The eye in rheumatology

TO Odufuwa, S Lightman

The eyes are involved in many different types of arthritis and different types of arthritis are associated with particular types of eye problems. Dry eyes are a feature of many patients with arthritis but other types of ocular involvement include scleritis and uveitis. Scleritis is most common in patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and Wegener's granulomatosis whereas uveitis occurs in ankylosing spondylitis, other seronegative arthritides, Behçet's disease and juvenile idiopathic arthritis (JIA).

Patients with polymyalgia rheumatica can have temporal arteritis, most commonly causing ischaemic optic neuropathy. Ophthalmic findings may be invaluable in helping to make a definitive diagnosis in rheumatology patients. Some findings can be sight threatening so require separate assessment and often management. Drugs required to control the arthritis or other complications such as vasculitis may also have side effects on the eye causing loss of vision.

RHEUMATOID ARTHRITIS

Dry eyes are the most common ophthalmic manifestation of RA. Patients complain of a foreign body sensation, grittiness and a dry feeling. Often ocular lubricants may be sufficient but if symptoms persist they need to be examined carefully on the slit lamp for presence of corneal inflammation and/or corneal thinning which is usually peripheral. Peripheral corneal thinning occurs because of an obliterative microangiitis at the level of the limbal vascular arcades, with deposition of immune complexes in the limbal vasculature. The area of tissue loss corresponds to the degree of vascular occlusion.

Patients who have RA do not typically develop uveitis, but do tend to develop scleritis, which can be anterior, posterior or both. Patients with scleritis typically complain of the severe pain which radiates from the orbit to the forehead and face and characteristically wakes them at night. It can be one of the most severe types of pain. The eye is red in anterior scleritis and this can be diffuse (*Figure 1)* or localized, and nodules (*Figure 2*) can form.

Posterior scleritis can be present in a white eye and the characteristic features of the pain help make the diagnosis which can be confirmed by measuring the thickness of the sclera on ultrasound (McCluskey et al, 1999). The inflammatory process can extend inside the eye causing uveitis, serous retinal detachments and optic nerve involvement (*Figure 3*). Necrotizing scleral disease can occur (*Figure 4*) which threatens the integrity of the eye and is an ophthalmic emergency. Corneal perforation can also occur. Treatment is with non-steroidal anti-inflammatory agents if no necrosis is seen and with high-dose steroids, with other immunosuppressive agents as required.

Figure 1. Diffuse scleritis.

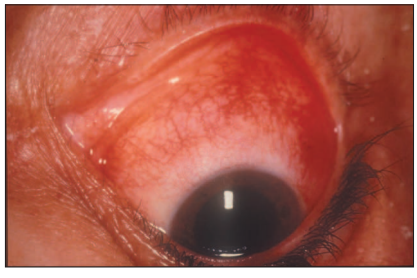
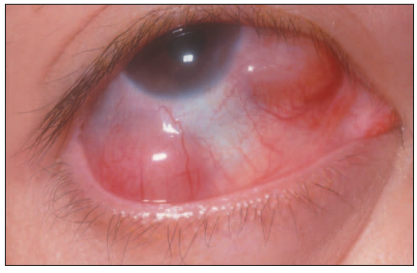


Figure 2. Nodular scleritis.



OTHER COLLAGEN DISEASES

Patients with SLE may get dry eyes and scleritis but can also have cerebral disease causing visual loss. Patients may have cotton wool spots and haemorrhages in the retina from microvasculopathy, and can also have features secondary to hypertension (Jacobsen et al, 1998). Patients with polychondritis can also have scleritis which can be extremely refractory to treatment (Hoang-Xaun et al, 1990).

WEGENER'S GRANULOMATOSIS

These patients can get necrotizing scleritis which may also involve the cornea causing perforation (*Figure 5*). They may also present with proptosis as a result of a granuloma in the orbit which can also involve the extraocular muscles causing squint and visual loss from optic nerve involvement. There

Figure 3. Optic nerve involvement in scleritis showing swollen nerve with cotton wool spots.

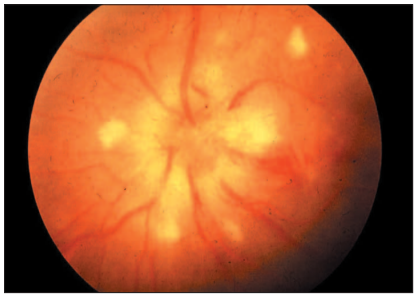
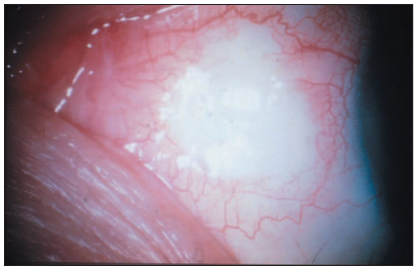


Figure 4. Necrotizing scleritis to show underlying choroid.



Miss TO Odufuwa is Specialist Registrar in Ophthalmology and **Professor S Lightman** is Professor of Clinical Ophthalmology and Consultant Ophthalmologist, Department of Clinical Ophthalmology, Institute of Ophthalmology, Moorfields Eye Hospital, London EC1V 2PD

Correspondence to: Professor S Lightman

may also be nose, lung, kidney or other organ involvement or the disease may be localized to the eye. Treatment is with high-dose steroids, usually with cyclophosphamide initially (Esper and Johnson, 1999). The scleritis tends to respond quickly and heal, but granulomas in the orbit may heal with scarring involving the optic nerve causing profound visual loss. Corneal perforation may require patch grafting but it may be possible to temporarily use corneal glue (Moschos et al, 1996–7) if the hole is small, until the tissue bed is less inflamed and necrotic.

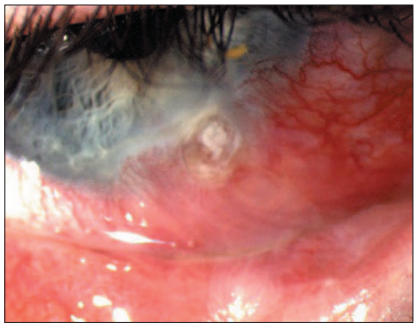
ANKYLOSING SPONDYLITIS AND THE SERONEGATIVE SPONDYLOARTHROPATHIES

Acute anterior uveitis occurs in 25–40% of patients with ankylosing spondylitis at some time in the course of the disease (Hamideh and Prete, 2001). It can vary in severity but is acute recurrent in type, each episode lasting less than 3 months and can be unilateral or bilateral.

Patients experience pain, redness and photophobia usually with signs confined to the front of the eye. Hypopyon can occur in very severe disease (Ramsay and Lightman, 2001). Very occasionally signs of posterior uveitis are reported to occur in patients with ankylosing spondylitis but this is more common in other spondyloarthropathies such as that associated with Crohn's disease, ulcerative colitis, psoriasis and Reiter's disease (Paiva et al, 2000). Patients usually respond rapidly to intensive topical steroids and mydriatics which are reduced in frequency over the following 6–8 weeks. Very occasionally the attack is very severe and refractory to topical steroids so that a short course of systemic steroids or periocular injection of longer acting steroids may be required.

Visual loss can occur during the attack as a result of macular oedema or after repeated attacks as a result of cataract, glaucoma or cystoid macular oedema. Some patients react to topical steroids and have a severe rise in intraocular pressure (called steroid-responders) and for this reason, patients should not self medicate unless it is absolutely certain that they do not have this problem. Mydriatics are extremely important to prevent the inflamed iris sticking to the lens (posterior synechiae), as this is associated with an increase in the future in visually compromising sequelae such as cataract, glaucoma and macular oedema.

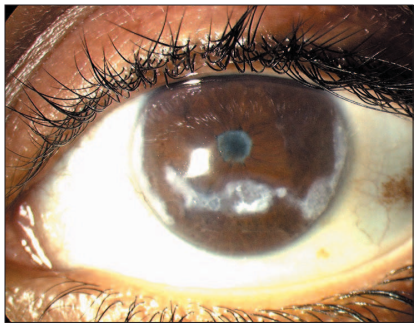
Figure 5. Corneal perforation with necrotizing scleritis.



JUVENILE IDIOPATHIC ARTHRITIS

Ocular involvement occurs most frequently in children with pauciarticular disease, many of whom are antinuclear factor (ANF) positive. Classically this uveitis is of the chronic anterior type and occurs in a white eye, which does not go red in stark contrast to the uveitis associated with the HLA B27 positive group of diseases. Children with juvenile sarcoidosis who may have a similar picture to that of JIA do, however, get red eyes and may also get posterior segment disease with floaters and visual loss.

Figure 6. Eye in juvenile idiopathic arthritis showing band keratopathy, bound down pupil and cataract.



Patients may have signs of uveitis when they first present with the arthritis or the uveitis may develop later. Children with JIA should be screened for uveitis at presentation and at appropriate intervals afterwards (American Academy of Pediatrics, 1993; Boone et al, 1998). This uveitis is chronic, lasts longer than 3 months and may be unilateral or bilateral. Posterior synechiae form easily and cataract, glaucoma, band keratopathy (*Figure 6*) and macular oedema may cause visual loss.

Treatment is with topical steroids and mydriatics, with the aim of quietening the cellular response as seen on the slit lamp, and with additional medication as required to control the intraocular pressure if it is raised. Cataract surgery is not straightforward in these children and requires a different approach from age-related cataracts (Kanski, 1992). The whole lens and its capsule is removed (lensectomy) with removal of the vitreous as well to prevent it providing a scaffold for cyclitic membrane formation which can cause major problems within the eye. Systemic medication may be required and methotrexate, often used to control the arthritis, may be helpful. More recently some children have been given etanercept (anti-tumour necrosis factor; TNF) with some success but care must be taken as the eyes may relapse while the arthritis is controlled (Reiff et al, 2001).

BEHÇET'S SYNDROME

About 70% of patients with Behçet's syndrome have ocular involvement which can vary from mild episcleritis to visually destructive uveitis. Classically the eye is said to be white and hypopyon is often present in active disease but when so inflamed the eye is often red. Visual loss is common from ischaemic retinal vasculitis affecting the optic nerve and macula (*Figure 7*). Vasculitis affecting the retinal veins and arteries can occur with neovascularization and vitreous haemorrhage causing visual loss.

Treatment is with steroids and other immunosuppressive agents over many years but many patients still lose

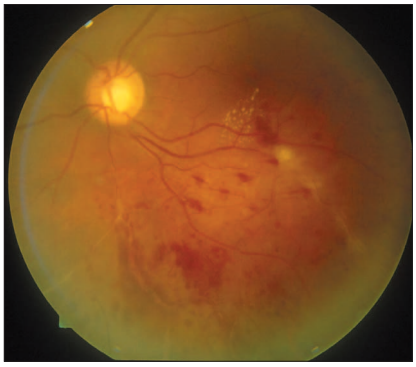


Figure 7. Retinal vascular occlusion with retinitis involving the macula in Behçet's disease.

vision. Infliximab (anti-TNF) (Sfikakis et al, 2001) and interferon-alpha (Zouboulis and Orfanos, 1998) have been used in small open studies in patients with severe Behçet's uveitis with remarkable results where other drugs have failed.

METASTATIC ENDOPHTHALMITIS

Patients of all ages with septic joints are at risk of haematogenous spread of the infection to the eye. Both fungi (Tanaka et al, 2001) and bacteria (Okada et al, 1994) can spread in this way and cause severe intraocular inflammation which often has devastating effects on vision. Complaints of the sudden onset of pain, redness and blurred vision by the patient should alert the physician to the possibility of endophthalmitis and the need for referral for urgent ophthalmic examination.

POLYMYALGIA RHEUMATICA

Patients with polymyalgia rheumatica may develop temporal arteritis and lose vision in one or both eyes. They can have a central retinal artery occlusion or ischaemic optic neuropathy, both of which result in permanent severe visual loss. In most patients, the erythrocyte sedimentation rate is raised and treatment with high-dose steroids is started urgently on clinical suspicion to prevent the second eye becoming involved. Temporal artery biopsy is useful to confirm the diagnosis and helps management in the future (Riordan-Eva et al, 2001).

DRUGS USED FOR THE MANAGEMENT OF ARTHRITIS WITH EYE EFFECTS

Long-term corticosteroid usage is associated with the formation of cataract (as is gold therapy) and in susceptible individuals (although much less commonly) can cause glaucoma. Hydroxychloroquine does not cause retinopathy (classically a bull-eye appearance at the macula) at currently recommended dosages (Royal College of Ophthalmologists, 1998) but chloroquine can and patients on this do need to be monitored. High-dose immunosuppression with methotrexate or other agents may lead to opportunistic infections and herpes viruses such as herpes zoster and cytomegalovirus can cause retinitis (Ng et al, 1998). Patients given interferon alpha can get a retinopathy characterized by cotton wool spots (Saito et al, 2001). HM

American Academy of Pediatrics Section on Rheumatology and Section on Ophthalmology (1993) Guidelines for ophthalmic examinations in children with juvenile rheumatoid arthritis. *Paediatrics* **92:** 295–6

Boone MI, Moore TL, Cruz OA (1998) Screening for uveitis in juvenile rheumatoid arthritis. *J Pediatr Ophthalmol Strabismus* **34:** 41–3

Esper GJ, Johnson JS (1999) Update on the treatment of Wegener's granulomatosis. *Bull Rheum Dis* **48:** 1–4

Hamideh F, Prete E (2001) Ophthalmologic manifestations of rheumatic diseases. *Semin Arthritis Rheum* **30:** 217–41

Hoang-Xaun T, Foster CS, Rice B-A (1990) Scleritis in relapsing polychondritis. Response to therapy. *Ophthalmology* **97:** 892–8

Jacobsen S, Petersen J, Ullman S et al (1998) A multicentre study of 513 Danish patients with systemic lupus erythematosus. I. Disease manifestations and analyses of clinical subsets. *Clin Rheumatol* **17:** 468–77

Kanski JJ (1992) Lensectomy for complicated cataract in juvenile chronic iridocyclitis. *Br J Ophthalmol* **76:** 72–5

McCluskey PJ, Watson PG, Lightman S, Haybittle J, Restori M, Branley M (1999) Posterior scleritis: clinical features, systemic associations, and outcome in a large series of patients. *Ophthalmology* **106:** 2380–6

Moschos M, Droutsas D, Boussalis P, Tsioulias G (1996–7) Clinical experience with cyanoacrylate tissue adhesive. *Doc Ophthalmol* **93:** 237–45

Ng P, McCluskey P, McCaughan G, Glanville A, MacDonald P, Keogh A (1998) Ocular complications of heart, lung, and liver transplantation. *Br J Ophthalmol* **82:** 423–8

Okada AA, Johnson RP, Liles WC, D'Amico DJ, Baker AS (1994) Endogenous bacterial endophthalmitis.Report of a ten-year retrospective study. *Ophthalmology* **101:** 832–8

Paiva ES, Macaluso DC, Edwards A, Rosenbaum JT (2000) Characterisation of uveitis in patients with psoriatic arthritis. *Ann Rheum Dis* **59:** 67–70

Ramsay A, Lightman S (2001) Hypopyon uveitis. *Surv Ophthalmol* **46:** 1–18

Reiff A, Takei S, Sadeghi S et al (2001) Etanercept therapy in children with treatment-resistant uveitis. *Arthritis Rheum* **44:** 1411–15

Riordan-Eva P, Landau K, O'Day J (2001) Temporal artery biopsy in the management of giant cell arteritis with neuro-ophthalmic complications. *Br J Ophthalmol* **85:** 1248–51

Royal College of Ophthalmologists (1998) *Ocular toxicity and Hydroxychloroquine: Guidelines for screening.* Royal College of Ophthalmologists, London

Saito H, Ebinuma H, Nagata H et al (2001) Interferon-associated retinopathy in a uniform regimen of natural interferon-alpha therapy for chronic hepatitis C. *Liver* **21:** 192–7

Sfikakis PP, Theodossiadis PG, Katsiari CG, Kaklamanis P, Markomichelakis NN (2001) Effect of infliximab on sight-threatening panuveitis in Behçet's disease. *Lancet* **358:** 295–6

Tanaka M, Kobayashi Y, Takebayashi H, Kiyokawa M, Qiu H (2001) Analysis of predisposing clinical and laboratory findings for the development of endogenous fungal endophthalmitis. A retrospective 12-year study of 79 eyes of 46 patients. *Retina* **21:** 203–9

Zouboulis CC, Orfanos CE (1998) Treatment of Adamantiades-Behcet disease with systemic interferon alfa. *Arch Dermatol* **134:** 1010–16