TREATMENT OF CHILDHOOD AUTOIMMUNE CHRONIC UVEITIS

Background

Childhood autoimmune chronic uveitis is a severe sight threatening condition that affects children of all ages. 20% to 25% of paediatric uveitis is associated with juvenile idiopathic arthritis (JIA) (1,2). Approximately 12% to 38% of patients with JIA develop uveitis within seven years of the onset of arthritis and about 50% to 75% of those with severe uveitis will develop visual impairment secondary to ocular complications such as cataract and glaucoma (3,4).

Corticosteroids and topical mydriatics are generally used as first line treatment for autoimmune uveitis. Disease modifying rheumatic drugs (DMARDs) such as methotrexate are used in treatment resistant cases or where corticosteroids are unable to be weaned (5). Methotrexate has a favorable effect in approximately 70% of cases of childhood autoimmune chronic uveitis (5). Methotrexate will not be an appropriate option in some patients due to intolerable side-effects (nausea in particular) or inefficacy.

TNF-α plays a pivotal role in the pathogenesis of intraocular inflammation (6). Adalimumab, a TNF-α blocking biologic disease modifying antirheumatic drugs (bDMARD), is a safe and effective treatment for chronic autoimmune uveitis (7). Multiple case series have supported the use of adalimumab in autoimmune uveitis (8,11,12) and it has been demonstrated to be superior to other TNF-α blocking agents including etanercept and infliximab in a recent systematic review (8). Placebo controlled randomized control trials assessing adalimumab in juvenile idiopathic arthritis associated uveitis are nearing publication and have been prematurely terminated due to superiority of adalimumab (9,10).

There is extensive evidence showing that adalimumab is effective in managing juvenile idiopathic arthritis (13). In Australia it is funded through the Pharmaceutical Benefits Scheme (PBS) for severe active polyarticular juvenile idiopathic arthritis where treatment with conventional DMARDs has failed. While adalimumab has recently been accepted for use in autoimmune uveitis by the US Food and Drug Administration (FDA), Australian patients with idiopathic uveitis and JIA associated uveitis with good arthritis control or non-polyarticular subtypes of JIA are not currently eligible for adalimumab through the PBS.

Other biologic therapies including infliximab, tocilizumab and abatacept may be used in refractory cases of childhood autoimmune chronic uveitis (8, 14, 15).

Recommendations

For management of childhood chronic uveitis at the Royal Children’s Hospital:

- First line therapy
  o Topical / locally injected / systemic corticosteroids
  o Topical mydriatics
- Second line therapy
  o Methotrexate

- Third line therapy
  o Biologic DMARDs (adalimumab)

Refer to figure 1 for commencement of systemic therapy in childhood chronic uveitis. Patients who are eligible for PBS funded adalimumab should apply through this scheme. Patients who are not eligible for PBS funded adalimumab but meet the criteria in figure 1 can use a streamlined drug usage committee (DUC) application attached. Patients who do not meet the criteria in figure 1 or who require treatment with another agent such as infliximab, tocilizumab or abatacept will need to make a DUC Individual Patient Approval.

Methotrexate should be commenced at a dose of 15mg/m² once per week in either oral or subcutaneous form.

Adalimumab should be commenced at a dose of 20mg subcutaneously every two weeks (<30kg) or 40mg subcutaneously every two weeks (>30kg). Several study protocols have suggested increasing adalimumab dosing to weekly if an insufficient response is noted (16). We propose that failure to completely respond within three months or loss of control after initial response is indication for a trial of weekly dosing.

Escalation and weaning of systemic therapies should be determined by the ophthalmology team based on regular monitoring using Standardized Uveitis Nomenclature (SUN) guidelines (17). Please refer to figure 2 for weaning recommendations.

Initial review prior to commencing bDMARD treatment should include screening investigations (FBE, UEC, LFT, ESR, CRP, QuantiFERON Gold +/- chest x-ray, hepatitis serology, varicella serology) and nursing education (drug administration, avoidance of live vaccines, etc). All patients should be reviewed at one month post commencement to ensure the medication is tolerated and to monitor for side effects. Blood tests (FBE, UEC, LFT, CRP, ESR) should be repeated at this stage. Patients on all DMARDs should be reviewed at least three monthly in the rheumatology clinic to monitor for complications of immunosuppression. Ophthalmology review is as indicated by activity of eye inflammation and sequelae.

References


10. Maire PQD. Effect of Adalimumab for the Treatment of Uveitis in Juvenile Idiopathic Arthritis (ADJUVITE).


RCH Drug Usage Committee (DUC) streamlined application for adalimumab for autoimmune chronic uveitis (initial application)

Date  
______________________________________

Patient name  
______________________________________

Patient UR  
______________________________________

Medication  
☐ Adalimumab 20mg subcut fortnightly (<30kg)  
☐ Adalimumab 40mg subcut fortnightly (>30kg)

Indication  
☐ Juvenile idiopathic arthritis associated uveitis  
☐ Idiopathic uveitis

Duration  
☐ Six months

Eligibility  
☐ Ongoing acute sight threatening complications and use of topical / locally injected / systemic corticosteroids and methotrexate for at least 4-6 weeks  
☐ Topical / locally injected / systemic corticosteroids and methotrexate for at least 3 months (or severe intolerance) with poor response or development of acute sight threatening complications

Rheumatologist  
______________________________________

Rheumatologist email  
______________________________________

Ophthalmologist  
______________________________________

Ophthalmologist email  
______________________________________

Comments  
__________________________________________________________________________
__________________________________________________________________________
RCH Drug Usage Committee (DUC) streamlined application for adalimumab for autoimmune chronic uveitis (continuing application)

Date
___________________________

Patient name
___________________________

Patient UR
___________________________

Medication
  □ Adalimumab 20mg subcut fortnightly (<30kg)
  □ Adalimumab 40mg subcut fortnightly (>30kg)

Indication
  □ Juvenile idiopathic arthritis associated uveitis
  □ Idiopathic uveitis

Duration
  Six months

Eligibility for continuation
  □ Ongoing uveitis (greater than 1+ anterior chamber activity)
  □ Ongoing corticosteroid requirement (greater than 1 drop of Prednefrin Forte daily)
  □ Immediate plans for cataract or glaucoma surgery

Rheumatologist email
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Ophthalmologist
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Ophthalmologist email
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Comments
___________________________________________________
___________________________________________________
Commencing systemic treatments for uveitis (figure 1)

- Idiopathic uveitis or juvenile idiopathic arthritis associated uveitis
  - Acute sight threatening complications requiring immediate treatment effect
    - Yes: Topical / locally injected / systemic corticosteroids AND Topical mydriatics AND methotrexate
      - ADD adalimumab if no response in 4-6 weeks and ongoing sight threatening complications
    - No: Topical / locally injected / systemic corticosteroids AND Topical mydriatics
      - Poor response or unacceptable reliance on corticosteroids
        - ADD methotrexate 15mg/m2
          - Poor response or unacceptable reliance on corticosteroids after at least 3 months of treatment
            OR severe intolerance to methotrexate and ongoing need for systemic therapy
            OR development of acute sight threatening complications
            - ADD adalimumab

- Adalimumab dose *
  - 20mg fortnightly (<30kg)
  - 40mg fortnightly (>30kg)

- Acute sight threatening complication:
  - IOP>21 mmHg requiring topical therapy; development of cataract; development of cystoid macular oedema or severe posterior uveitis

- Poor response:
  - Ongoing ocular inflammation despite current treatment or 1+ or greater anterior chamber activity

- Unacceptable reliance on corticosteroids:
  - Prednefrin Forte two drops daily or more
  - OR Complications from corticosteroids such as cataract or glaucoma
  - OR Ongoing need for systemic or locally injected corticosteroids
Ceasing systemic treatment for uveitis (figure 2)

Methotrexate and/or adalimumab treatment

Quiescent eye disease for at least six months

Yes

Minimal or no corticosteroid use (Prednefrin Forte 1 drop daily or less)

Yes

Quiescent eye disease: 0 to 1+ anterior chamber activity and at least 2 grades better than activity present when treatment commenced

If both adalimumab and methotrexate are used concurrently then adalimumab should be weaned first

No

Continue

Immediate plans for cataract or glaucoma surgery?

Yes

Continue with plan to cease if quiescent for 3 months following last planned surgery

No

Wean or cease medication