Sjögren's Disease

Sjögren's disease (SD) is a chronic, systemic autoimmune disorder primarily affecting the exocrine glands, especially the salivary and lacrimal glands. It leads to xerostomia (dry mouth) and keratoconjunctivitis sicca (dry eyes), often accompanied by systemic symptoms.

Key Features

Feature	Description
Etiology	Autoimmune; predominantly T and B cell-mediated responses
Classic symptoms	Dry eyes, dry mouth, fatigue, joint pain
Systemic involvement	Skin, lungs, kidneys, GI tract, CNS, peripheral nerves
Autoantibodies	Anti-SSA/Ro and Anti-SSB/La
Histology	Focal lymphocytic sialadenitis in minor salivary gland biopsy
Epidemiology	More common in middle-aged women (F:M ≈ 9:1)

Neurological Involvement

* **Peripheral Nervous System:**

1. Small fiber neuropathy
2. Trigeminal neuralgia
3. Mononeuritis multiplex

* **Central Nervous System:**

1. Cognitive dysfunction
2. Myelopathy
3. Rare MS-like syndromes

Classification

- **Primary Sjögren's disease:** Occurs without another autoimmune disease
- **Secondary Sjögren's disease:** Occurs with diseases like rheumatoid arthritis or systemic lupus erythematosus

⚙ Diagnosis

Based on ACR/EULAR 2016 criteria, including:

- Ocular staining score
- Unstimulated salivary flow rate
- Positive minor salivary gland biopsy
- Anti-SSA/Ro antibodies

- Symptoms > 3 months

Treatment

- **Symptomatic:**
  1. Artificial tears/saliva
  2. Sialogogues (e.g., pilocarpine)
- **Systemic disease:**
  1. Hydroxychloroquine
  2. Corticosteroids
  3. Rituximab (in refractory cases)

⚠ Risk

- Increased risk of non-Hodgkin lymphoma in long-standing disease.

Cross-sectional observational studies

In a cross-sectional observational study using immunohistochemistry and serology to assess human cytomegalovirus (HCMV) activity in salivary gland tissue and serum samples, Pantalone et al. (Karolinska Institutet, Stockholm; Turku University, Finland) — published in Clinical Immunology — investigated the presence and potential role of HCMV in patients with Sjögren's disease (SD).

Their findings showed:

- SD patients had significantly higher expression of HCMV proteins in salivary gland tissue:
  1. HCMV-IE: 88.9%
  2. HCMV-LA: 69.2%
  3. HCMV-pp65: 45.8%
- HCMV-specific IgM was more frequent in SD patients than in controls (32.1% vs. 13.4%, $p = 0.04$)
- HCMV-IgG titers were significantly elevated in the SD group ($p < 0.0001$)

These results suggest a possible role of **active or latent HCMV infection** in the pathogenesis of Sjögren's disease, although a causal relationship has not been established.

[1)]

Takeaway Message for Neurosurgeons

While **Sjögren’s disease** is primarily a **rheumatologic** condition, this study provides important implications for neurosurgeons:

- The presence of **active HCMV infection** in **autoimmune disease** reinforces the hypothesis that **viral latency and reactivation** may be a cofactor in **neuroinflammation**, **cognitive**

dysfunction, and **chronic fatigue syndromes** often seen in SD patients.

- **Neurological manifestations** of Sjögren's include:
  1. Sensory and small-fiber neuropathies
  2. Trigeminal neuralgia
  3. Myelopathy or MS-like presentations
  4. Cognitive fog and mood changes
- Given the **neurotropic potential of HCMV**, this study supports further investigation into whether **latent viral infections** play a role in **neuroimmune dysregulation**, especially in patients with overlapping symptoms (e.g., unexplained neuropathies or cognitive decline).
- In neurosurgical patients with **autoimmune backgrounds**, especially those with unexplained CNS or PNS involvement, consider exploring **viral serology** (HCMV, EBV, HSV) as a potential contributor.

1. Association ≠ Causation

The authors repeatedly suggest a *pathogenic role* of HCMV in SD. But this is a **cross-sectional observational study**, making causal inference **methodologically impossible**. The presence of viral proteins or antibodies does not establish **temporal or mechanistic causality**.

→ *They detect smoke, then hypothesize arson, without checking for a fireplace.*

2. Serology Without Functional Insight

The serologic data are underwhelming:

- IgM: 32.1% in SD vs. 13.4% in controls (P=0.04)
- IgG: Higher titers in SD (P<0.0001)

But no **viral DNA quantification** (e.g., qPCR), **no longitudinal viral kinetics**, and **no cytokine profiling** were performed to support active reactivation or its functional relevance. → *This is viral presence by suggestion, not by demonstration.*

3. Biased Interpretation from Prior Commitments

Several authors (e.g., Söderberg-Nauclér) have long promoted the role of HCMV in chronic diseases. This study reads like **confirmation bias in action**. The data are made to fit the theory, rather than challenge it.

→ *When you carry a viral hammer, every immune disease looks like a nail.*

4. Control Group Weakness

While the inclusion of "Sicca but not SD" patients is commendable, the selection and matching criteria are unclear. Were comorbidities, age, immunosuppressive use, or HCMV exposure history balanced?

→ *Without proper matching, you're comparing weather across cities with different climates.*

5. Clinical Relevance: Zero

No treatment implications. No biomarker validated. No outcome tracked. Despite its title, the study offers **no actionable insight** for the diagnosis, management, or prevention of SD.

→ *It's all noise and no signal — or worse, signal misinterpreted as insight.*

Final Verdict

This study is **scientifically decorative**, not **clinically transformative**. It's another installment in the long tradition of elegant immunohistochemistry papers that propose bold pathogenic hypotheses without adequate mechanistic or temporal evidence.

> **Clever staining. Careless thinking.**

[1)]

Pantalone MR, Xu X, Almazán NM, Gerstner C, Fischer M, Kvarnström M, Söderberg-Nauclér C, Wahren-Herlenius M, Rahbar A. High activity of human cytomegalovirus in patients with Sjögren's disease. Clin Immunol. 2025 Jun 18:110545. doi: 10.1016/j.clim.2025.110545. Epub ahead of print. PMID: 40541820.