Anti-Adalimumab Antibody Development in Adults Treated for Non-infectious Uveitis With Adalimumab Biologic Therapy

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Background

Adalimumab - a fully human therapeutic monoclonal antibody directed against TNFα - has been shown to be an effective glucocorticoid-sparing agent for the treatment of non-infectious uveitis[1]. Anti-adalimumab antibodies (AAA) are used in combination with clinical features to determine treatment failure, where levels >10AU/mL are considered positive. However, the influence of AAA on the efficacy of adalimumab therapy is not yet fully understood.

Currently, there are no clinical guidelines regarding AAA testing or the management of patients with positive levels. Therapeutic decisions are made on a case-by-case basis.

Objectives

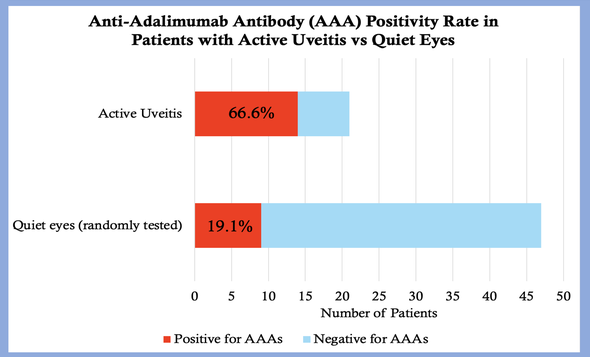
1. To investigate the rate of positive AAA in patients with non-infectious uveitis treated with adalimumab in a single tertiary uveitis service.

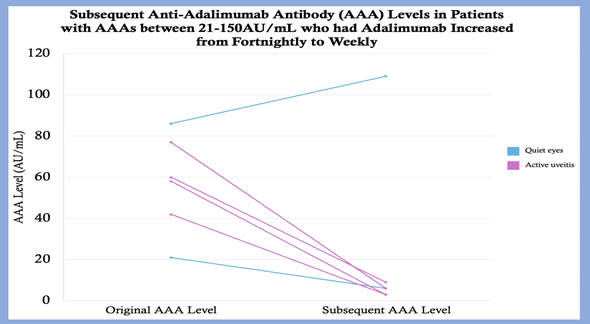
2. To review the clinical decision making for patients with detectable AAA dependent on disease activity.

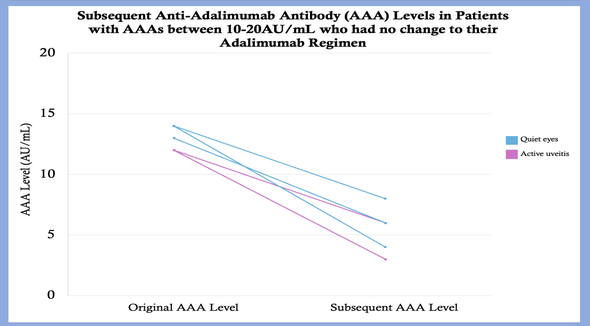
Methods

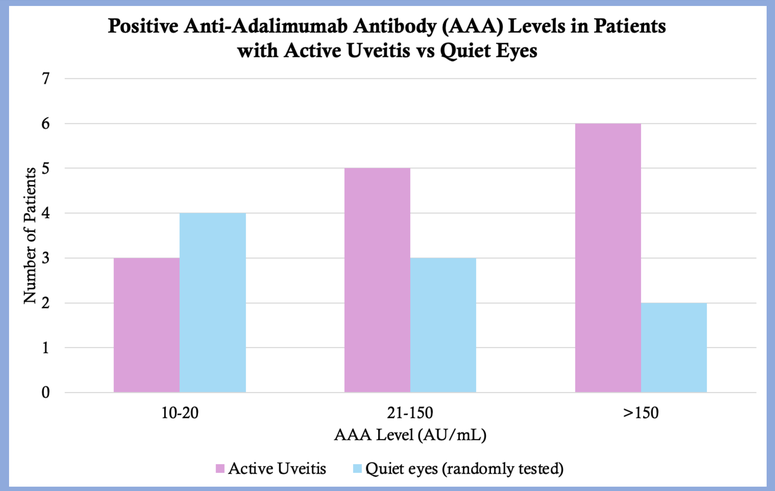
- Retrospective analysis of medical records.
- 149 adults treated with adalimumab for non-infectious uveitis between September 2008-September 2024.
- Primary outcomes: patient demographics, length of adalimumab therapy, presence or absence of active uveitis, AAA levels, reason for testing, adjuvant immunosuppressive treatment, therapeutic approach in cases with positive AAA.

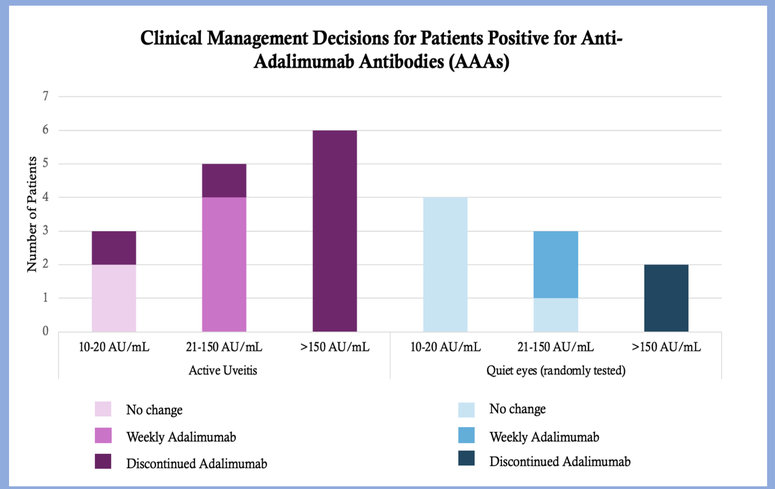
Results





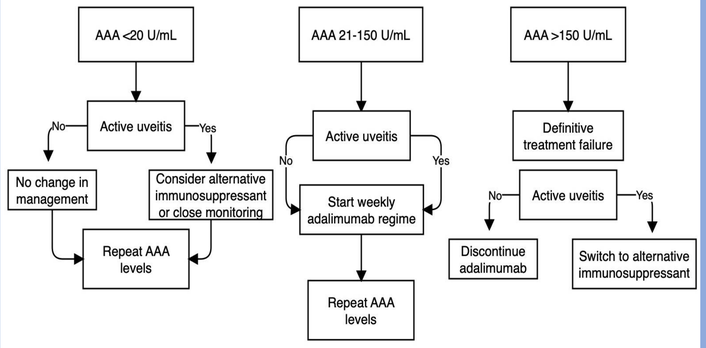






Conclusions

- In our cohort, although anti-adalimumab antibodies (AAA) are more likely to be raised in the presence of active uveitis (66.6%), AAA can also be raised in those with quiet eyes (19.1%). To enable the early identification of AAA and the adjustment of treatment accordingly, we recommend routine monitoring of AAA in all patients taking adalimumab regardless of disease activity, corroborating conclusions from another recent study.[2]
- We propose a clinical management algorithm for the management of positive AAA:



- Despite our small cohort, we infer that the threshold of positive AAA that requires a change in treatment in patients with quiet eyes could be raised from 10 U/mL to 20 AU/mL.
- A range of clinical management decisions were undertaken for patients with AAA between 10-20 AU/mL with active uveitis. These included no change in treatment, commencing an additional immunosuppressant alongside adalimumab or discontinuing adalimumab and starting an alternative biologic therapy. Although subsequent AAA levels for these patients became negative, management decisions in our cohort were variable.
- Where AAAs were positive within the range of 21-150 AU/mL, in both active uveitis and quiet eyes, we found increasing adalimumab from fortnightly to weekly led to undetectable AAA levels in most patients.[3]
- Regardless of whether they had active uveitis or quiet eyes, adalimumab was discontinued in all patients with AAAs greater than 150AU/mL as this was considered definite treatment failure.
- Larger prospective studies are necessary to formulate clinical guidelines for the management of uveitis patients taking adalimumab who develop antibodies, taking into consideration disease activity and level of AAA.

References:
1. Jaffe GJ et al. Adalimumab in Patients with Active Noninfectious Uveitis. N Engl J Med. 2016 Sep 8;375(10):932-43
2. Zur Bonsen LS, et al. Adalimumab Autoantibodies in Uveitis Patients: Do We Need Routine Drug Monitoring? Biomedicines. 2024 Dec 6;12(12):2782.
3. Bartelds GM, Wijbrandts CA, Nurmohamed MT, Stapel S, Lems WF, Aarden L, Dijkmans BA, Tak PP, Wolbink GJ. Clinical response to adalimumab: relationship to anti-adalimumab antibodies and serum adalimumab concentrations in rheumatoid arthritis. Ann Rheum Dis. 2007 Jul;66(7):921-6.