eight samples from RA patients treated with biopharmaceuticals were collected and tested with the ADA assay methods. The rate of samples that are defined to be potentially positive for ADA varied depending on biopharmaceuticals. In the case of adalimumab and tocilizumab, the combination with methotrexate tended to reduce ADA production. Comparing subcutaneous and intravenous administration of tocilizumab, it was suggested that subcutaneous administration has more potential to induce ADA production. Two hundred twelve samples from RA patients who have not received biopharmaceuticals were also tested, and several samples were potentially positive for ADA. One of the possibilities explaining this result is existence of pre-existing antibodies in some patients before the administration of biopharmaceuticals. More investigations are clearly needed to reveal this phenomenon.

[Conclusions] Current results showed impact of administration routes and concomitant methotrexate administration on ADA production.