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Successful IVIG treatment without Discontinuation of TNF α blocker in GBS Induced by Adalimumab

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Introduction

Adalimumab, one of the anti-tumor necrosis factor (TNF) α blockers, is known to be associated with the development of Guillain-Barre syndrome (GBS). Although not clearly decided so far, discontinuation of adalimumab is recommended when GBS occurs during adalimumab treatment. Until now, however, there has been no report that showed improvement of GBS after intravenous immunoglobulin (IVIG) treatment without discontinuation of adalimumab.

Case

A 33-year-old woman who had suffered from Crohn's disease (CD) for 14 years complained of weakness of both the upper and lower extremities after the fourth injection of adalimumab. Before GBS occurred, her gastrointestinal symptoms of CD were well controlled through adalimumab treatment, unlike other treatments that had caused unbearable side effects. After obtaining informed consent, she began to receive treatment for GBS with IVIG, but without adalimumab discontinuation because she wanted to continue the adalimumab treatment. In spite of treatment continuing using adalimumab, she recovered considerably from her neurologic abnormality, which remained tolerable for one year without recurrence of GBS.

Discussion

The association between adalimumab and GBS needs to be elucidated, but one of the hypotheses is that adalimumab can trigger the syndrome by promoting its autoimmune reactions by alteration of the antigen-presenting cell function and reduction of autoreactive T-cell apoptosis through the blocking of TNF-α. In addition, TNF-α blocking therapy can interfere with the intrinsic immunity given by TNF- α and other cytokines in the peripheral nervous system, arousing the syndrome in immune-genetically highly susceptible individuals. Despite the broad efficacy of IVIG therapy on GBS, the mechanism of IVIG on GBS has not been clearly elucidated. Recently, however, it was demonstrated that IVIG induces the amelioration of antibody-dependent autoimmune processes by several steps. First, IVIG therapy induces immunomodulatory effects by resetting the threshold for innate immune effector cell activation. The up-regulation of the inhibitory receptor Fcγ (FcγRIIB) on human B cells induced by IVIG may increase their sensitivity to apoptosis and thus may have a direct impact on auto-antibody production. Secondly, IVIG inhibits the toll-like receptors (TLR) 9 and TLR 7, mediates B cell activation and suppresses TLR-induced production of pro-inflammatory cytokine, which causes up-regulating T-cell-dependent inflammation. Considering these aspects, IVIG may have an immediate impact on autoantibody-induced inflammation. Although the mechanism of GBS is not clear,

continuous treatment with adalimumab did not trigger GBS in the patient in our study after recovering almost completely from the disease. We hypothesize that a transient production of auto-antibodies which cause GBS may be ameliorated by immunomodulatory actions of IVIG therapy.