

Relapsing polychondritis and eye disease

D. A. R. MCKAY, P. G. WATSON, AND A. J. LYNE

Scleritis Clinic, Professorial Unit, Moorfields Eye Hospital, City Road, London, EC1V 2PD

Relapsing polychondritis was first recognized as a clinical entity in 1923 by Jaksch-Wartenhorst (1923) and reported by him under the title "polychondropathia". The term "relapsing polychondritis" was first used by Pearson, Kline, and Newcomer (1960). Up to 1966, 49 cases had been described in the literature and these were reviewed by Dolan, Lemmon, and Teitelbaum (1966). So far 114 clinical cases have been described in the general medical literature.

Migratory arthritis is frequently the earliest sign of the disease and is often accompanied by a febrile illness. Chondritis, involving typically the external ear, follows at a variable interval after the onset of the disease. First one and then the other auricle becomes painful, swollen, and inflamed so that the pinna becomes distorted and floppy. The nasal, costal, tracheal, and laryngeal cartilage may also become involved, causing a characteristic saddle-nosed deformity, tracheal collapse which may require urgent tracheostomy, or eventual death from acute bronchial collapse. Involvement of the inner ear may lead to auditory impairment, tinnitus, and vertigo. Myocardial and aortic involvement can result in valvular disease and aneurysm formation. Anaemia and a raised erythrocyte sedimentation rate (ESR) are common, and abnormal liver function tests have been recorded.

Ocular signs were found in 60 per cent. of reported cases (Dolan and others, 1966). The first accurate description was that of Rucker and Ferguson (1965), and Anderson (1967) and Bergaust and Abrahamsen (1969) have since added further cases to the ophthalmic literature.

In this Unit we have seen three cases of this condition, in one of whom the ocular manifestations were the primary presentation.

The diagnosis of relapsing polychondritis should not be made until at least two or possibly three different sites are affected.

Case reports

Case 1, a man aged 38, first attended the Scleritis Clinic of Moorfields Eye Hospital, City Road, in May, 1965, with red eyes. A diagnosis of bilateral diffuse anterior necrotizing scleritis was made. He had been admitted to St. Andrew's Hospital, Bow, 8 months before with central chest pain and a swollen right ankle. He had a persistent fever and ulceration of the mouth and during admission he developed a mild jaundice which settled over a 2-week period. All investigations were normal including an electrocardiogram (ECG). 1 month later he developed a painful swollen left wrist and ankle. ACTH therapy was then started and led to a rapid improvement in his overall condition. 4 months before the eye signs appeared he again developed ulceration of his mouth and was given prednisolone 45 mg./day, which produced some improvement.

On his first admission to Moorfields (May, 1965) with bilateral scleritis more severe in the right eye than the left, the visual acuity was 6/9 right, 6/6 left, unaided. Ocular examination was normal in all other respects. He had mild anaemia (Hb 80 per cent.) and an ESR of 29 mm./1st hr. An initial diagnosis of Behçet's disease was made; he was therefore given prednisolone 60 mg./day and his condition improved. He was discharged 1 month later on prednisolone 40 mg./day and Predsol eye drops.

He required readmission 2 months later with severe pain in the right eye which improved with an increase in his steroid dosage to 80 mg. daily. About this time he developed an acutely inflamed right pinna, followed by severe tinnitus, vertigo, and deafness.

In October, 1965, he was admitted to the Metabolic Unit, St. Mary's Hospital, under Professor V. Wynn, for assessment of the steroid therapy, and his management has been shared since then. He was eventually stabilized on prednisolone 15 mg./day. In January, 1966, the left pinna became swollen and the patient himself commented on the increasing deformity of the nasal cartilage. He again developed a severe left scleritis, and the steroid dose was temporarily increased to 80 mg./day with a good response. He was again extensively investigated but the only abnormal laboratory finding was an ESR of 39 mm./1st hr.

Over the next 2 months he had further attacks of arthritis, mouth ulceration, and chest symptoms, all of which settled with boosting of the steroid intake. The various several attacks of scleritis have also responded well, and his present visual acuity is 6/6 right and left; the maintenance dose of prednisolone is 5 mg. three times a day.

Case 2, a man aged 57 years, first presented to our Unit in October 1968, with a painful red left eye. A diagnosis of simple episcleritis was made, and the condition responded well to Predsol eye drops 2-hourly; 12 months later the right eye became involved, and responded similarly.

In June, 1970, he had a bilateral inguinal hernia repaired and about this time both ears became red and swollen, followed 1 month later by swelling of both knees and the left wrist. He was investigated by Dr. B. Gottlieb at St. Mary Abbots Hospital, London.

He was found to have a mild anaemia (Hb 85 per cent.), and the ESR was 55 mm./1st hr, negative Waaler-Rose test, negative urinary mucopolysaccharide, and a slight rise in the gamma globulin fraction of the serum proteins. Biopsy of the left ear showed necrotic cartilage and an inflammatory cell infiltrate, which consisted mainly of plasma cells. Anticartilage antibodies were demonstrated by an immunofluorescent technique (Godtfredsen, 1949). An audiogram showed high-tone deafness.

Once the diagnosis of relapsing *polychondritis* was made, he responded well to prednisolone by mouth and was maintained on 5 mg. three times a day.

During the next 12 months he was troubled by recurrent attacks of episcleritis, swelling of the left knee and both wrists, and further swelling and destruction of both external ears. He also had recurrent urinary tract infection and a sterile urethral discharge, and he passed a renal stone in July 1971. He has had one episode of right-sided laryngeal swelling. Recurrent skin rashes have also occurred, including a thoracic herpes zoster, necessitating a reduction in his steroid intake.

At present his visual acuity is 6/9 right and left (corrected) and he is on maintenance therapy with prednisolone 15 mg./day and local steroid preparations to the eyes when necessary. Intraocular pressure has never been raised and there is as yet no sign of cataract formation.

Case 3, a married woman aged 42 years, first attended the ophthalmic department in February, 1970, when she was complaining of proptosis of the right eye for 1 week, and aching of the eye and orbit. She had also experienced double vision in all directions of gaze. The only significant past medical history was of thyrotoxicosis 10 years before, which had been treated with potassium perchlorate; the patient rapidly became euthyroid and there had since been no symptoms of thyroid dysfunction. Shortly after this episode she had noticed that the end of her nose had become depressed.

She had been deaf since early childhood and there was a family history of perceptive deafness, her father and brother having similar symptoms. She had been helped by a hearing aid.

Examination (February, 1970)

Diplopia was present in all directions of gaze but most marked on elevation. There was definite proptosis and even more marked downward displacement of the right eye. The subconjunctival tissues in the region of the superior rectus were infiltrated. The corrected visual acuity was 6/6 in the right eye and 6/5 in the left. Central field testing showed no defect. There were no fundus abnormalities at this time. The intraocular pressure was 21 mm.Hg in the right eye and 19 mm.Hg in the left.

Full investigations, which included x rays of the chest, skull, sinuses, orbits, small bones of the hands, feet, and wrists, and the neck, and full serological tests, were all negative. The erythrocyte sedimentation rate was 23 mm./1st hr (Westergren).

Two biopsies of the infiltrated region of the superior rectus muscle revealed a lymphomatous type of deposit, and a non-specific chronic inflammatory reaction. It was therefore felt that this lesion was most likely to be an orbital lymphoma. Ear, nose and throat and neurosurgical opinions were sought, but no evidence of sinus or intracranial involvement was found.

Progress

After 3 months the proptosis had become more marked and an area of scleral thinning had appeared superiorly. The visual acuity remained unchanged but examination of the fundus showed retinal striae at the posterior pole. The vitreous remained clear and the disc margins were well defined.

The scleral thinning suggested the presence of a posterior scleritis. The patient was therefore given systemic prednisolone 30 mg. daily. A dramatic improvement occurred within a few days, the proptosis resolved, and the pain disappeared.

At this time the diagnosis of chronic relapsing polychondritis was made, and a maintenance dose of 10 to 15 mg. prednisolone daily was continued.

The nose was operated upon in 1970; a plastic implant was inserted, but this unfortunately came out when the patient blew her nose. The Figure shows the facial appearance after the extrusion of the implant.



FIGURE *Destruction of nasal cartilage in a patient with relapsing polychondritis (Case 3), giving rise to a depression of the tip of the nose*

Biopsies of the nasal cartilage and of a section of the sixth costal cartilage were taken at the time of operation. The former showed aseptic necrosis and the latter was normal.

Shortly after the birth of a normal female infant in May, 1972, she suffered a relapse with recurrence of the proptosis and blurred vision. The corrected visual acuity was 6/18, and the optic disc showed surrounding swelling with some small haemorrhages. Her condition returned to normal when the steroid dosage was increased.

During April, 1974, she noticed a rapid loss of vision in the right eye; the visual acuity was reduced to counting fingers, the left remaining normal at 6/4.

The pupillary reaction of the right eye was sluggish but the fundus showed no abnormality. The left eye was normal.

The steroid dosage was increased to 20 mg. daily, and the visual acuity returned to normal within 5 days.

Discussion

The ocular manifestations of relapsing *polychondritis* are many and varied. The most common are episcleritis, scleritis, iritis, and keratoconjunctivitis sicca, but sclerokeratitis, conjunctivitis, exudative chorio-retinitis, exudative retinal detachment, optic neuritis, cataract, proptosis, and muscle paresis have been reported. In a case described by Rucker and Ferguson (1965) of a 41-year-old female patient, there was acute left proptosis with diplopia due either to lateral rectus involvement or to a sixth nerve paresis. This settled on treatment with steroids. Later the right eye became proptosed and also settled with treatment. Recently, Davies and Karseras (1971) have described a further case of anterior and posterior scleritis with proptosis and a partial third nerve lesion. The seven cases reported by Anderson (1967) included signs of episcleritis, exudative retinopathy, which they describe as resembling Coats's disease, sclerokeratitis with progressive scleral thinning, and iritis. Bergaust and Abrahamsen (1969) described a case with multiple ocular complications including four attacks of sclerokeratitis, one attack of sclero-iritis, one of bilateral pan-uveitis, and an exudative chorio-retinopathy, also resembling Coats's disease.

Eventual blindness has twice been described (Hilding, 1952; Barth and Berson, 1968). The first was due to a severe iritis with secondary glaucoma, leading to phthisis bulbi, and the second to bilateral corneal perforation.

The most common manifestations seem to be episcleritis, iritis (Matas, 1970), and keratoconjunctivitis sicca.

The first patient, who presented with a diffuse anterior necrotizing scleritis of the type commonly seen in patients with connective tissue disorders, had a severe generalized disease. The second patient never had any scleral involvement, the inflammation being confined to the episclera only. This presentation is unusual when other systemic connective tissue disease is present but does occur from time to time, particularly in patients with mild rheumatoid arthritis. The third patient presented with a posterior scleritis, proptosis, and reduced visual acuity due probably to the involvement of the sclera in the region of the optic nerve and posterior pole; in this respect the patient was similar to others we have seen with posterior scleritis both in presentation and in dramatic response to treatment. The usual exudative changes were absent in this patient. Because of the physiogenetic similarity between cartilage and sclera, the varied modes of presentation of these patients may be a manifestation of the inflammation of similar tissues at different sites.

AETIOLOGY

The aetiology of this condition is still obscure, although it is thought to belong to the family of "collagenoses" with an autoimmune complex background. Jaksch-Wartenhorst (1923), in his original article, attributed the cause, perhaps light-heartedly, to excessive consumption of alcohol! Dolan and others (1966) attempted to demonstrate immunofluorescent antibodies to cartilage with inconclusive results. These antibodies were found in Case 2; this patient also had raised gamma globulin fractions in the plasma proteins.

Other laboratory investigations have also proved generally unhelpful. A high ESR is usually present, with a mild anaemia, but specific tests show no definite pattern. Anti-rheumatoid factor has been present in some cases, and an antithyroid antibody has been demonstrated in others. Kaye and Sones (1964) described a method of estimating urinary acid mucopolysaccharide, which was raised in patients with *polychondritis*, and Riggs and Wilson (1967) also found that such a test warranted inclusion in their investigation

Hughes, Berry, Seifert, and Lessof (1972) discussed the use of tests for anticartilage antibodies, and also described the estimation of glycoaminoglycans in the cartilage matrix of affected individuals.

Biopsy of affected cartilage and histological changes have been reported by Harwood (1958), who found replacement of cartilage by fibrous connective tissue, scattered calcification, and non-specific inflammatory signs. Verity, Larson, and Madden (1963) reported in detail the histological changes and, although there is no pathognomonic finding, the basophilic staining of the normal cartilage is usually lost while the diseased cartilage becomes acidophilic, dissolving and fragmenting from the edge towards the centre. The chondrocytes lose their cytoplasm, and eventually only nuclear remnants are found. The destroyed cartilage is replaced by fibrous connective tissue, often vascularized, growing in from the edges of the lesion. Similar changes were found in Case 3.

DIFFERENTIAL DIAGNOSIS

Before the diagnosis of relapsing polychondritis can be made, two or three sites including the ocular structures have to be involved. It is little wonder that diagnosis is difficult in the early stages as this has to be made on clinical grounds alone. This condition should be considered not only in patients presenting with scleral disease but also those who develop diffuse joint disease. It is interesting to note that two excellent reviews of ocular and joint disease (Godtfredsen, 1949; Stanworth, 1951) do not mention this condition.

As demonstrated by Case 1, both Reiter's disease and Behçet's disease can present a very similar picture and follow a similar course. Other conditions, including rheumatoid arthritis, Still's disease, Wegener's granulomatosis, Cogan's syndrome, and Sjögren's syndrome, enter the differential diagnosis. Inflammation of the eye associated with inflammation and eventual destruction of the aural and nasal cartilage is diagnostic, and the condition should be suspected if there is associated chest pain (from involvement of the costal cartilages), tracheo-bronchial symptoms, migratory arthritis, or middle and inner ear disease.

COURSE AND TREATMENT

The cases so far described in the literature are equally spread between the sexes. The age at onset varied from 2 to 61 years (average 32). The duration of the disease varied from 1 to 24 years. The reported cause of death is usually acute respiratory collapse, and a number of survivors have required urgent tracheostomy. Other deaths have been caused by ruptured aortic and cerebral aneurysms and by myocardial valvular involvement.

The disease may, in fact, run an acute fulminating course, but it more commonly follows a slow, low-grade, relapsing pattern.

Treatment is essentially with anti-inflammatory agents. Steroids in an initial dosage of prednisolone 60–80 mg./day or its equivalent bring about a marked and rapid improvement and this is the treatment of choice. A maintenance dose seems to be necessary to suppress the condition. If there is an exacerbation then the steroids must again be given in full dosage for a short period.

Kaye and Sones (1964) reported good results with salicylates in a dosage of 2 to 5 g./day, but had no success with Plaquenil. The articular complications were successfully controlled with chloroquine on one occasion and our first patient responded well at one stage to systemic Tanderil.

There is no doubt, however, that systemic steroids are the mainstay, and they can be supplemented by local steroids for recurrent ocular problems. Subconjunctival steroids should at all times be avoided – diseased sclera may often rupture at the site of such injections (Watson, 1972).

Summary

Three patients with relapsing polychondritis, who presented in the first instance to an eye department, are described. One patient had a diffuse anterior necrotizing scleritis, the second a simple episcleritis, and the third a posterior scleritis. All have made satisfactory progress with maintenance of good vision. Systemic steroid therapy appears to be the only satisfactory treatment; it must be given initially in high doses and reduced to a maintenance dose as soon as the ocular and systemic manifestations regress. All three patients still require maintenance dosage even after 10, 7, and 4 years respectively. A brief review of the literature of this rare and interesting condition is included, and the aetiology discussed.

References

- ANDERSON, B. (1967) *Amer. J. Ophthalm.*, **64**, 35
 BARTH, W. F., and BERSON, E. L. (1968) *Ibid.*, **66**, 890
 BERGAUST, B., and ABRAHAMSEN, A. M. (1969) *Acta ophthalm. (Kbh.)*, **47**, 174
 DAVIES, M. S., and KARSERAS, A. G. (1971) *Brit. J. Ophthalm.*, **55**, 196
 DOLAN, D. L., LEMMON, G. B., and TEITELBAUM, S. L. (1966) *Amer. J. Med.*, **41**, 285
 GODTFREDSSEN, E. (1949) *Brit. J. Ophthalm.*, **33**, 261
 HARWOOD, T. R. (1958) *Arch. Path.*, **65**, 81
 HILDING, A. C. (1952) *Arch. intern. Med.*, **89**, 445
 HUGHES, R. A. C., BERRY, C. L., SEIFERT, M., and LESSOF, M. H. (1972) *Quart. J. Med.*, **41**, 363
 JAKSCH-WARTENHORST, R. (1923) *Wien. Z. inn. Med.*, **6**, 93
 KAYE, R. L., and SONES, D. A. (1964) *Ann. intern. Med.*, **60**, 653
 MATAS, B. R. (1970) *Arch. Ophthalm. (Chicago)*, **84**, 474
 PEARSON, C. M., KLINE, H. M., and NEWCOMER, V. D. (1960) *New Engl. J. Med.*, **263**, 51
 RIGGS, R. H., and WILSON, J. W. (1967) *Laryngoscope*, **77**, 534
 RUCKER, C. W., and FERGUSON, R. H. (1965) *Arch. Ophthalm. (Chicago)*, **73**, 46
 STANWORTH, A. (1951) *Trans. ophthalm. Soc. U.K.*, **71**, 189
 VERITY, M. A., LARSON, W. M., and MADDEN, S. C. (1963) *Amer. J. Path.*, **42**, 251
 WATSON, P. G. (1972) "Contemporary Ophthalmology Honouring Sir Stewart Duke-Elder", ed. J. G. Bellows, p. 77. Williams and Wilkins, Baltimore; Churchill Livingstone, Edinburgh.