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SPECIAL REVIEW

Marathon of eponyms: 19 Sjögren syndrome

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The use of eponyms has long been contentious, but many remain in common use, as discussed elsewhere (Editorial: Oral Diseases. 2009: 15; 185). The use of eponyms in diseases of the head and neck is found mainly in specialties dealing with medically compromised individuals (paediatric dentistry, special care dentistry, oral and maxillofacial medicine, oral and maxillofacial pathology, oral and maxillofacial radiology and oral and maxillofacial surgery) and particularly by hospital-centred practitioners. This series has selected some of the more recognized relevant eponymous conditions and presents them alphabetically. The information is based largely on data available from MEDLINE and a number of internet websites as noted below: the authors would welcome any corrections. This document summarizes data about Sjögren syndrome.

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Also known as

Gougerot-Houwer-Sjögren syndrome
Gougerot-Sjögren syndrome
Sjögren disease (Karl Gustaf Torsten Sjögren)
von Mikulicz-Gougerot-Sjögren syndrome

The condition

Sjögren syndrome (SS) is a chronic autoimmune disease – an inflammatory exocrinopathy– affecting mainly postmenopausal women (80–90%) or younger women after artificial menopause. It is characterized by the occurrence of xerostomia, pharyngolaryngitis sicca, rhinitis sicca, enlarged salivary glands, keratoconjunctivitis sicca, dry skin, decreased sweating, dryness and crusting of the nasal passages, blocking of the Eustachian tubes which can cause deafness, vaginal dryness which can cause dyspareunia, a patchy alopecia, decrease of scalp and body hair, areas of hyperpigmentation and hypopigmentation of the skin, vasculitis, purpura, cataracts and Raynaud syndrome.

The most common type is *secondary* SS (SS-2) which comprises dry eyes and dry mouth and a connective tissue or autoimmune disease, usually rheumatoid arthritis or primary biliary cirrhosis. Perversely, SS occurs in only approximately 20% of patients with rheumatoid arthritis, whereas it occurs in nearly all patients with primary biliary cirrhosis. However, as rheumatoid arthritis is so much commoner, most cases of secondary SS occur in these patients. The same clinical features in the absence of a systemic disease are sometimes termed sicca syndrome, now referred to as *primary* SS (SS-1).

In SS there is focal lymphocyte-mediated destruction of salivary, lacrimal and other exocrine glands directed against alpha fodrin, a cytoskeletal protein involved in actin binding. An infective aetiology, possibly by human retrovirus 5 (HRV-5), and a genetic predisposition may be implicated. An SS type of disease may follow infection with HIV, EBV or HCV, *Helicobacter pylori* or graft-versus-host disease.

Chemokines expressed by epithelial cells can attract T lymphocytes and dendritic cells that produce proinflammatory cytokines, which induce apoptosis in the acinar and ductal epithelial cells. The autoantigens SS-A and SS-B are translocated to the apoptotic blebs and trigger infiltrating B lymphocytes to produce autoantibodies against them. Germinal-centre-like structures can form within glandular lymphocyte foci, facilitating the antigen-driven B-cell activation. Type I interferon (IFN) may drive these reactions. One hypothesis is that viral infection induces type I IFN production in salivary glands with a subsequent activation of the adaptive immune system, producing autoantibodies that form nucleic-acid-containing immune complexes that can trigger further type I IFN production. Type I IFN and inflammatory cytokines may cause engagement of the toll-like receptor TLR3 within the salivary glands, resulting in a rapid loss of gland function. IFN gamma (type 2 IFN) can induce class II MHC, Fas and CD40 on salivary epithelial cells, and also induces T cell-attracting chemokines, such as IP-10 (CXCL10; chemokine [C-X-C motif] ligand), Mig (CXCL9) and I-TAC (CXCL11). IFN gamma dysregulation in SS salivary

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glands may also contribute to the decreased production of TGF beta from salivary epithelial cells. SS salivary epithelial cell death requires the cooperation of Fas and CD40.

Oral features of SS (often the presenting feature) may include:

- xerostomia,
- difficulty in eating dry foods (the cracker sign),
- soreness,
- difficulties in controlling dentures in speech and swallowing,
- disturbed taste,
- salivary gland swelling.

Sore and red oral mucosa, and angular stomatitis are usually the result of candidiasis. Dental caries tends to be severe and difficult to control. Ascending (suppurative) sialadenitis is a hazard. Salivary swelling is occasionally massive and associated with enlarged regional lymph nodes – pseudolymphoma. B cell lymphoproliferation may actually become malignant, with a true lymphoma.

Diagnosis is mainly from history and clinical examination. Salivary flow rate is reduced. Vital staining with Rose Bengal and slit lamp examination is a sensitive test for corneal drying and has largely replaced the Schirmer test.

Helpful investigations can include:

- Serum autoantibodies – particularly rheumatoid factor (RF) and antinuclear antibodies (ANA) known as SS-A (Ro) and SS-B (La). SS-A is common in many autoimmune diseases [e.g., systemic lupus erythematosus (SLE), SS/SLE overlap syndrome, subacute cutaneous LE (SCLE), neonatal lupus and primary biliary cirrhosis] including secondary SS. In contrast, anti-La/SSB is more associated with primary SS.
- anaemia
- increased erythrocyte sedimentation rate (ESR) or plasma viscosity
- labial gland biopsy
- salivary studies.

Drugs to control underlying autoimmune disease are largely experimental (e.g., ciclosporin and rituximab). About 5% of patients with SS develop lymphoid malignancy. Patients with severe SS are most likely to develop lymphomas – usually salivary extranodal marginal zone B cell (MALT) or diffuse large B-cell lymphomas.

Background to eponym

Gougerot in 1925 described three cases of salivary gland atrophy associated with dry eyes, mouth and vagina. Houwer (1927) and Wisssmann (1932) noted the joint occurrence of keratoconjunctivitis sicca and arthritis. Sjögren in 1933 published the complete disease picture.

The main persons

Henrik Samuel Conrad Sjögren was born on 23 July 1899, in Köping on Mälaren, Scheele, Sweden. He graduated in Medicine from the Karolinska Institutet, Stockholm, in 1922 and was appointed at the Serafimerlasarettet in 1925. There he first met a patient with 'his' syndrome, a 49-year-old woman. In 1927, he qualified as a physician. Shortly afterwards, he was employed at the Sabbatsbergs sjukhus, and had soon accumulated another four cases, published in 1930. Sjögren described his syndrome in 1933 in his doctoral thesis 'Zur Kenntnis der keratoconjunctivitis sicca'. In 1936, Sjögren took up an appointment in eye medicine at the hospital in Jönköping, and was appointed as a 'lasarettsläkare' there in 1938. In 1943, his paper was translated into English. In 1957, Sjögren became an associate professor at the University of Göteborg and in 1961 honorary professor. He was elected honorary member of The Australian Ophthalmological Society in 1951, of the American Rheumatism Organisation in 1970 and of Svensk Reumatologisk Forening and of the Royal College of Physicians and Surgeons of Glasgow in 1976. He died in Lund on 17 September 1986.

Henri Gougerot was born on 2 July 1881, in Saint-Ouen-sur-Seine, France. He qualified as doctor of medicine from the University of Paris in 1908, and became professor agrégé at the faculty of medicine in 1910. During World War I, he served in the French Army, being awarded the Croix de Guerre. In 1928, he was appointed to the Chair of dermatology and syphilology at Paris and became chief physician at the Hôpital St Louis.

He wrote on numerous aspects of dermatology, including hemisporosis, sporotrichosis, sarcoidosis, lupus and cutaneous papillomatosis. With Ferdinand-Jean Darier and Raymond Jacques Adrien Sabouraud, he edited the text Nouvelle Pratique Dermatologique (1936) and was made an honorary foreign member of the British Association of Dermatology.

Gougerot died in 1955 – with a list of no less than 2500 publications.

Jan Mikulicz-Radecki (Johannes Freiherr von Mikulicz-Radecki) was born on 16 May 1850, in Czerniowce, Bukowina, Romania. He studied in Vienna from 1869, received his medical doctorate there in 1875 and then worked for 3 years as an apprentice in surgery under Theodor Billroth and then as an assistant until 1882, when he became Professor ordinarius of surgery and Director of the surgical clinic in Kraków in 1882. In 1887, he became Professor ordinarius of surgery at the University of Königsberg, and then from 1890 worked at Breslau.

Mikulicz contributed prodigiously to cancer surgery, especially on organs of the digestive system. With Bernhard Naunyn, Mikulicz-Radecki founded *Mitteilungen aus dem Grenzgebieten der Medizin und Chirurgie* in 1896. He died in Breslau on 4 June 1905.

Associated persons

Henri Gougerot
Jan Mikulicz-Radecki
Adriaan Willem Mulock Houwer
Henrik Samuel Conrad Sjögren

Source internet sites (accessed 21 February 2009) and further reading

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