Episode 107 – Sjögren Syndrome April 26, 2024

Overview

Sjögren syndrome[1] is a chronic, systemic, inflammatory, autoimmune disorder[2] affecting exocrine glands, primarily the salivary and lacrimal glands, and any organ that depends on exocrine glands. It can occur alone or with other autoimmune conditions (e.g., rheumatoid arthritis, systemic lupus erythematosus, systemic sclerosis,[3] vasculitis, mixed connective tissue disease, Hashimoto thyroiditis, primary biliary cirrhosis, chronic autoimmune hepatitis). There is no cure for Sjögren syndrome, but various strategies exist to manage the symptoms. [1] [2] [3] [4] [5] [6]

Prevalence

Sjögren syndrome is the second most prevalent autoimmune disease. It usually occurs after age 45 but can also affect young adults and children. Around 1% of the general population is affected by primary or secondary Sjögren syndrome, with over 85% of the cases reported in females, and more commonly in females aged 50 years or older, with up to 3% of females over 50 being affected. [3] [7]

Pathophysiology

Leukocytes[4] infiltrate and damage exocrine glands, and sometimes other organs are damaged. Specifically, salivary, lacrimal, and other exocrine glands are infiltrated with CD4+ T cells[5] and some B cells.[6] The T cells produce inflammatory cytokines. Salivary duct cells also produce cytokines, eventually damaging the secretory ducts. Lacrimal gland secretory epithelium atrophy causes cornea and conjunctiva[7] dryness (termed keratoconjunctivitis sicca). Lymphocytic infiltration and intraductal cellular proliferation in the parotid gland cause luminal narrowing and in some cases gland atrophy. [2]

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[1] Sjögren syndrome, also known as Sjögren's disease, was named after Swedish physician Henrik Sjögren who first described the condition in 1933. He had been treating a group of females whose chronic arthritis was accompanied by dry eyes and mouth. He used the term "sicca syndrome" to describe the ocular and oral dryness. [7] [12] [25]

[2] Refer to Episode 45 to learn more about the immune system and autoimmune disorders.

[3] Refer to Episode 62 for information on lupus and systemic sclerosis.

[4] Refer to Episodes 44 and 45 for additional information on leukocytes and the immune system.

[5] CD4+ T cells are leukocytes that help B cells produce antibodies against foreign antigens, help killer T cells become active, and stimulate macrophages, enabling them to ingest infected or abnormal cells more efficiently.

[6] B cells secrete antigen-specific antibodies which circulate in the blood and act upon extracellular microbes and their toxins.

[7] The conjunctiva is the thin clear membrane that covers the sclera and the inner surface of the eyelid to protect the eye.

Types

Sjögren syndrome is classified as primary or secondary.

- Primary Sjögren syndrome occurs in the absence of another underlying rheumatic disorder. Most individuals with primary Sjögren syndrome have two specific antibodies against SS-A (or Ro) and SS-B (or La) antigens.
- Secondary Sjögren syndrome is associated with another underlying rheumatic disease, such as systemic lupus erythematosus, rheumatoid arthritis, or scleroderma.

Given the overlap of Sjögren syndrome with many other rheumatic disorders, it is sometimes difficult to determine whether a clinical manifestation is solely from Sjögren syndrome or due to a concurrent disorder. [1] [8]

Symptoms

Sjögren syndrome can affect individuals differently, and symptoms can cycle between mild and severe. The clinical features of Sjögren syndrome are often divided into those related to exocrine dysfunction (i.e., glandular manifestations) and those that affect organs other than the exocrine glands (i.e., extraglandular or systemic manifestations). [1] [9]

Glandular manifestations

Two main symptoms of Sjögren syndrome are xerophthalmia (dry eyes) and xerostomia (dry mouth). In some individuals, only the mouth or eyes are dry (a condition called sicca syndrome or sicca complex). [5]

Dry eyes can cause a sandy, gritty sensation. Eyes may be red, itchy, and painful. The cornea can become severely damaged. The dryness may cause blurry vision or sensitivity to bright light. The eyelids may get irritated and itchy due to inflammation. Symptoms typically worsen throughout the day, probably due to evaporation of the already scanty aqueous layer. Some individuals awaken with matting in their eyes and, when severe, have difficulty opening their eyes in the morning.

Xerostomia from diminished saliva can cause trouble swallowing, speaking, tasting, and wearing dentures or other oral appliances, which may lead to decreased food intake and poor nutrition. It also increases the risk of dental caries,[8] periodontal disease, salivary gland stones, and oral infections, such as candidiasis. Candidiasis can present with burning pain (i.e., secondary burning mouth syndrome).[9]

Parotid gland enlargement occurs in about 33% of individuals. Submandibular and sublingual gland swelling may also take place. Salivary gland enlargement tends to correlate with the severity of the disease. Chronic salivary gland enlargement is rarely painful unless there is obstruction or infection. Salivary gland enlargement can come and go or remain constant; it can be bilateral or unilateral. Bilateral parotid swelling is the most common sign of Sjögren syndrome onset in children. [5] [8]

[8] Refer to Episodes 86 and 87 for detailed discussion on dental caries.
[9] Refer to Episode 106 for additional information on burning mouth syndrome.

Saliva can be thick, ropey, and mucinous, or it may be altogether absent. Oral mucosal changes are those typical of xerostomia. They include dry, red, and wrinkled mucosa and a cobblestone appearance of the tongue due to atrophy of the papillae. Tongue fissuring and angular cheilitis are also common. [8]

Clients may describe the effects of dry mouth as:

- Inability to eat dry food (e.g., crackers) because it sticks to the roof of the mouth
- Tongue sticking to the roof of the mouth
- Putting a glass of water on the bed stand to drink at night (resulting in nocturia, the need to get up at night regularly to urinate)
- Difficulty speaking for long periods or the development of hoarseness
- Altered sense of taste
- Difficulty wearing dentures or other oral appliances
- Mouth pain
- Difficulty swallowing and food becoming stuck in the throat [8]

Glandular manifestations can also affect the skin and other mucous membranes. For example, dryness may develop in the skin and mucous membranes of the nose, throat, larynx, bronchi, vulva, and vagina. Hair may be dry, sparse, and brittle. Diffuse alopecia may involve the scalp and other areas of the body. Partial or complete loss of sweating may be present. Sense of smell can be diminished, and dryness of the respiratory tract may cause cough. [3] [5] [7] [8] [10] [11]

Extraglandular manifestations

Extraglandular signs and symptoms may include:

- Arthralgia (joint pain affects 50% of people, most often smaller joints)
- Arthritis (affects 33% of people and affects the same joints as rheumatoid arthritis, but joint inflammation of Sjögren syndrome tends to be milder and is usually not destructive)
- Generalized lymphadenopathy
- Skin rashes (including purpura - red or purple-coloured spots on the skin of the lower legs from small blood vessel leakage under the skin)
- Prolonged fatigue
- Impaired concentrating ability
- Raynaud phenomenon[10]
- Myalgia (muscle pain)
- Pulmonary disease
- Gastrointestinal disease
- Leukopenia
- Anemia
- Neuropathy
- Vasculitis
- Pancreatic insufficiency

[10] Raynaud phenomenon is a condition in which arterioles, usually in the fingers or toes, overly constrict in response to cold exposure, causing fingers or toes to become pale or bluish, numb, and tingle. [26]

- Pancreatitis
- Chronic hepatobiliary disease
- Alopecia
- Kidney problems (e.g., kidney stones, glomerulonephritis, renal tubular acidosis)
- Lymphoma (more common among people with Sjögren syndrome than the general population) [2] [8] [10]

Etiology

The precise etiology of Sjögren syndrome is unknown. Genetic susceptibility and environmental factors, for example, stress, hormones, and viruses (e.g., Epstein-Barr virus (EBV), human T-lymphotropic virus type 1 (HTLV-1),[11] human herpesvirus 6 (HHV-6), HIV, hepatitis C virus, cytomegalovirus) may play a role. Research has also shown an increased risk of Sjögren syndrome with COVID-19 infection. [5] [8] [9] [12] [13] [14]

Risk factors

Sjögren syndrome typically occurs in individuals with one or more known risk factors, such as:

- Age (usually diagnosed in people >45).
- Female sex (females are more likely to develop Sjögren syndrome).
- Rheumatic disease (common for people with Sjögren syndrome to concurrently have a rheumatic disease, such as rheumatoid arthritis, lupus, etc.). [10]

Complications

The most common complications involve the oral cavity and the eyes, including:

- Dental caries due to xerostomia, especially cervical, root, or incisal and cuspal tip dental caries.
- Oral candidiasis.
- Infection of the parotid gland, typically staphylococcal, streptococcal, or pneumococcal. Presentation may include unilateral worsening of symptoms, along with tenderness, warmth, and erythema.
- Parotid tumours may present as unusually hard or unilateral parotid enlargement
- Vision problems such as ocular dryness can lead to light sensitivity, blurred vision, and corneal damage.

Less common complications include:

- Pneumonia, bronchitis, or other lung problems from lung inflammation.
- Problems with kidney function.
- Hepatitis or cirrhosis of the liver.
- Peripheral neuropathy with numbness, tingling, and burning in the hands and feet.
- Lymphoma (cancer of the lymph nodes). [4] [8] [10]

[11] Human T-lymphotropic virus type 1 (HTLV-1) can cause a type of cancer called adult T-cell leukaemia/lymphoma (ATL) and a progressive nervous system condition known as HTLV-1-associated myelopathy or tropical spastic paraparesis (HAM/TSP). [28]

Diagnosis

Sjögren syndrome can be challenging to diagnose because the signs and symptoms may fluctuate, vary from person to person, and be similar to those caused by other diseases. Side effects of many medications also mimic some signs and symptoms of Sjögren syndrome. People with undiagnosed Sjögren syndrome may consult several specialists about Sjögren-related symptoms, not knowing these symptoms are connected, and healthcare providers may not ask about symptoms unrelated to their specialty. On average, it may take up to five years to receive a diagnosis. [15] [16]

Usually, a rheumatologist diagnoses the disease. However, eye care practitioners (e.g., ophthalmologists, optometrists) or dental specialists may also perform specific tests to help make the diagnosis. [1] [17]

There is no single test that will confirm the diagnosis of Sjögren syndrome. Diagnosis begins with a complete health history and physical examination. Diagnosis is based on:

1) Clinical criteria,
2) Eye and salivary gland testing,
3) Blood tests, and
4) Salivary gland biopsy. [2]

Clinical criteria

The key to prompt diagnosis is clinical evaluation of clients with symptoms of oral or ocular dryness. This evaluation should include a complete review of the body systems, including specific questions to assess oral and ocular dryness, clinical examination, and investigations to assess the degree of exocrine gland dysfunction, the presence of relevant immunologic abnormalities, and the extent of organ involvement. [2] [5] [9]

Certain criteria are used to help diagnose primary Sjögren syndrome. These criteria are applied to people who have at least one symptom of ocular or oral dryness. The eye and oral symptoms are as follows:

- Eye symptoms: Daily, persistent, troublesome dry eyes for ≥3 months, recurrent sensation of sand or gravel in the eyes, or use of tear substitutes ≥3 times a day.
- Oral symptoms: Daily dry mouth sensation for >3 months or daily use of liquids to aid in swallowing dry food.

However, it is important to note some people with Sjögren syndrome may not fulfill these strict criteria for eye or oral symptoms. Once eye or oral symptoms are confirmed, criteria are used to determine whether the person has other symptoms to support the diagnosis of Sjögren syndrome.

Criteria are also used to exclude other disorders. The differential diagnosis of Sjögren syndrome is extensive because oral and ocular dryness can be attributed to several different clinical entities. [9]

Differential diagnosis

The following should be considered in the differential diagnosis of Sjögren syndrome:

- Medications (xerostomia is associated with >500 medications, e.g., diuretics, antihistamines, antidepressants)[12]
- Viral infections (e.g., HIV infection, hepatitis C virus infection, mumps)[13]
- Tumours (e.g., parotid gland tumour)
- Bulimia (self-induced vomiting can lead to salivary gland enlargement, e.g., parotid, sometimes submandibular)[14]
- Metabolic disorders (e.g., diabetes mellitus)[15]
- Radiation therapy to the head or neck[16]
- Sarcoidosis
- Chronic graft-versus-host disease
- Lymphoma
- Amyloidosis
- IgG4-related sialadenitis[17]
- Autoimmune thyroid disease
- Dehydration
- Complications from contact lenses
- Mouth breathing[18] [2] [5] [8] [9]

Eye tests

Assessment of lacrimal gland function may include:

- Schirmer test to estimate the quantity of tears from lacrimal glands produced in five minutes. The test is done by placing a filter paper strip under each lower eyelid, waiting five minutes, and observing how much of the strip is moistened. If the amount of the tears secreted onto the paper strip is less than or equal to 5mm in at least one eye, it confirms a dry eye. A person with Sjögren syndrome may produce less than one-third of the normal amount.
- Ocular surface staining to examine the surface of the eyes for damage and dryness. Yellow fluorescein dye is instilled into the eyes, and with the use slit lamp and blue light, the amount of staining on the cornea is given an ocular stain score. A score of ≥5 indicates dry eye disease.
- Van Bijsterveld score to assess the surface of the eye using rose bengal or lissamine green dyes. After the dye is instilled, a white light is used to count the number of dry spots in the conjunctiva. A score of ≥4 indicates a dry eye. [2] [16] [18]

[12] Refer to Episode 62 for additional information on drug-induced xerostomia.
[13] Refer to Episode 61 for information on HIV, hepatitis C, and mumps.
[14] Refer to Episodes 95 and 96 for detailed discussion on eating disorders.
[15] Refer to Episodes 91, 93, and 94 for additional information on diabetes.
[16] Refer to Episodes 68, 78, and 92 for additional information on head and neck radiation therapy.
[17] IgG4-related sialadenitis is an autoimmune disorder that can affect major salivary glands and lacrimal glands. Glands are painlessly enlarged bilaterally, but usually, their function is not impaired. [27]
[18] Nonexhaustive list.

Salivary gland tests
Salivary gland tests may include:

- Salivary flow test can help confirm abnormally low saliva production, which includes collecting unstimulated saliva in a graduated tube (≤ 1.5 mL/15 min, ≤ 0.1 mL/min) (>1.5 mL in 15 min is considered normal).
- Modified Schirmer test to measure unstimulated saliva flow.
- Other tests such as salivary scintigraphy (nuclear medicine), sialography (x-ray), and ultrasounds may help to evaluate salivary gland functioning.
- Qualitative methods to evaluate saliva production, such as:
    - Looking for normal pooling of saliva under the tongue.
    - Tongue blade held against the buccal mucosa for 10 seconds, if the blade falls off immediately when released, salivary flow is considered normal. The more difficulty removing the tongue blade, the more severe the dryness.
    - Lipstick sign, where lipstick adheres to the front teeth of the wearer, may indicate dry mouth. [2] [16] [19] [20]

Blood tests
Blood tests are used to determine complete blood count and for viral testing (e.g., hepatitis C virus, HIV). Blood tests can identify antibodies to help determine autoimmunity and Sjögren syndrome, such as:

- SS-A (or Ro) antibodies: detected in ≥70% of people with Sjögren syndrome
- SS-B (or La) antibodies: detected in 40% of people with Sjögren syndrome
- Antinuclear antibodies (ANA): detected in 70% of people with Sjögren syndrome and those with other autoimmune diseases
- Rheumatoid factor (RF): detected in 60-70% of people with Sjögren syndrome and those with other autoimmune diseases

Erythrocyte sedimentation rate (ESR), a test that measures the rate at which erythrocytes settle to the bottom of a test tube, is elevated in about 70% of people. About 33% of people have a decreased number of erythrocytes (i.e., anemia), and up to 25% have a reduced number of certain leukocytes (i.e., leukopenia). [5] [9] [16]

Although blood tests can help diagnose Sjögren syndrome, they alone cannot confirm a definite diagnosis because the abnormalities they detect are sometimes present in healthy people or people with other disorders. [5]

Salivary gland biopsy
Labial minor salivary gland biopsy is often used to diagnose Sjögren syndrome because it is less invasive than obtaining a biopsy sample from one of the major salivary glands or the lacrimal glands. Histologic examination of minor salivary is to determine the presence of lymphocytic infiltrates around the salivary gland epithelium, a hallmark of Sjögren syndrome. [3] [9]

Prognosis
Prognosis is generally good, with overall health and life expectancy mainly unaffected in those whose only symptoms are dry eyes and mouth. However, if the lungs, kidneys, or lymph nodes are damaged by autoantibodies, pneumonia, kidney failure, or lymphoma

may result. Individuals with Sjögren syndrome have a higher risk of developing any type of lymphoma than people who do not have Sjögren syndrome. [5]

Management

No cure for Sjögren syndrome is available, but symptoms can be managed. A team of healthcare professionals is often involved in symptom management, including rheumatologists, physicians, nurse practitioners, eye care practitioners (optometrists or ophthalmologists), other specialists (e.g., nephrologists, respirologists, oncologists), and oral health professionals. Management may include measures to relieve dry eyes and xerostomia, avoiding aggravating factors, and using certain medications for symptom relief and severe disease.

Dry eyes

Dry eye relief may include:

- Using preservative-free artificial teardrops during the day and eye lubricants at night. Eye lubricants do not have to be applied as often as artificial tears, but their thicker consistency can blur vision, so overnight is often recommended.
- Increasing indoor humidity.
- Reducing evaporation of tears by wearing protective eyewear outdoors to protect eyes from air and wind and avoiding sitting in front of a fan or air conditioning vent.
- A simple surgical procedure to seal the tear ducts (i.e., punctal occlusion). Collagen or silicone plugs are inserted into the tear ducts in the corner of the lower eyelids to help tears stay on the eye longer.
- Prescription eyedrops such as cyclosporine (e.g., Restasis) or lifitegrast (Xiidra) may be recommended for moderate to severe dry eyes to help decrease eye inflammation. [5] [15]

Xerostomia

Salivary gland dysfunction increases the risk of halitosis,[19] dysgeusia (altered taste), oral candidiasis, traumatic oral lesions, dental caries, periodontal disease, and tooth loss. It can also lead to diminished quality of life and costly dental treatment. Management of xerostomia is to alleviate symptoms and prevent oral complications.

Strategies to help prevent complications and provide xerostomia relief may include:

- Increasing fluid intake by sipping fluids, particularly water, throughout the day.
- Stimulating saliva flow with sugarless chewing gum or lozenges (e.g., sweetened with xylitol).
- Using saliva replacement products (e.g., mouthrinses,[20] gels) with neutral pH for dentate clients.
- Brushing and cleaning between teeth after every meal (e.g., water irrigation devices)[21]
- Using topical fluoride represents best clinical practice for those with dry mouth (e.g., fluoride trays, high fluoride toothpaste, fluoride varnish, sodium fluoride mouthrinse).

[19] Refer to Episode 67 for discussion on halitosis.
[20] Refer to Episode 103 for the role of mouthrinses in oral care.
[21] Refer to Episode 89 for additional information on oral self-care.

- Avoiding toothpaste with sodium lauryl sulphate (SLS) to help reduce oral irritation.
- Pilocarpine (Salagen) may be prescribed to help increase saliva production among individuals with residual gland function. Pilocarpine use showed statistically significant improvements in oral, ocular, nasal, vaginal, and skin dryness and salivary flow rates. Side effects of pilocarpine can include sweating, abdominal pain, flushing, runny eyes and nose, and increased urination.
- Decreasing mouth breathing by using nasal saline spray to help moisturize and clear nasal passages to help nasal breathing.
- Avoiding tobacco products.[22]
- Avoiding drinking coffee or alcohol, which can exacerbate xerostomia.
- Avoiding acidic beverages (e.g., soft drinks, sports drinks) to protect teeth from erosion.[23]
- Limiting intake of fermentable carbohydrates.
- Avoiding medications (if possible) that reduce saliva flow (e.g., decongestants, antidepressants, antihistamines).
- Using a humidifier.
- Chlorhexidine administered by varnish, gel, or rinse may be considered in those with dry mouth and high root caries rate. Note: The strength of this recommendation is rated as weak because of a lack of evidence and potential side effects associated with chlorhexidine use.
- Nonfluoride remineralizing agents may be considered as an adjunct therapy in those with dry mouth and a high root caries rate. Note: The moderate strength of this recommendation was based on studies that demonstrated the benefit of calcium phosphate rinse in preventing caries.
- Scheduling regular oral health appointments to ensure early detection and treatment of oral complications (e.g., dental caries, oral candidiasis, periodontal diseases, salivary gland enlargement). [5] [9] [11] [15] [21] [22] [23]

<u>Other oral conditions</u>

- Salivary gland stones should be promptly removed to preserve viable salivary tissue. Painful, enlarged salivary glands can be alleviated with analgesics (e.g., nonsteroidal anti-inflammatory drugs) and warm, moist compresses after ruling out bacterial infection and lymphoma.
- Oral candidiasis is treated with antifungal medications.
- Dental implants may be an option to replace missing teeth since some people with Sjögren disease may have difficulty wearing dentures due to dry and sensitive oral mucosa. [2] [5] [9] [15] [24]

Medications

The following medications may be prescribed depending on the symptoms:

- Nonsteroidal anti-inflammatory drugs (NSAIDs) may help arthritis symptoms.
- Antimalarial drugs (e.g., hydroxychloroquine [Plaquenil]) to treat arthralgia and inflammation and myalgia.

[22] Refer to Episode 101 for information on tobacco use and cessation.
[23] Refer to Episode 82 for information on tooth wear, including dental erosion.

- Methotrexate may also be given alone or in combination with antimalarial drugs to suppress immune response when antimalarial drugs do not successfully relieve joint symptoms.
- Corticosteroids (e.g., prednisone) or sometimes rituximab (a monoclonal antibody) may be needed in severe disease, such as peripheral neuropathy, severe parotid swelling, severe lung involvement, or inflammatory arthritis that does not respond to other therapies. [2] [5] [9] [15]

Addressing other symptoms

Strategies for other areas of dryness include:

- Avoiding hot water when bathing or showering if dry skin is a problem. Pat skin dry with a towel and apply moisturizer when the skin is still damp.
- Using rubber gloves when doing dishes or housecleaning to protect the skin.
- Vaginal moisturizers and lubricants can help with vaginal dryness. [15]

There is no clearly effective treatment for fatigue in people with Sjögren syndrome. [5]

People with secondary Sjögren syndrome receive additional treatment for concurrent diseases (e.g., lupus, rheumatoid arthritis, etc.). [5]

Take home messages

- Dry mouth may signal the presence of Sjögren syndrome, particularly when it is associated with dry eyes.
- Oral health practitioners may be the first to detect Sjögren syndrome.
- Early recognition and referral to appropriate specialists for diagnosis and treatment are essential to ensure proper monitoring, timely treatment, and prevention of serious complications associated with Sjögren syndrome.
- Regular oral health appointments are vital to monitor and manage oral symptoms and to help prevent potential complications.

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Client Resources

Dry mouth, ODHA factsheet
https://odha.on.ca/wp-content/uploads/2016/08/ODHA-Facts-Dry-Mouth.VFS18-copyright.pdf

Sjögren's Society of Canada
https://sjogrenscanada.org/what-is-sjgrens/diagnosis.html

Sjögren's Foundation
https://sjogrens.org/

Arthritis Society of Canada
https://arthritis.ca/about-arthritis/arthritis-types-(a-z)/types/sjogren-syndrome

Additional Resources

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