SJÖGREN'S SYNDROME

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Abstract
Sjögren's syndrome is a systemic autoimmune disease that affects connective tissues, primarily involving the exocrine glands—mainly the salivary and lacrimal glands—in the pathological process and progresses chronically. As a result of this process, dryness of the mouth (xerostomia) and dryness of the eyes (xerophthalmia) are observed. The disease can occur independently in its primary form or develop as a secondary form together with other autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus. This article provides a scientific analysis of the pathogenetic mechanisms, clinical features, diagnostic criteria, and preventive measures of Sjögren's syndrome. The results of the study emphasize the scientific and practical significance of early detection and effective management of the disease to promote a healthy lifestyle among the population.
Keywords: Sjögren's syndrome, xerostomia, xerophthalmia, rheumatoid arthritis, systemic lupus erythematosus, lymphocytic infiltration, autoimmune damage, apoptotic products, perforin mechanisms, pSS (primary Sjögren's syndrome).

INTRODUCTION

Sjögren's syndrome is a chronic, systemic autoimmune disease primarily characterized by lymphocytic infiltration of the exocrine glands. This results in symptoms such as dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca). The disease was first described in 1933 by the Swedish ophthalmologist Henrik Sjögren. It mainly affects middle-aged women and often occurs in association with other autoimmune diseases such as rheumatoid arthritis or systemic lupus erythematosus. The exact etiology of Sjögren's syndrome has not yet been fully elucidated, but it is believed to result from the interplay of genetic, hormonal, and environmental factors, leading to an immune system attack against glandular tissues. In addition to classic glandular symptoms, patients may also experience systemic complications involving the musculoskeletal system, lungs, kidneys, and nervous system. Early detection and multidisciplinary management are crucial, as they help alleviate symptoms, prevent complications, and improve the patient's quality of

life.This article provides a scientific analysis of the main clinical features, pathogenic mechanisms, diagnostic criteria, and modern treatment approaches for Sjögren's syndrome. It also highlights the importance of a healthy lifestyle in preventing the syndrome and aims to improve public medical literacy.

Main Body

Sjögren's syndrome is a chronic systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands. It can manifest as a primary form (pSS), occurring independently, or as a secondary form (sSS), associated with other autoimmune diseases. Primary Sjögren's syndrome predominantly affects women, especially Caucasian women, typically between the ages of 40 and 50. Clinical manifestations can range from mild to severe, including classic symptoms such as dry eyes, dry mouth, keratoconjunctivitis sicca, and xerostomia, to severe systemic involvement affecting multiple organ systems.Various autoantibodies may be detected in the disease, including anti-SSA/Ro, anti-SSB/La, rheumatoid factor, cryoglobulins, and antinuclear antibodies, which can complicate the diagnostic process. The variability of symptoms and signs has led to the development of several classification criteria. However, there is currently no single internationally accepted diagnostic criterion for Sjögren's syndrome. Epidemiological studies on Sjögren's syndrome are limited, and the prevalence and incidence rates vary depending on the criteria used. Data accuracy is also affected by selection and classification biases, making precise estimates challenging.

Pathogenesis

The pathogenesis of Sjögren's syndrome involves several interconnected processes. Although a detailed discussion is beyond the scope of this article, the main mechanisms include:

a) Early changes in glandular cells and blood vessels, which occur before lymphocytic infiltration [2].

b) Activation of the innate (HLA-independent) immune system, which can respond to apoptotic products, including RNA-protein complexes containing SS-A particles [3].

c) Partial destruction of the glands via granzyme/perforin mechanisms [4].

d) Dysfunction of the remaining glands (affecting approximately 50% of the original ducts and acini) caused by disruption of matrix signaling through inflammatory cytokines (e.g., IL-1, TNF), autoantibodies (e.g., anti-muscarinic M3 receptor antibodies), and metalloproteinases. These factors reduce neurotransmitter release from the remaining neurons and impair the response of the glands to existing neurotransmitters [5].

Each stage is influenced by genetic factors (i.e., the acquired immune system) and environmental factors (i.e., HLA-independent innate immune system), which together can lead to glandular dysfunction/destruction and lymphoproliferation. Sjögren's syndrome also illustrates an interesting interaction between local mucosal inflammation and the central nervous system, as seen in the perception of dryness. Understanding that urine and tear production are functional circuit outcomes has led to new therapeutic approaches [6]. For example, patients with Alzheimer's disease or multiple sclerosis often experience significant dryness due to changes in subcortical white matter involved in functional circuits. This has led to the use of drugs like Cevimeline, initially developed as a muscarinic agonist for Alzheimer's treatment, as a therapy to stimulate salivation.

Classification Criteria and Diagnostic Evaluation

Since the 1970s, various classification criteria for Sjögren's syndrome have been developed and evaluated. Recently, the existing U.S. criteria (2012) were integrated into the current classification system by major societies, namely ACR (American College of Rheumatology) and EULAR (European League Against Rheumatism).In patients experiencing sicca symptoms for at least 3 months, classification relies on additional functional tests (e.g., Schirmer's test), serological tests (Anti-Ro/SSA), and histological evaluation (labial salivary gland biopsy). Among these, anti-Ro/SSA antibodies and abnormal labial salivary gland biopsy have the highest specificity and are considered the most valuable criteria. A minimum score of 4 points is sufficient to classify a patient as having Sjögren's syndrome. Diagnostic algorithms illustrate how the revised classification criteria, combined with various disease manifestations, guide the diagnosis.

Key Points:

Sjögren's syndrome should be suspected if sicca symptoms persist for more than 3 months after excluding drug side effects and other possible causes.

ANA titers >1:160 with fine granular ANA pattern indicate the presence of anti-Ro/SSA and/or anti-La/SSB antibodies.

Anti-Ro/SSA antibodies and abnormal labial salivary gland biopsy provide the highest diagnostic specificity for Sjögren's syndrome.

Assessment of quality of life, organ-specific manifestations, and lymphoma risk is crucial for interdisciplinary treatment and monitoring.

Extraglandular manifestations are treated according to the affected organ using immunosuppressants or DMARDs; the efficacy of biologic agents for these indications is not yet fully established.

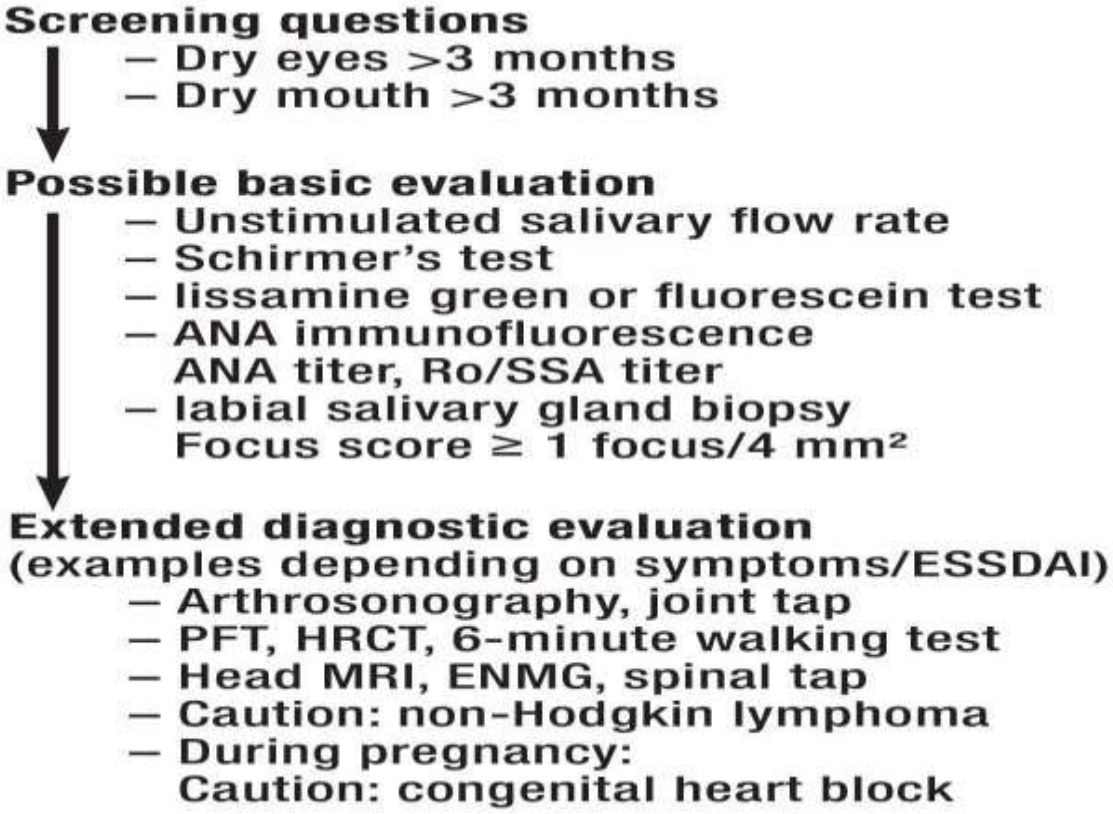

Figure: Diagnostic Algorithm for Sjögren's Syndrome

Abbreviations:

ANA – antinuclear antibodies

ENMG – electroneuromyography

ESSDAI – Sjögren's Syndrome Disease Activity Index (developed by EULAR)

HRCT – high-resolution computed tomography

PFT – pulmonary function test [7]

Treatment

Efficacy of Specific Therapeutic Agents in Current Clinical Practice currently, no immunosuppressive drug has been approved specifically for patients with primary Sjögren's syndrome (pSS). However, limited evidence and clinical experience allow for a clinical perspective based on expert opinion.

Glucocorticoids

No large clinical trials have been conducted to assess the benefit of glucocorticoids for glandular manifestations of Sjögren's syndrome. Nevertheless, clinical experience suggests that glucocorticoids may help reduce gland enlargement but do not improve sicca symptoms. Short-term use of glucocorticoids usually helps control glandular swelling. In a small randomized clinical trial, patients treated with prednisolone (30 mg daily) or piroxicam (20 mg/day) showed no significant changes in salivary or lacrimal gland function or salivary gland histopathology compared to placebo after

six months [8].Long-term use of glucocorticoids is not recommended for pSS patients due to potential adverse effects, including osteoporosis, hyperglycemia, weight gain, nervousness, tissue damage, and increased susceptibility to infections. These risks are similar to those observed in other autoimmune diseases. In pSS, there is also an increased risk of oral candidiasis (fungal infection) and accelerated dental erosion, further limiting long-term or high-dose glucocorticoid therapy [9, 10].

Glucocorticoids are occasionally used to treat systemic manifestations of pSS, similar to their use in other systemic rheumatic or autoimmune diseases [11]. A review of 1,120 Spanish pSS patients showed that low-dose glucocorticoids (around 20 mg/day prednisolone equivalent) were used for this purpose in 19% of patients [12].Until the risk–benefit ratio of glucocorticoids is reliably established, their dose and duration should be limited, and complete avoidance is recommended whenever possible.

Conclusion

In the treatment of Sjögren's syndrome (pSS), it is crucial to assess patients individually and evaluate disease severity. Currently, no drug is specifically approved for pSS. Treatment strategies focus on symptomatic relief, reduction of immune-mediated inflammation, and prevention of complications.In mild cases, therapies include agents to reduce eye and mouth dryness, secretagogues, and hygiene measures.In moderate to severe cases, antimalarials, immunosuppressive drugs, and biologics (e.g., rituximab) are recommended.In organ-damaging forms of the disease, treatment follows protocols used for systemic autoimmune diseases.Recent studies have highlighted the interaction between the immune and nervous systems in pSS pathogenesis, leading to exploration of new targeted therapeutic approaches. Effective management of Sjögren's syndrome requires a comprehensive, multidisciplinary approach and regular patient monitoring.

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