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Efficacy and Safety of Adalimumab Therapy for the Treatment of Non-infectious Uveitis: Efficacy comparison among Uveitis Aetiologies

（非感染性ぶどう膜炎に対するアダリムマブ療法の有効性と安全性：病因別の有効性の比較）

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Introduction

Non-infectious uveitis (NIU) is predominantly T-cell mediated intraocular autoimmune inflammatory disease. It can be associated with systemic disorders, such as Behçet's disease, and is presumably the cause of blindness in 10% of the affected individuals in developed countries. Although corticosteroids remain the first-line treatment for NIU, additional immunosuppressive treatments may be administered to avoid the risk of corticosteroid-related adverse events. In Japan, adalimumab (ADA), a fully human monoclonal IgG1 tumor-necrosis factor-alpha (TNF-α) antibody, was approved for the treatment of non-infectious intermediate and posterior uveitis and panuveitis in 2016. The efficacy and safety of ADA for NIU have previously been demonstrated; however, reports regarding the use of ADA in Asian populations are limited. We studied the efficacy and safety of ADA in the treatment of Japanese patients with NIU. The efficacies of ADA treatment were also compared among patients with distinct uveitis aetiologies.

Methods

The retrospective study included patients with chronic active NIU, who had been treated with ADA for >6 months from September 2016 to October 2020 at the uveitis centre of Hiroshima University Hospital.

The primary objects were to control ocular inflammation and evaluate treatment safety. The secondary objects included evaluating changes in systemic treatments, best-corrected visual acuity (BCVA), laser flare photometry results, and potential optimization of ADA regimen.

The outcome variables included anterior chamber cell grade, vitreous haze grade, retinal/choroidal lesion status, cystoid macular oedema (CME), BCVA, change in systemic immunosuppressive treatment, relapse rate, and laser flare photometry values. Treatment failure was defined as two-step increase in the level of inflammation, an increase from grade 3+ to 4+ in the anterior chamber or vitreous haze score new CME or retinal/choroidal lesion activity, and/or a requirement for corticosteroid or other immunosuppressive rescue therapy.

Results

Forty-eight patients were enrolled in the study. The median follow-up period was 15.5 months. The majority of patients had panuveitis and bilateral involvement. The most common diagnosis were Vogt-Koyanagi-Harada disease (VKH) (n=12) and Behçet's disease (n=11). Undifferentiated inflammation was seen in 18 patients. Among 44 patients who were followed up for ≥6 months, approximately 60% and 90% were corticosteroid free at 3 months and 12 months, respectively. More than 80% of the patients achieved anterior chamber cell grade and vitreous haze grade ≤0.5+ at all evaluation points. The proportions of eyes with CME and eyes with active retinal/choroidal lesions also decreased from baseline. The mean BCVA improved from 2.76 to 0.07 logMAR at 3 months, while the mean relapse rate score significantly decreased from 2.76 at baseline to 0.18 at 12 months (P<.0001). Treatment failure occurred in 16 patients with a median survival time of 38 months.

Inflammation was successfully controlled with ADA alone in 63.6% of the patients at 12 months.

No patients with Behçet's disease received new treatment with MTX, while 10 out of 14 patients with VKH/SO required concomitant MTX; 50% of whom received it by 3 months. Although the survival curves of patients with VKH/SO and those with Behçet's disease did not show statistically significant difference,

the survival rate tended to be lower in patients with VKH/SO than in patients with Behçet's disease.

The mean laser flare photometry value of patients with uveitis duration <15 months significantly decreased from 17.7 ph/ms at baseline to 5.8 ph/ms at 12 months; it remained high in patients with uveitis duration ≥15 months. High laser flare values were related to high frequencies of intraocular surgeries.

Optimization of ADA was performed in 9 patients who achieved remission after ADA treatment, at a median of 15 months from ADA initiation. Relapses occurred in 6 patients during optimization at a median of 15 months after optimization.

There were no serious side effects of ADA which led to treatment discontinuation.

Discussion and Conclusion

Our findings indicate that ADA is effective for controlling ocular inflammation and can reduce the relapse rate in the Japanese population. More than 90% of the included patients were systemic corticosteroid-free at 12 months. Ocular inflammation was controlled with ADA alone in 63.6% of the patients at 12 months, without re-administration or increased dose of systemic corticosteroid.

Our study also suggests possible differences in rates of response to ADA treatment among patients with distinct uveitis aetiologies. More patients with VKH/SO on ADA seemed to require additional immunosuppression for controlling ocular inflammation. Approximately 40% of the relapses in patients with VKH/SO occurred during the first 3 months after initiation of ADA; 50% of the patients with VKH/SO received concomitant MTX at 6 months. TNF-α may play a greater role as a proinflammatory cytokine in Behcet's disease than in VKH/SO.

In conclusion, this study demonstrated that ADA treatment is efficacious and safe for Japanese patients with NIU. The findings suggest differences in the efficacy of ADA treatment between patients with VKH/SO and those with Behcet's disease, as well the potential need to implement ADA and MTX combination therapy in patients with VKH/SO.