The management of chronic uveitis

A 40-year-old company executive is referred from another unit with recurrent anterior and posterior uveitis for 12 months and the inflammatory markers are raised.

Review of systems

This is a case of chronic uveitis which needs a thorough workup and systemic management. He has been extensively investigated by his referring ophthalmologist and GP and has had a range of blood tests and imaging. His blood tests have shown a low white cell count, raised C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), normal live function, normal urea and electrolytes, and negative T-spot, Venereal Disease Research Laboratory (VDRL) and Mantoux. His chest x-ray has been reported as showing bilateral hilar lymphadenopathy consistent with sarcoidosis and his ACE is significantly elevated. The patient is due to have further investigations including a high resolution CT scan and lung function testing.

Deciding whether immunosuppression is warranted

The general approach to assessing such a patient is first to determine whether this is an infective condition and whether there is any evidence of 'sight threatening' ocular inflammation.

Inflammation is graded according to the SUN classification [1]. Sight threatening inflammation may include cystoid macular oedema, occlusive vasculitis, vasculitis involving the posterior pole or involvement of the optic nerve. Multifocal choroiditis and secondary choroidal neovascular membranes may also occur.

The duration of uveitis is also relevant. Uveitis may be acute, recurrent, where the relapse occurs after a period of at least three months after resolution of the previous episode, or chronic, where inflammation is always present, or where there is recurrence without a three month period of quiescence.

The initial treatment of significant bilateral non-infective posterior uveitis is generally with systemic steroids. If inflammation is limited to one eye, peri-ocular steroid injections may be used. Otherwise, systemic steroids given either intravenously, intra-muscularly or orally usually bring about remission.

Chronic steroid use for more than three months at a dose greater than 7.5mg per day is associated with adverse effects. A higher cumulative dose makes this more likely and therefore, immunosuppressive medications are often considered.

The aims of these therapies are to limit long-term steroid dosing (i.e. steroid sparing) and to prevent flare-ups of uveitis and cystoid macular oedema. Without adequate control, each episode carries a risk of potential damage to the retina or macula, with potential visual loss.

Preparing to start immunosuppression

Immunosuppression is generally started and overseen by a rheumatologist, medical ophthalmologist or uveitis specialist.

Importantly, patients need to be aware of the requirement for blood monitoring, contraception and family planning, and increased risk of infection and possible increased risk of malignancy.

Which agent to use?

The choice of immunosuppressant for particular subtypes of chronic inflammatory disease will generally be dictated by the current literature and evidence base. In our patient's case azathioprine, mycophenolate mofetil or methotrexate might be considered.

Pretreatment testing

Pretreatment assessments should be undertaken for infection (including an interferon gamma release assay (IGRA) test when anti tumour necrosis factor (TNF) therapy is considered), baseline blood tests including full blood count, renal function and liver function and a baseline chest x-ray prior to methotrexate and anti-TNF therapy. Where cyclosporine is considered the blood pressure and the mean of two serum creatinine levels should be established prior to treatment so that dosage may be adjusted to ensure serum creatinine rises to no more than 130% of baseline and effects on BP are monitored. For azathioprine thiopurine methyl transferase activity (TMPT) should be estimated prior to commencement of therapy. Up to date vaccination is recommended prior to starting immunosuppression. Whilst on immunosuppression, live vaccines are contraindicated.

Monitoring of the patient on immunosuppression

Patients should be followed up in secondary care or in some cases monitoring can be passed to primary care according to an agreed shared care guideline.

Ensuring good outcomes

The effectiveness of therapy is usually gauged after a period of three to six months. Outcome measures include vision, resolution of cystoid macular oedema, a decrease in inflammatory activity and ability of the patient to reduce systemic steroid to a dose of less than 7.5mg orally per day, without disease flare-up. Compliance with medication is central to successful outcomes.

Reference

1. SUN WORKING GROUP. Standardization of Uveitis Nomenclature for Reporting Clinical Data. Results of the First International Workshop. *American Journal of Ophthalmology* 2005;**140(3)**:509-16.

TAKE HOME MESSAGE

Optimal management of such patients generally requires a patient focused team based approach.

Miss Erika Damato,
FRCOphth,
Consultant Ophthalmologist,
Birmingham & Midland Eye Centre.

Once any chronic inflammatory disease has been diagnosed, the optimal management of such patients generally requires a patient-focused team based approach.

I find it useful to think of the systems required in terms of the 'Wagner' model for chronic disease management, which requires an 'activated' team (which has protocols and policies in place, together with expert and knowledgeable team members), an 'activated' patient (the patient fully understands the nature of their condition) and an effective supportive IT and administrative system for managing and auditing the process that links patients with all clinicians in the team.

Our goal to optimise chronic disease management requires the active participation of the patient in therapeutic decision-making so that the risks and benefits of the introduction of immunosuppression can be fully understood.

For this to be achieved, prior to consideration of the introduction of immunosuppression, the team should ensure that the associated risks of disease progression and the concept of the association between the control of inflammation and the development of irreversible damage caused by an uncontrolled inflammatory process. Only then may the important and often risk based decisions surrounding the introduction of such therapy be made safely in partnership. In general this requires sufficient time for discussion supported by a specialist nurse with access to paper based or online information leaflets (BSR). This information should be supported by access to a dedicated helpline or other means of support (e.g. dedicated email or online support), with written instructions summarising for the patient what to do if things go wrong (who to contact for advice, where to go if things go wrong, what to do if you develop an infection, fever or systemic symptoms, what particular drugs to avoid or interactions to be aware of, e.g. trimethorim / septrin with methotrexate, what are the implications for family and pregnancy planning). The BSR is a useful source of this material which includes the following key principles to be observed when monitoring:

1. It is important to note that in addition to absolute values for any haematological or biochemical indices, a rapid unusual fall or rise or a consistent downward or upward trend in any value should prompt caution and extra vigilance.
2. Extra caution is required before advising patients about immunisations, as live vaccines are not recommended when patients are on certain immuno modulators.
3. Drug interactions are important and should always be weighed against the clinical need.
4. Pregnancy and related issues such as breastfeeding must be addressed when patients are receiving a disease-modifying anti-rheumatic drug (DMARD). It is necessary to be absolutely certain about the effect of the DMARD on the foetus as well as on lactation.
5. All monitoring activity for early detection of toxicity should also be documented in case notes and the patient should be informed as well.
6. Although side-effects are not mentioned with each individual DMARD, users of this document are requested to also consult the British National Formulary (BNF) and individual drug summary of product characteristics (SPC) wherever needed.
7. ALL patients should be provided with a patient-held booklet of their DMARD monitoring records with clear mention of all current results where appropriate.
8. Patients should be encouraged to take part in a self management programme to monitor their own therapy, as studies have shown that patients like to be involved in their continuing care rather than just informed about the therapy.
9. All patients should ideally go through a regular educational programme before prescribing the DMARD.
10. It is desirable that some form of outcome assessment is undertaken and all contacts between the health professional and the patient for the purpose of monitoring should be taken as an opportunity for teaching and training about the role of the DMARD in rheumatoid arthritis (RA) or other similar diseases.

With uveitis, the effectiveness of therapy is usually assessed by the ophthalmologist after a period of three to six months, so regimes that require dose escalation or titration according to response will require tight communication channels between rheumatologist and ophthalmologist.

Dr Deva Situnayake,
FRCP,
Consultant Rheumatologist,
Sandwell & West Birmingham Hospitals NHS Trust.

Mr Yajati K Ghosh,
Top Tips section editor, MBBS, FRCSEd Ophthal, Consultant Ophthalmic Surgeon, Birmingham & Midland Eye Centre, UK.

E: yajati_ghosh@hotmail.com

After nearly five years of section editing Top Tips, it is now time for me to pass on the reins to my colleague Erika Damato. It only seems yesterday that I took over from Tom Stumpf and then in a blink it is time for a change again. I have thoroughly enjoyed these years and my negotiating skills and perseverance has reached such epic proportions, that my colleagues are very cautious about responding to my emails and phone calls, lest it be a 'Top Tips' call! A very big thank you to all the contributors, who have made me look good.

Like all other things, work and other commitments are making increasingly unreasonable demands and I have used up all of my 'ask for a favour' cards many times over. I have tried to keep the interest going in this popular section and, in the process, have had a refresher course in significant topics in ophthalmology, from people who do it well and love doing so.

It gives me great pleasure to hand over to Erika, who is a uveitis specialist and has a special interest in Behçet's disease and its ocular manifestations. I am sure she will bring in new ideas and continue to attract readers to this section. It is also fitting that this month's Top Tips features her article.

I will be missing the editorial gang and their wonderful support, including the 'gentle reminders'.

Thank you all and goodbye,

Yajati Ghosh

The editors and publishers of *Eye News* would like to express their gratitude to Yajati for his dedicated work on the Top Tips section of the magazine. He will be greatly missed, but we look forward to taking the section forward with new section editor Erika Damato at the helm.