KERATO-CONJUNCTIVITIS SICCA AND RHEUMATOID ARTHRITIS

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Although the ophthalmic lesions which constitute kerato-conjunctivitis sicca have long been known, the nature of the condition has remained obscure. Duke-Elder (1930) reviewed those rare cases in which lesions of the lacrimal secretory nerves or of the gland parenchyma (including congenital aplasia, surgical extirpation, infiltrations by sarcoid, leukemic or malignant tissue) resulted in deficient lacrimal secretion and the subsequent development of corneal and conjunctival lesions of the sicca type. These rare cases, however, accounted for only a small proportion of all the patients suffering from kerato-conjunctivitis sicca, and in the majority no local ophthalmic cause for deficient lacrimation and sicca lesions could be found.

Sjögren (1933) described in detail his observations on eighteen patients with idiopathic kerato-conjunctivitis sicca and drew attention to its frequent association with such clinical features as polyarthritis, xerostoma, and salivary gland enlargement, occurring especially in middle-aged women. To this triad the name Sjögren's syndrome was given, but the variations and increasing complexity of the condition soon became apparent. Holm (1949) reviewing 440 cases of rheumatoid disease stated that "The conception of kerato-conjunctivitis sicca as a disease sui genesis (Sjögren) is fundamentally incorrect": but he considered that rheumatoid arthritis was of importance as an aetiological factor.

The term Sjögren's syndrome continued to be applied to any condition in which the classical triad of kerato-conjunctivitis sicca, polyarthritis, and salivary gland enlargement was present, as well as those in which arthritis was absent (approximately 40 per cent. of all cases of kerato-conjunctivitis sicca). Writers, however, remained cautious of associating the condition with rheumatoid arthritis. Coverdale (1948) considered that "Sjögren's syndrome" indicated a general constitutional or systemic disturbance of unknown origin, while Henderson (1950) stated: "I do not feel that poly-

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arthritis is an integral part of the symptom complex. It is my feeling that the arthritis is an incidental finding." Ellman, Weber, and Goodier (1951) remarked that: "rheumatoid arthritis is fairly common among women, and that very few patients with rheumatoid arthritis ever manifest any symptoms resembling Sjögren's disease". They recorded the case history and autopsy findings in a patient who did suffer from rheumatoid arthritis, but in whom the symptoms of xerostoma, salivary gland enlargement, and ocular inflammation preceded the development of the arthritis by several years.

However, Reader, Whyte, and Elmes (1951) confirmed the opinion of Holm (1949) that many patients who suffered from rheumatoid arthritis also had a deficiency of lacrimal secretion, as estimated by Schirmer's test. Other workers have been more inclined to consider kerato-conjunctivitis sicca and its allied pathology as part of the wider concept of rheumatoid disease; this view was expressed by Littler (1951), Gurling (1953), and Morgan (1954).

During the past 3 years, we have treated eighteen patients with severe or moderate kerato-conjunctivitis sicca, fourteen of whom (77.7 per cent.) had rheumatoid arthritis. An additional sixteen patients with milder symptoms and signs, consistent with a condition of conjunctivitis sicca, and also suffering from rheumatoid arthritis, have also been examined and treated. The high percentage of cases associated with polyarthritis is due to the fact that most of the cases were identified at a rheumatic unit. The ophthalmic features, associated lesions, and complications noted in these patients have some points of interest, and are recorded together with some observations on the results of treatment of the ocular lesions.

Incidence

Kerato-conjunctivitis sicca is not the rarity it was once considered to be. It is, indeed, the commonest ocular complication of rheumatoid arthritis. In a recent study of 210 former in-patients of the Rheumatic Diseases Unit, Northern General Hospital,
Edinburgh, we found evidence of lesions of the sicca type in thirty patients, an incidence of 14·3 per cent. In comparison with this, there were only seven patients (3·5 per cent.) who showed signs of active or old uveitis. No cases of episcleritis, scleromalacia perforans, or superficial punctate keratitis were identified in this series. These findings accord with those of Holm (1949), who diagnosed keratoconjunctivitis sicca in 13·4 per cent. of 440 rheumatoid patients, and of Rosenberg (1949) who reported uveitis in 3 to 5 per cent. of cases.

Of the thirty patients with keratoconjunctivitis sicca in our series, all of whom had had ophthalmic symptoms, six had gross corneal and conjunctival lesions, eight had conjunctival lesions of moderate severity and had only slight corneal changes in addition, and sixteen had conjunctival lesions only, and could be considered to be examples of conjunctivitis sicca.

Sex Ratio

Sjögren (1933) stated that the syndrome occurred most commonly in middle-aged women. Holm (1949) found that female cases predominated, but that in his rheumatoid patients the sex incidence of keratoconjunctivitis sicca paralleled the sex distribution of the arthritis, being approximately 2·5 females to 1 male. Of the thirty patients in our series, 26 were females, making a ratio of 6·5 females to one male. The sex ratio of the 210 patients studied was only 2·7 females to one male.

Description

Ophthalmic Features.—The classical symptoms and signs of keratoconjunctivitis sicca are those of conjunctivitis associated with filamentary keratitis and reduction of lacrimal secretion, and the diagnosis can be substantiated by Schirmer’s test for lacrimal secretion and the staining reaction with 1 per cent. aqueous Rose-Bengal solution.

In the present series, several ophthalmic features of interest were noted. The ocular symptoms ran a course of remissions and exacerbations, but symptoms were rarely completely absent in severe cases of keratoconjunctivitis sicca. The waxing and waning of the ophthalmic symptoms in those patients who also had rheumatoid arthritis often occurred independently of any changes in the arthritic condition. Furthermore, the severity of the ocular changes in such patients was not proportional to the severity of the arthritis, some of the most marked examples of keratoconjunctivitis sicca being encountered in patients with mild or quiescent rheumatoid arthritis.

Although ocular discomfort, photophobia, and mild impairment of vision are well recognized as symptoms of keratoconjunctivitis sicca, the more serious risks to vision have not been fully appreciated. In the present series, corneal ulceration was noted in three cases. In two instances the ulcers were of the small marginal type which healed without incident. The third patient, however, suffered from bilateral corneal ulceration, and was initially referred to hospital when perforation of a central corneal ulcer necessitated enucleation of the eye. One patient also had a small pannus involving the infero-lateral quadrant of the cornea.

Pathology.—Sjögren (1933) also described the histological features in the lacrimal and salivary glands and in the conjunctiva. In the lacrimal glands the changes consisted of round cell infiltrations, atrophy and destruction of the acini, and replacement fibrosis in the later stages (Fig. 1).

The lesions in the lacrimal glands were considered to be mainly responsible for the dryness of the eyes and the subsequent epithelial changes, but primary degenerative changes in the conjunctival epithelium could also contribute to the developed appearances in keratoconjunctivitis sicca. The histological changes in the lacrimal glands are similar to those
noted in the salivary glands, but one important difference is that while secretory ducts may be blocked in the salivary glands, this does not occur in the lacrimal glands (Morgan, 1954). This is in keeping with the clinical observation that enlargement of the salivary glands is not uncommon in Sjögren's syndrome, but that enlargement of the lacrimal glands is never seen.

**Associated Clinical Features.**—The principal conditions, already recorded as associated with keratoconjunctivitis sicca, and accepted as components of Sjögren's syndrome, are shown in Table I.

<table>
<thead>
<tr>
<th>Clinical Features</th>
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<tr>
<td>Rheumatoid polyarthritis</td>
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<tr>
<td>Xerostoma</td>
<td>14</td>
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<tr>
<td>Salivary gland enlargement</td>
<td>6</td>
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<tr>
<td>Laryngo-pharyngo-rhinitis sicca</td>
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<tr>
<td>Bronchitis and pulmonary atelectasis</td>
<td>5</td>
</tr>
<tr>
<td>Achlorhydria (five cases examined)</td>
<td>5</td>
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<tr>
<td>Vaginitis</td>
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<td>Alopecia</td>
<td>5</td>
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<tr>
<td>Peripheral vascular symptoms</td>
<td>4</td>
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<tr>
<td>Ichthyosis</td>
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It is exceptional for a patient to exhibit most or even many of these features, and usually only polyarthritis and xerostoma are seen. Many of the associated features can be attributed to a deficiency of epithelial glandular secretions and consequent dryness of cutaneous and mucosal surfaces. The co-existence of Sjögren's syndrome and Felty's syndrome, previously noted by Gurling (1953), is further evidence of the common identity of Sjögren's syndrome and rheumatoid disease.

The clinical features in our eighteen cases of severe or moderate keratoconjunctivitis sicca are shown in Table II. Fourteen of the patients, of whom thirteen were women, had associated rheumatoid polyarthritis. The four patients who had no evidence of arthritis comprised one man and three women. In only two instances had ocular symptoms been noticed before the age of 40 years. The nail changes and otitis externa noted in the present series are worthy of special mention.

The nail lesions, seen in both fingers and toes, consisted of dry, longitudinally fissured nails (onychorrhexis), stained brownish-yellow. Those most severely involved were rough and irregularly heaped up, due to subungual hyperkeratosis, and such nails grew slowly, gradually separated and sloughed (onycholysis) and then further nail growth commenced from the irregular nail bed. Similar changes in the nails have been recorded in rheumatoid arthritis (Ragan, 1954), but are only rarely encountered, so that their frequency in the present series is especially noteworthy. The most severe nail lesions occurred in a patient who also had arthritis, alopecia totalis, and several other features of the syndrome. This patient received oral cortisone, 100 mg. daily, and normal nail growth was restored (Fig. 2), but there was no improvement in the alopecia.

**Table II**

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The occurrence of external otitis in three patients is probably a significant finding in a syndrome where deficiency of epithelial secretions is common. Deficient secretion of cerumen and resultant impairment of normal lubrication of the outer ear passages would predispose to dryness and irritation by dust. The appearances in the affected cases were those of dry, sore ears with small, tender fissures in the

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Fig. 2.—Close-up of left hand of a patient suffering from rheumatoid arthritis, who also exhibited many of the features of Sjögren's syndrome, taken after 2 months' treatment with cortisone, 100 mg. daily. There is a clear line of demarcation between the former discoloured nail and the apparently normal new nail formation.
external meatus and helix. The ear wax was dry and powdery, but there was no suppuration or damage to the ear drum. The changes may be described as an otitis externa sicca, comparable to rhinitis sicca.

Treatment

General treatment, by such measures as large doses of vitamins, thyroid extract, and oestrogens, has not proved to be of any value. Local treatments have been directed towards relieving the ocular symptoms. Gifford, Puntenney, and Bellows (1943) employed parasympathomimetic drugs such as pilocarpine nitrate and prostigmine hydrobromide, in an attempt to stimulate lacrimal secretion, and reported success in the treatment of early cases. However, the results have not been impressive in more severe cases, and intestinal cramps limit the dosage of such drugs.

Saline and antibiotic eye drops are not usually helpful because of rapid evaporation. In our experience, artificial tears, which do not evaporate so rapidly, have been of benefit in many mild cases. Methylcellulose drops have been used, and another suitable preparation, suggested by Gifford and others (1943), is:

- Gelatin ........ 0.3 g.
- Chlorbutal ...... 0.3 g.
- Locke's solution .. 30 ml.

One drop of these “tears” can be instilled into the conjunctiva, three to six times daily.

Deep x-ray therapy has been used successfully in reducing the size of the enlarged parotid glands, but no constant improvement has been noted after treatment of the lacrimal glands (Beetham, 1935).

ACTH and cortisone have been administered systemically with conflicting reports of their effect upon lacrimal secretion. In early cases some return of lacrimal secretion has been noted, but side-effects and complications, common to the prolonged administration of high doses of these hormones, have limited the value of this form of treatment. In severe and chronic cases of keratoconjunctivitis sicca the systemic administration of steroid hormones may relieve the ocular symptoms even though unsuccessful in increasing lacrimal secretion.

Topical administration of cortisone and hydrocortisone has, in our experience, proved to be a safe and useful means of treating mild and moderate cases of keratoconjunctivitis sicca (Eadie and Thompson, 1955). The eye drops may be prepared in strengths ranging from 0.5 to 2 per cent., and we employed a saline suspension of cortisone acetate diluted in a buffered base. The drops were instilled three to six times daily, according to the severity of the symptoms, and in no instance has any undesirable side-effect been noted as a result of this treatment. Hydrocortisone drops and cortisone eye ointment were used in the treatment of some patients, but did not appear to confer any extra benefit. The local application of these hormones has been shown to be effective solely by virtue of their anti-inflammatory action, as no increase in lacrimal secretion has been noted during their use.

The operation of sealing both lacrimal puncta, in order to conserve diminished secretions, was introduced by Beetham (1935), and has proved to be an effective surgical procedure. Gifford and others (1943) have reported favourably on its value, and we have found it to be helpful in more severe cases of keratoconjunctivitis sicca that were not adequately controlled by local cortisone therapy. This operation, conveniently done by thermal cauterization of the canaliculus, should not be performed in early or mild cases in whom a remission may be expected, as subsequent improvement in lacrimation would lead to epiphora. In some cases only slight increase in lacrimal secretion, as measured by Schirmer’s filter-paper may occur after operation, but in spite of this there may be an appreciable subjective and objective improvement in the eyes. In very severe cases of keratoconjunctivitis sicca adjuvant therapy with cortisone eye drops or artificial tears may be necessary even after sealing of the lacrimal puncta.

Summary

The clinical features of keratoconjunctivitis sicca have been described and its occurrence in patients suffering from rheumatoid arthritis has been studied. It is considered to be the most common ocular complication of this disease, having been identified in 14.3 per cent. of a series of 210 patients. Mild cases of keratoconjunctivitis sicca are especially common, and the minor, recurrent, conjunctival inflammation noted in many patients with rheumatoid arthritis is conjunctivitis sicca, without corneal lesions.

The associated clinical findings have been described in a series of eighteen patients who exhibited the features of Sjögren’s syndrome. Changes in the nails and otitis externa sicca have been described. The hazard to vision resulting from corneal ulceration has been emphasized. The treatment of the ocular symptoms has been discussed.

We gratefully acknowledge the invaluable advice and co-operation of Dr. J. J. R. Duthie of the Northern General Hospital, Edinburgh, and of Professor G. I. Scott of the Edinburgh Royal Infirmary. During the period when this work was undertaken the Rheumatic Unit, Northern General Hospital, Edinburgh, was in
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receipt of grants from the Nuffield Foundation and Medical Research Council, and one of us (S.E.) received a grant from the W. H. Ross Foundation (Scotland) for the Prevention of Blindness.

The cortisone and ACTH used in the treatment of several of these patients was supplied by the Medical Research Council, to whom we are indebted.

REFERENCES

La kerato-conjonctivite sèche et l'arthrite rhumatismale
RéSUMÉ
On décrit les caractères cliniques de la kerato-conjonctivite sèche et on étudie sa fréquence parmi les sujets atteints d'arthrite rhumatismale. On considère que c'est la complication oculaire la plus fréquente, l'ayant identifié dans 14,3% d'une série de 210 malades. Des cas bénins de kerato-conjonctivite sèche sont particulièrement répandus et l'inflammation mineure et récurrente des conjonctives, observée chez nombreux rhumatisants est, en réalité, une conjonctivite sèche sans lésions de la cornée.

On décrit les manifestations cliniques secondaires chez 18 malades présentant des traits du syndrome de Sjögren, en particulier les altérations des ongles et l'otite externe sèche. On souligne le danger de l'ulcération de la cornée et on discute le traitement oculaire.

La kerato-conjonctivitis sicca y la artritis reumatoide
SUMARIO
Se describen los rasgos clinicos de la kerato-conjonctivitis sicca y se estudia su ocurrencia en sujetos con artritis reumatoide. Se considera que se trata aqui de la complicación ocular la más frecuente, habiéndola identificado en el 14,3% de una serie de 210 enfermos. Casos benignos de kerato-conjonctivitis sicca se ven corrientemente y la inflamación menor y recurrente de las conjuntivas observada en numerosos enfermos con artritis reumatoide representa realmente una conjuntivitis secas sin lesiones de la cornea.

Se describen las manifestaciones clínicas secundarias en 18 enfermos presentando rasgos del síndrome de Sjögren, particularmente las alteraciones unguals y la otitis externa sèche. Se subraya el peligro de la ulceración de la cornea y se discute el tratamiento ocular.
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