Clinical Topics

Scleritis and associated disease

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Summary and conclusions

One hundred patients (66 women and 34 men) who presented consecutively to Moorfields Eye Hospital with scleral disease underwent medical examination. Thirteen were found to have seropositive rheumatoid arthritis and another 16 also had rheumatoid factor present (Rheumaton test). Autoantibodies were present in 35% of patients, being most common in the elderly and most frequent in cases of necrotising and diffuse scleritis.

Although scleral disease is uncommon, it is associated with connective-tissue disorders. Scleritis may be severe and destructive locally, and one series showed that 27% of patients who develop necrotising scleritis are dead from systemic complications within five years. It is therefore important for it to be correctly diagnosed and effectively treated at an early stage.

Introduction

The ocular complications of rheumatoid arthritis are particularly important because slight inflammatory changes may cause severe interference with vision. The symptoms and signs may be ignored by both the patient, who is suffering great pain elsewhere, and the doctor, who is concentrating on the joint disease. This can lead to inadequate treatment of early progressive lesions, and blindness with its devastating consequences may result.

Scleritis occurs in about 0.6% cases of rheumatoid arthritis¹ and is much less common than keratoconjunctivitis sicca, which occurs in about one-third. Nevertheless, since rheumatoid arthritis is so common all rheumatologists will encounter it. Scleritis also occurs in other disorders in connective tissue, and is sometimes the first sign of these. In most cases presenting to the ophthalmologist, however, no immediate cause for the condition is apparent.

We undertook this study to assess how often an underlying medical condition could be detected. One hundred patients attending the scleritis clinic at Moorfields Hospital over two years were given a thorough medical examination, investigated, and classified according to the type of scleritis.

Patients and examination

MEDICAL EXAMINATION

All patients (66 women and 34 men) underwent medical examination. Investigations included a full blood count; measurement of

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plasma protein, complement, urea, sugar, urate, and cholesterol concentrations; immunofluorescence tests for rheumatoid factor, LE cells, and autoantibodies; and screening tests for syphilis. Urine analysis and radiographs of chest, hands, feet, and sacroiliac joints were obtained. Tissue-typing was carried out on 54 patients. Fifty controls matched for age and sex, who were undergoing cold eye surgery at Addenbrooke's Hospital, were also examined.

OPHTHALMOLOGICAL EXAMINATION

Scleritis must be distinguished from episcleritis. As the name implies, episcleritis affects only the superficial covering of the sclera, the fascia bulbi or Tenon's capsule, which has a parietal and visceral layer. Characteristically, the onset is acute, the eye flushing red within a few minutes. There is no discharge and pain, if present, is mild and confined to the eye. The attacks are self-limiting over 7 to 10 days and are notoriously recurrent. The attacks may be due to an allergic reaction or hyperuricaemia (when crystals or urate may be seen with the slit-lamp).

Pain is more prominent in scleritis than in episcleritis and may be widely radiated. The more serious scleritis can often be distinguished from episcleritis simply by examining the patient with the naked eye in daylight. The colour of the sclera in scleritis is bluish red as opposed to the bright fiery redness of episcleritis; necrosis can easily be seen, as can any areas of increased translucency that accompany or follow the healing of scleritis. Beta-scan ultrasonography has shown that this is not always consistent with scleral thinning.²

Areas of anterior scleral swelling and the associated displacement and dilatation of the different plexuses of vessels are easily identified on slit-lamp examination. As soon as the eye is inflamed three separate vascular plexuses become visible. Close to the surface are (1) the subconjunctival vessels, which when inflamed show up as a bright-red superficial network that is easily moved on the underlying episclera; (2) the episcleral vessels, which run radially, and when inflamed are salmon pink, and (3) the scleral vessels, which form a deep meshwork and are deep purple and closely attached to the scleral surface. These differences in colour are best seen in daylight and do not show up at all well in artificial light.

If difficulty is experienced in determining which layer of vessels is displaced, red-free light makes the vessels more easily visible, and if there is still doubt 1/1000 adrenaline blanches the conjunctival and episcleral vessels but not the sclera. The slit-lamp detects the depth of maximum vascular congestion and site of oedema, thus allowing episcleritis to be distinguished from scleritis. There is often a region of episcleritis overlying and secondary to a patch of scleritis. The reverse does not occur. The cornea should also be examined for evidence of keratitis, marginal ulcers, or, rarely, keratolysis.

Posterior scleritis is rare and if present is difficult to diagnose (see below).

TYPES OF SCLERITIS

The classification of the types of scleritis is on a clinical basis. Histologically there is granuloma formation very similar to a rheumatoid nodule.

Nodular—These are localised round lesions caused by oedema of the sclera. As the oedema resolves the inflammation causes changes in the sclera so that characteristic blue patches appear, which are caused by the choroid showing through the now translucent sclera. Scleral nodules that resemble nodular episcleritis on cursory examination can easily be distinguished by their immobility and the intense inflammation and pain to which they give rise.

Diffuse—There may be severe brawny inflammation, which is spread all over the sclera and episclera. More often, however, the generalised diffuse changes are much less conspicuous, but nevertheless should be treated promptly to avoid ocular complications, the most serious of which is glaucoma.

Necrotising scleritis is the most severe form. The prognosis is poor: 60% develop ocular or systemic complications, 40% lose some visual acuity, and 29% die within five years. Pain is the prominent feature. It is severe and disabling, often being referred to the side of the face and the jaw, characteristically waking the patient in the early hours of the morning. Several patients have had neurosurgical investigation in the belief that the pain was due to a cerebral tumour. The sclera usually becomes red in one place, sometimes with an avascular patch indicating vasculitis at its centre. The inflammation, which is the result of granuloma formation, spreads out both ways from the original focus, progresses around the globe, and, unless stopped by vigorous systemic steroid treatment, will destroy the eye. This type of scleritis is most likely to be associated with connective-tissue disease. While necrotising scleritis may start as a diffuse or nodular scleritis, it is usually obvious from the start, either because of avascular patches in episcleral tissue or by the intensity and progressive nature of the disease.

Scleromalacia perforans—This unusual but highly characteristic form of necrotising scleritis almost always occurs in patients who have had rheumatoid arthritis for at least 15 years. There is a progressive loss of episcleral tissue over many years, presumably due to a mild occlusive vasculitis, and then a localised necrotic nodule forms with very little surrounding inflammation. After a variable period, sequestration of sclera occurs leaving bare choroid, and the sclera appears to melt away. This destructive process will not necessarily be halted by systemic steroid treatment unless the disease is detected and treated while the overlying episcleral tissue is still intact.

Posterior scleritis often presents as a problem in diagnosis between scleritis and invasion by an orbital granuloma. Patients often present with an exudative retinal detachment. The eye may just be proptosed and not red, and there may be periorbital oedema and limited extraocular movements. Fluorescein angiography may show the lesion, and ophthalmoscopy may show vessels displaced forwards by patches of scleral oedema.

Results

The patients' ages ranged from 15 to 85 and the average age was 46.6 years. Many had associated diseases (table I).

The average age of the 50 patients (33 women and 17 men) in the control group was 44.3 years. Fewer diseases were found in this group, and in particular no patient had rheumatoid arthritis or circulating rheumatoid factor. Four patients were diabetics, one patient had had a myocardial infarction, and one patient was an epileptic. The high incidence of diabetes found is because such patients are prone to develop ocular complications requiring eye surgery.

TABLE I—Incidence of associated disease in patients with scleritis

Disease	Men	Women	Total
Rheumatoid arthritis	5	8	13
Sjögren's syndrome (2 with rheumatoid arthritis)	0	3	3
Pulmonary fibrosis (+ rheumatoid arthritis)	1		1
Cutaneous vasculitis (+ rheumatoid arthritis)	1	1	2
Temporal arteritis		1	1
Gout	3		3
Acne rosacea	2		2
Hypertension and angina	1	3	4
Hypothyroidism		2	2
Syphilis (1 congenital, 1 acquired)	1	1	2
Sarcoidosis		2	2
Psoriasis		2	2
Diabetes		1	1
Carcinoma of breast		1	1

TABLE II—Association of disease with types of scleritis

	Diffuse (n = 30)	Nodular (n = 25)	Necrotising (n = 18)	Scleromalacia perforans (n = 2)	Posterior (n = 8)
Rheumatoid arthritis	3	2	4	1	2
Rheumatoid factor	10	5	9	2	8
Autoantibodies	11	6	9	1	4

LABORATORY INVESTIGATIONS

The sedimentation rate was found to rise with activity of the scleritis. The other laboratory investigations showed no deviation from normal apart from the rheumatoid factor and autoantibodies.

Twenty-nine patients had rheumatoid factor. Of these, 13 had clinical rheumatoid arthritis and seven had a family history of rheumatoid arthritis. These results are similar to those of McGavin *et al.*¹ The reason for the presence of rheumatoid factor is not known, but McCormick³ has suggested that it may be produced by the scleral nodule in the eye.

One or more autoantibodies were found in 35% of the patients with scleritis, smooth-muscle antibodies being most often detected: smooth-muscle (11 cases), thyroglobulin (6), gastric parietal (5), thyroid microsomal (3), muscle (1), salivary duct (1), nuclear (7), reticulin (5), neural (5), thyroid mucosa (2), and ocular (1). Autoantibodies were most common in middle-aged patients and most frequent in cases of necrotising or diffuse scleritis. In contrast only 6 (12%) patients in the control group were found to have autoantibodies. Two patients had antibodies to thyroid microsomes, two to smooth muscle, one to gastric parietal cells, and one to nuclei.

When the clinical and immunological results were correlated with the type of scleritis (table II), several associations could be detected (though it was not possible to classify all patients with scleritis). Autoantibodies were found most often in patients with necrotising or diffuse scleritis. It was the necrotising group that was associated with the vasculitic and systemic complications of rheumatoid arthritis.

The distribution of histocompatibility antigens was examined in 54 patients.⁴ The incidence of HLA-B27 was not increased nor was there a significant preponderance of any other type.

Discussion

The association of scleral disease and "rheumatism" has been recognised since McKenzie's report in 1830.⁵ Van der Hoeve⁶ first described the association of scleromalacia perforans and rheumatoid disease, and Verhoeff and King⁷ noted the similarity of the scleral lesion to a subcutaneous rheumatoid nodule. Recent reviews of scleritis and rheumatoid arthritis confirm a correlation.⁸⁻¹⁰ McGavin *et al.*¹ confirm that rheumatoid arthritis is less commonly associated with episcleritis than with scleritis.

Scleritis is rare. Williamson¹¹ estimates that it is responsible for 0.08% of new patient referrals to eye departments. Nevertheless, the condition must be taken seriously because it can lead to blindness. It first must be distinguished from episcleritis as they are two distinct conditions showing differences in their clinical pattern and in their ultimate effects on the eye, episcleritis being the milder condition.

Scleritis is often difficult to diagnose as oedema may hide the necrotising process, and the disease may progress until it is too late to be treated. In one series of 30 eyes with a primary histological diagnosis of scleritis 43% had not had the diagnosis made in life; in most cases the diagnosis was secondary glaucoma from a primary anterior uveitis.¹² The overlying episcleral congestion that is always present if the sclera is inflamed must be ignored and the presence of scleral oedema confirmed with a slit-lamp. The occurrence of avascular patches in the scleral and episcleral vessels indicates vasculitis and calls for immediate treatment. Only rarely does the sclera ulcerate.

Scleral inflammation is rarely affected by local treatment so some form of systemic treatment should be given. Of the many anti-inflammatory drugs tested, only phenylbutazone, its derivatives, and indomethacin have so far proved effective. The reason is unclear. If there is no response to one of these drugs

within a few days patients should be given systemic steroid treatment. For the short term, high doses of prednisone (60 mg decreasing to maintenance doses of 15 mg) are effective and produce dramatic relief of the pain in the eye within 12 hours. If avascular areas are present systemic steroids, 60 mg/day or even more, should be given until new vessels start to grow into the areas. As soon as the inflammation is suppressed dosage can be reduced rapidly. It is important not to biopsy scleral nodules or inject hydrocortisone subconjunctivally, because the sclera will not heal and perforation may be induced at the injection site.

Whereas some forms of scleritis are harmless and subside with treatment, others are severe and destructive. Necrotising scleritis is particularly sinister as it may be associated with systemic disease. Watson found in one series that 27% of patients who developed necrotising scleritis were dead within five years.¹³ In patients with mild rheumatoid arthritis the onset of scleritis may, in about 30% of cases, be associated with the development of "malignant" rheumatoid disease with vasculitis, and may precede it. In these patients, prompt diagnosis and systemic treatment may control both scleritis and rheumatoid arthritis.

Widespread systemic involvement, particularly of cardiovascular, respiratory, and renal systems, may be associated with scleral disease in patients with rheumatoid arthritis.¹⁴ Jayson and Jones¹⁰ found pericarditis in two of 12 patients with scleritis and rheumatoid arthritis, one of whom also had pleurisy. They noted arteritis in 10 of 14 cases of scleritis. McGavin *et al*¹ found ischaemic changes on electrocardiography in 60% of patients examined, and nearly 33% had Sjögren's syndrome. They also found an increase in pulmonary complications, including pleurisy, pneumonitis, pleural effusion, and rheumatoid nodules of the lung. The extra-articular features were consistently more evident in patients with rheumatoid arthritis and scleritis than in a control group with rheumatoid arthritis alone.

Not only are the extra-articular manifestations more often present where the eye is affected, but also the patients have more severe disease, more advanced radiological changes, and higher

sedimentation rates and higher titres of rheumatoid factor. Ocular changes tend to occur in patients with more severe rheumatoid disease, especially vasculitis, and exacerbation occurs at times of increased activity.

The increased incidence of systemic features is reflected in a decreased life expectancy. Jones and Jayson¹⁵ found that about 36% had died within three years compared with about 19% of the control group. It is important for the rheumatologist to remember that the development of necrotising scleritis in a rheumatoid patient may shortly be followed by systemic complications.

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Changing pattern of drugs used for self-poisoning

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Summary and conclusions

In 1967-76 the annual number of admissions to a poisoning treatment centre rose from 964 to 2134. The proportion of admissions caused by taking barbiturate hypnotics and methaqualone fell considerably while that caused by taking benzodiazepines and tricyclic antidepressants increased. As a result the proportion of patients admitted unconscious fell from 23% to 15%. The declining contributions of barbiturates and methaqualone and increased importance of tricyclic antidepressants were significant

in all grades of coma. The change in drugs taken, however, has not yet reduced the percentage of unconscious patients needing endotracheal intubation or assisted ventilation, and hypothermia remains as common. Only hypotension has become less frequent as antidepressants replace barbiturates as the main cause of drug-induced coma. The use of salicylates for self-poisoning is declining slowly, and paracetamol poisoning is now as common.

Introduction

The epidemic of self-poisoning will be remembered as one of the major medicosocial phenomena of the past 30 years. Many reports testify to its impact on the work load of general hospitals throughout Britain¹⁻⁷ and in several areas the incidence continues to rise inexorably.^{1 5-7} In most cases the physical consequences of self-poisoning are minor, and the episode is more important as a manifestation of interpersonal and social strife or, less often, of psychiatric illness. The medical seriousness of other cases, however, is reflected in 1875 official deaths

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