Rheumatoid arthritis and the eye

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Patients with rheumatoid arthritis may develop serious eye conditions that can threaten their vision.

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Rheumatoid arthritis (RA) is a common disease affecting about 1% of the population. Ocular complications affect up to 25% of all patients with RA and can significantly impact their quality of life. Treating these ocular complications is an important aspect of managing the patient's disease. For optimal care, these patients are best managed in a multidisciplinary team involving an ophthalmologist, a rheumatologist and a GP.

KERATOCONJUNCTIVITIS SICCA

Keratoconjunctivitis sicca, or 'dry eye', is a common complication of RA and affects between 15 and 25% of patients (Figure 1).[1-3] It occurs from dysfunction of the lacrimal glands secondary to immune-mediated destruction and chronic inflammation.

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Patients complain of a burning, foreign body sensation, dryness, irritation and tiredness in the eyes. In more severe cases, episodes of blurred vision result from an uneven tear film over the surface of the eye.[4]

The mainstay of treatment for dry eye is regular, frequent (and often lifelong) ocular lubricants, which may be difficult for patients with RA to self-administer. A range of treatments may be needed in patients with severe disease, including punctal plugs, autologous serum drops and topical cyclosporin as well as treatment for the frequently associated posterior blepharitis and consideration of any allergic eye disease. Nonpreserved lubricants are often required to minimise preservative toxicity.

SCLERITIS

Scleritis affects about 2% of patients with RA.[5] It represents a serious vision-threatening ocular manifestation of RA, patients who develop it having a substantially increased risk of mortality due to the subsequent development of rheumatoid vasculitis.[6,7]

The preponderance of patients affected by scleritis are women (almost two-thirds of cases) with a mean age of onset in men and women of about 50 years. It may be bilateral in 30 to 50% of cases.[8] Scleritis is classified into anterior or posterior scleritis, and can be further subdivided into necrotising and non-necrotising. The most common variant encountered is anterior non-necrotising scleritis, which accounts for almost 50% of cases; however, necrotising scleritis has the strongest association with systemic disease and increased risk of mortality.[7] Scleritis in patients with RA is a chronic, relapsing manifestation that, without appropriate treatment, may persist for months to years. It typically requires systemic immunomodulatory therapy, such as methotrexate, azathioprine, mycophenolate mofetil or cyclosporin or the newer biological agents infliximab and rituximab, to modify the course of the disease.

Scleritis almost always presents with severe, boring pain that may wake the patient from sleep (Box). The pain may be worse

SCLERITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

History
- Severe, boring pain, often waking the patient from sleep
- Blurred vision in association with a red eye
- Known history of a connective tissue/joint disease

Examination
- Intensely red eye, either diffuse or sectoral
- Eye tender to touch (not seen in any other eye disease)
- If keratitis present, staining is noted on instillation of fluorescein drops
- Normal pupil

Differential diagnosis
- Episcleritis
- Conjunctivitis
- Uveitis
- Acute angle closure

Management
- Refer to ophthalmologist

when the eye is moved. Patients describe the eye as being tender to touch, and it is typically intensely red (Figure 2). Anterior scleritis may be associated with uveitis, which may cause blurred vision; posterior scleritis may be associated with blurred vision due to oedema of the macula and optic nerve.

Differential diagnosis

The differential diagnosis for scleritis includes conjunctivitis, episcleritis, corneal ulceration (keratitis), uveitis and acute angle closure.[6]

Episcleritis is a separate entity from scleritis and is not vision threatening. It represents inflammation of the episcleral layer of the eye and may be difficult to distinguish from scleritis because the pattern of injection is similar and the two conditions can coexist. The key differentiating features are that episcleritis causes mild pain, is not tender to touch and usually resolves over

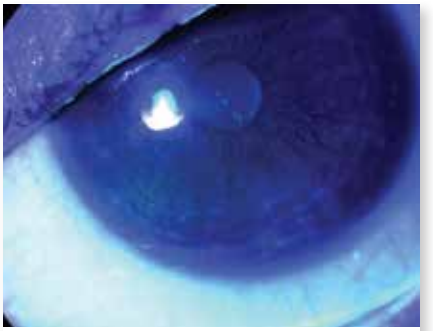

Figure 1. Keratoconjunctivitis sicca or dry eye. Note the multiple punctate erosions highlighted with fluorescein at the 7 o'clock position.

days to weeks. The simplest test to differentiate episcleritis from scleritis is the application of 10% phenylephrine drops, which will result in blanching of the redness of episcleritis but not of scleritis. It is important to differentiate the two conditions because episcleritis is relatively common, is not associated with systemic disease and does not need to be further investigated.

Management

All patients with scleritis need to be referred to an ophthalmologist for investigation and management. About half of patients with scleritis have an identifiable cause, of which RA is the most common association (10 to 33%). Therefore, all patients with scleritis warrant systemic investigations. Apart from RA, commonly associated systemic diseases include antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (especially granulomatosis with polyangiitis [Wegener's disease]), inflammatory bowel disease and relapsing polychondritis.[9,10]

Initial management is to make the correct clinical diagnosis (a high index of suspicion is needed in patients with RA presenting with a red, painful eye), investigate for systemic associations and treat the underlying disease. Treatment options for scleritis can be considered along a therapeutic ladder starting with oral NSAIDs, which a GP can commence with relative safety.

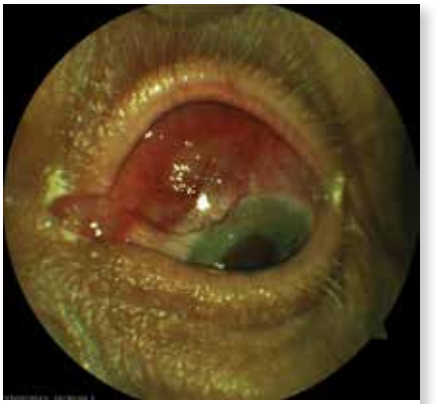

Figure 2. Necrotising scleritis. Note the intense redness to the eye seen in scleritis. The area of necrosis is seen superiorly.

Beyond this, treatment is best managed under the care of an ophthalmologist and rheumatologist, with the GP acting as the primary liaison. The mainstay of treatment for patients with more severe disease is high-dose oral corticosteroids (up to 1 mg/kg/day prednisolone). However, local injections of corticosteroid may be used in selected cases and spares the patient the risks associated with systemic corticosteroid treatment.

Additional immunosuppression is essential in the following circumstances:
- in patients with necrotising scleritis
- in severe cases where treatment with high-dose oral corticosteroid has not halted progression of the disease
- when there is difficulty reaching an acceptable oral corticosteroid maintenance dose – generally considered if the patient cannot be weaned below 10 mg/day of prednisolone for longer than three months.

At least 25% of patients need immunosuppressive therapy, which typically has included methotrexate, azathioprine or mycophenolate mofetil. Newer biological agents (tumour necrosis factor blockers) have revolutionised the treatment of patients with aggressive scleritis. The foremost of these is rituximab, a monoclonal antibody directed against the CD20 antigen expressed on B cells.

Figure 3. Peripheral ulcerative keratitis. Central corneal melt with perforation.

Figure 4. Tectonic corneal grafting to seal a perforated peripheral ulcerative keratitis. Note the corneal guttering and thinning in the 5 to 9 o'clock position.

KERATITIS

The development of peripheral ulcerative keratitis implies severe disease and poor control in patients with RA. Keratitis is much more uncommon than scleritis; however, 30 to 40% of all cases of peripheral ulcerative keratitis are associated with RA.[11,12] Peripheral ulcerative keratitis tends to occur in patients with long-standing RA (mean of 20 years between diagnosis of RA and development of keratitis) and has an equal gender distribution. It may be bilateral in up to 40% of cases[13] and is more likely to occur in patients with dry eye. The classic history is that of ocular pain and redness, and vision may deteriorate with worsening disease.

Different types of keratitis may develop. Peripheral ulcerative keratitis results in thinning at the periphery of the cornea but generally spares the central cornea. The eye is typically red, but a 'silent' variety exists where central or eccentric thinning occurs without a red eye. Severe cases can lead to corneal melt and perforation, which is an ocular emergency (Figure 3). More severe forms, such as sclerosing keratitis, are often associated with adjacent scleritis (often the necrotising type) and result in severe inflammation and scarring of the cornea. This form starts at the periphery of the cornea and can extend centrally if the inflammation is not controlled, directly affecting visual acuity.

As with scleritis, patients with keratitis require investigation. An underlying connective tissue disease should be sought, with RA representing the aetiology in up to 40% of cases.

Patients with RA-associated keratitis often require admission to hospital for intensive treatment to control the disease. Once infection has been ruled out, high-dose systemic corticosteroid (1 mg/kg of prednisolone equivalent) and often immunomodulatory therapy (methotrexate, azathioprine or, commonly, cyclophosphamide) is needed. If severe thinning or corneal perforation occurs, gluing of small perforations with tissue glue or 'tectonic' corneal grafting for larger defects may be needed to seal the perforation and stabilise the eye (Figure 4).

As in scleritis, a multidisciplinary team approach is needed to optimise patient care.

CONCLUSION

Patients with known RA may develop dry eye, scleritis and keratitis. Although uncommon, scleritis and keratitis are serious and potentially threaten vision; patients with these conditions need urgent referral to an ophthalmologist. Much more common is the complaint of dry eyes, which can be managed with copious use of lubricants and high-quality posterior blepharitis care. Preservative-free lubricants are preferred when the frequency of use exceeds four times a day. MT

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