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SJÖGREN'S DISEASE, WITH DRYNESS OF THE BRONCHIAL MUCOSA AND UNCERTAIN LUNG LESION

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Henrik Sjögren (1933, 1935, 1938, 1943), of Jönköping, by the careful study of cases of kerato-conjunctivitis sicca, has succeeded in establishing the existence of a syndrome, or rather a disease, which in its complete form includes kerato-conjunctivitis sicca, xerostomia, rhinitis sicca, pharyngitis sicca, and laryngitis sicca, but the disease is far more often incomplete. The eye lesion need not be the presenting condition, and patients may first seek medical advice because of enlargement of salivary glands or because of xerostomia.

The chronic inflammatory changes in the parotid glands, usually without suppuration but with recurrent exacerbations, tend to produce permanent enlargement, sclerosis, or atrophy in irregular combination. Analogous changes occur in the other salivary glands and in the oral mucosal glands; and also in the lacrimal glands, though usually without obvious clinical enlargement. It seems certain that many cases have been labelled as Mikulicz's disease or Mikulicz's syndrome. The skin, especially the sweat glands, and the stomach (acid-producing glands) may be involved in some cases. The clinical onset, often more pronounced on one side than the other, is intermittent and insidious. The patients are mostly middle-aged women. Clinical accompaniments may include accelerated blood-sedimentation rate, alterations in the blood count, in the body temperature, and in the blood-sugar curve, and not rarely arthritic symptoms (rheumatoid arthritis).

In regard to the eye condition Sjögren concluded: "The morbid changes appear to find their simplest explanation in the fact that, owing to intense diminution or complete abolition of the lacrimal secretion, the conjunctiva itself

is obliged to provide for the entire secretion of fluid. As the result of this a chronic oedema arises, which gradually leads to degeneration and atrophy of the epithelium." One may suggest an analogous explanation for the secondary changes in the oral mucosa when they arise in cases of chronic xerostomia of any nature. According to Sjögren's investigations it seems clear that the dryness of the mouth and eyes is preceded by changes (microscopical) in the salivary and lacrimal glands.

Non-ocular features of the disease (Weber, 1945), in addition to the changes in the salivary glands and mouth, may include dryness in the nose, pharynx, and larynx; secondary dysphagia (Plummer-Vinson syndrome); secondary cough (from dryness of mouth and pharynx); achlorhydria; dryness of skin; dryness and atrophic change in the vagina; almost complete alopecia; accelerated blood-sedimentation rate; hypochromic anaemia; low blood pressure; low blood sugar; low blood calcium; Raynaud-like blueness of hands and feet; telangiectasis on lips and tips of fingers; telangiectatic and pigmentary scleroderma-like changes in the legs (Sheldon, 1938-9); and delusional mental symptoms and occasional epileptic fits (Sheldon, 1938-9). But some of these features may possibly be regarded as superadded conditions, not directly connected with Sjögren's disease. However, in regard to the curious pigmentary scleroderma-like dermatosis in Sheldon's case, one of us (Weber, 1945) has heard of another case of Sjögren's disease with similar leg pigmentation.

In the present case the unusual feature is the occurrence of dryness of the bronchial mucosa with some radiological basal pulmonary shadowing of uncertain nature, which may perhaps be interpreted as an infected (granulomatous) atelectasis due to breakdown of the natural defence owing to the dry bronchial mucosa.

Case Report

The patient is a delicately built woman of medium height, aged 34 on Nov. 13, 1948, thin, but apparently not losing weight. Her father died at 57 of heart failure; he suffered from bronchitis. Her mother died at 69 of "sugar diabetes." The parents had eight children, of which the patient is the seventh; all the others are said to be living and healthy. The patient herself has always been thin and delicate-looking, and since the age of 13 has been subject to short Raynaud-like attacks in the fingers—the tips turn white and then blue—relieved by putting the hands into hot water. She had measles at 17 and scarlet fever at 21. While still in the fever hospital after the scarlet fever she developed temporary swellings on both sides of the face, which were considered possibly mumps. About 1940 she noticed a peculiar dryness of the lips and mouth, which she did not get rid of. In January, 1942, painless cherry-sized parotid swellings developed, one on each side, and were diagnosed as Mikulicz's disease. For these she received deep x-ray treatment at the Cancer Hospital (six séances) and they disappeared, but not the dryness of the mouth.

Menstruation, which began at 12 years of age, has remained normal. She married in February, 1939, and in December, 1943, a child (boy) was delivered by caesarean section owing to the presence of a uterine fibroid, which was removed at the same time. The boy was normal at birth and has remained healthy. After suckling him for 8½ months she developed two small painless lumps (September, 1944), one on each side, under the lower jaw. With deep x-ray treatment (six séances) they disappeared. She received further deep x-ray treatment in February, 1946, but for the past eighteen months she has had a small painless swelling in the right sublingual region. About September, 1944, her eyes felt hot, dry, and irritable, and a doctor told her she had conjunctivitis. It cleared up, but has returned on and off ever since.

In April, 1946, she suffered from "dry pleurisy," first on one side and then on the other. For this she was in bed for three weeks only, but never got rid of the dry cough and since then

has never felt quite well. Since then also the eyes have been drier, and in February, 1948, they became much worse and "follicular" conjunctivitis was diagnosed.

In May, 1948, a stiff neck was followed by painful swelling in the knuckles, and pain and stiffness in the wrists, knees, feet, and left shoulder, with some fever. This polyarthritides of the rheumatoid arthritis type, for which she was referred to one of us (P. E.) by Dr. W. Edwards and treated at the Leatherhead Hospital, has now nearly subsided. Her dry cough has become much worse, and when she is talking she has to sip water frequently to relieve the dryness.

Present Condition

She complains of dryness of eyes, mouth, and throat and irritable dry cough, much worse on talking. Sometimes she has slight difficulty in swallowing. Most of her teeth have been extracted. By palpation with the finger and thumb a painless cherry-sized swelling can be felt below the tongue to the right of the middle line. There is slight symmetrical enlargement of the thyroid gland, but no clinical evidence of thyrotoxicosis.

A blood count (Aug. 14, 1948) showed: haemoglobin, 98%; erythrocytes, 4,980,000; colour index, 0.99; leucocytes, 6,000. Another blood count (Dec. 31) gave: haemoglobin, 103%; erythrocytes, 5,700,000; colour index, 0.9; leucocytes, 7,600 (polymorphs 81%, lymphocytes 18%, monocytes 1%). Urine showed nothing abnormal. Blood pressure was 120/80 mm. Hg. Blood Wassermann reaction was negative. Blood sedimentation rate was not raised on June 28, 1948, when it was 5; but on Sept. 26 it was 22 (normal 4 to 8). Blood calcium was 10.6 mg. per 100 ml., blood phosphorus 3.9 mg. per 100 ml., and blood alkaline phosphatase 9 units. There has been no sputum at present. There was no clinical evidence of disease of the heart, abdomen, or central nervous system. In the lungs there is diminution of air-entry at both bases, breath sounds are tubular in type at the left base, and numerous dry crepitations can be heard at both bases, but are especially marked at the left base.

X-ray examination of the chest (July 11, 1947) showed diminished translucency in the left lower lobe, with pleural involvement. On Aug. 16, 1948, there was an area of consolidation in the left lower lobe, with some scattered opacities in the right lower lobe. The heart, mediastinum, and trachea were centrally placed, the left diaphragm was obscured, and the heart was normal in shape, size, and position. A further skiagram on Nov. 30, 1948, showed little appreciable change. Bronchoscopy was negative, except for dryness of bronchial mucosa; no secretion was obtained (Mr. W. P. Cleland, St. Helier Hospital, Carshalton). Electrocardiogram was normal. The hands showed soft-tissue swelling of the proximal interphalangeal joints but no bony changes, nor were there any bony changes in the other joints.

The following additional investigations were carried out at the Hammersmith Hospital. The sputum showed Gram-positive cocci and diphtheroids on direct smear, and *Staphylococcus aureus* on culture. Fractional test meal gave normal secretion of hydrochloric acid. Urinary excretion of 17-ketosteroids and the glucose-tolerance test were normal. Schirmer's lacrimation test showed moistening along 0.5 cm. of the filter paper compared with 3 to 5 cm. in controls. Salivation test, consisting of collection of saliva for three minutes after chewing and swallowing fruit, gave 0.8 ml., whereas control subjects produced 5 to 9 ml. A heating test for sweating gave normal response. A liver biopsy (performed because pulmonary sarcoidosis had been suggested) showed normal histology.

Treatment

Treatment was directed symptomatically to the dry eyes, dry mouth, and dry bronchial mucosa. So far as the eyes are concerned cod-liver oil drops gave symptomatic relief. Attempts were made to increase the salivary secretion by pilocarpine, mechohine, and physostigmine. These produced no appreciable response as shown by the salivation test. In the hope that the changes at the base of the left lung might be improved an attempt was made to alleviate dryness of the bronchial mucosa by keeping the patient for a fortnight in a steam tent (Hammersmith Hospital). This had no beneficial effect on the respiratory condition and the patient thought that

the dampness aggravated the arthritis. Breathing exercises and postural drainage produced no significant result. She was given vitamin A, 150,000 units daily, empirically, as it was thought that this could not possibly do any harm and might conceivably do some good. Closure of the lacrimal ducts by local diathermy was not carried out, since the eye symptoms were not the most troublesome. The patient thinks that inhalation therapy helped her at the Hammersmith Hospital.

Discussion

This case seems to be one of Sjögren's disease, which, we think, may be regarded as a lymphoid granulomatous condition, affecting especially the salivary and lacrimal glands and giving rise to dryness of the mouth and conjunctivae. The presence of slight rheumatoid arthritis may be regarded as a point in favour of this diagnosis. In the present instance the bronchial mucosa is specially affected, and there are pulmonary lesions of uncertain nature, probably granulomatous. Dryness of the bronchial mucosa seems as yet not to have been noted in Sjögren's disease, though its occurrence might have been expected in some cases.

The main salivary gland swellings have disappeared under deep x-ray therapy, but the dryness of the mouth and conjunctivae has increased if anything, and there is a swelling in the right sublingual region. Further treatment of the case, beyond inhalation therapy, is problematic, but we think that the lacrimal ducts should now be closed by diathermy in order to diminish the conjunctival dryness. Mikulicz's disease is a lymphoid granulomatous condition of the salivary and lacrimal glands very susceptible to x-ray treatment, and it is a question how far it can be distinguished from Sjögren's disease, to which perhaps it may be an allied condition (variant). The advisability of further deep x-ray treatment is a matter for consideration—in regard both to the sublingual nodule and to the lungs.

There is also the question of the lung condition being of sarcoid nature, but the negative liver biopsy makes this unlikely. We need not therefore consider the further question of a possible relationship between Sjögren's disease, Mikulicz's disease, and sarcoidosis. The replacement of glandular tissues in Sjögren's disease and Mikulicz's disease by a kind of lymphoid granulomatous tissue reminds one, it may be noted, of the gradual replacement of thyroid glandular tissue by lymphadenoid tissue in cases of so-called lymphadenoid goitre.

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The Ministry of Health states that in many hospitals and clinics the arrangements for the reception and treatment of out-patients in the past have left much to be desired. It suggests that boards and committees should have in mind the elimination of unnecessary out-patient attendances, the reduction of waiting-time to a minimum, and the maximum convenience and comfort of the out-patient. "The institution of an effective appointment system is probably the biggest single contribution that can be made to the convenience and comfort of out-patients." It adds that the resulting saving of space should make possible the replacement of unsightly and uncomfortable forms by cheap but comfortable chairs, and a canteen for out-patients is an amenity which should be provided. Particular attention should be given to the holding of treatment clinics such as physiotherapy and rehabilitation in the evening or at other times outside the normal working hours of patients, so that working time need not be lost by patients unnecessarily.