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THE SILENT AUTOIMMUNE: SJÖGREN'S SYNDROME IN A YOUNG MALE

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ABSTRACT

Background: Sjögren's syndrome (SS) is a systemic autoimmune exocrinopathy primarily targeting salivary and lacrimal glands. Its occurrence in young males is uncommon, and its association with hypokalemic paralysis mediated by distal renal tubular acidosis (dRTA) type 1 is an exceptionally rare and diagnostically challenging presentation. Anti-Jo-1 antibody positivity further distinguishes this case as a unique overlap with inflammatory myopathy. **Case Presentation:** We report a 27-year-old male who presented with dry eyes and dry mouth, with a prior hospitalization for hypokalemic quadriplegia. Ophthalmological assessment confirmed severe bilateral keratoconjunctivitis sicca (Schirmer's test: <5 mm/5 min bilaterally). Serological workup revealed isolated Anti-Jo-1 antibody positivity on ENA/ANA qualitative profile, while Anti-Ro/SSA and Anti-La/SSB antibodies were negative. Labial minor salivary gland biopsy demonstrated focal lymphocytic sialadenitis consistent with primary Sjögren's syndrome. The 2016 ACR/EULAR classification criteria were fulfilled with a score of ≥5. **Conclusion:** This case underscores the importance of considering Sjögren's syndrome in young male patients presenting with hypokalemic paralysis. Seronegativity for classical antibodies does not exclude the diagnosis. Minor salivary gland biopsy remains the histopathological cornerstone, and the oral pathologist plays a pivotal diagnostic role. Multidisciplinary management is essential to address both glandular and extraglandular manifestations.

KEYWORDS: Sjögren's syndrome; hypokalemic quadriplegia; Anti-Jo-1 antibody; minor salivary gland biopsy; keratoconjunctivitis sicca; seronegative.

INTRODUCTION

Sjögren's syndrome (SS) is a chronic, progressive systemic autoimmune exocrinopathy characterized by lymphocytic infiltration of the exocrine glands, principally the salivary and lacrimal glands, resulting in xerostomia and keratoconjunctivitis sicca. Its global prevalence ranges from 0.01% to 0.72%, with a striking female predominance (female-to-male ratio approximately 9:1), most commonly affecting individuals in the fourth to fifth decade of life.[1,2] Occurrence in young males, as in the present case, is distinctly uncommon and warrants detailed clinicopathological documentation.

The syndrome may manifest as primary Sjögren's Syndrome (pSS) or secondary to another autoimmune connective tissue disease. Extraglandular manifestations are well recognized in pSS and include musculoskeletal, pulmonary, renal, and neurological involvement.[3] Among the renal complications, distal renal tubular acidosis (dRTA) type 1 is the most frequent, characterized by impaired urinary acidification and potassium wasting, which may precipitate hypokalemic paralysis, a potentially life-threatening manifestation that is often the presenting event in younger patients.[4] This clinical pathway, though recognized, remains infrequently documented particularly in young males.

The presence of Anti-Jo-1 antibodies characteristically associated with inflammatory myopathies such as polymyositis in a patient with clinical features of SS raises the possibility of an autoimmune overlap syndrome. Anti-Jo-1 is the most common anti-aminoacyl tRNA synthetase antibody and defines the Anti-Synthetase Syndrome (ASSD), which may encompass sicca features alongside inflammatory myopathy, interstitial lung disease, and arthritis.[5] The coexistence of SS features with Anti-Jo-1 positivity creates a complex diagnostic scenario requiring careful multidisciplinary evaluation.

The diagnosis of SS is currently guided by the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria.[6] Minor salivary gland biopsy (MSGB) remains the histopathological cornerstone, with focal lymphocytic sialadenitis (FLS) and a focus score of ≥1 per 4 mm² fulfilling the highest-weighted histopathological criterion (3 points). The oral pathologist is therefore uniquely positioned to contribute to the definitive diagnosis of this systemic autoimmune condition.[7,8]

CASE REPORT

Patient History and Chief Complaint

A 27-year-old male patient referred by a physician for minor salivary gland biopsy to evaluate for any pathology like Sjogren's Syndrome to the Department of Oral Pathology and Microbiology. His habit history was significant for kharra (smokeless tobacco) chewing at 1–5 sachets per day.

History of Present Illness

Approximately one month prior to presentation, the patient had been admitted to a private hospital with an acute episode of hypokalemic quadriplegia. He presented with acute-onset, rapidly progressive limb weakness involving all four limbs, with inability to stand or walk, along with muscle cramps. Neurological consultation documented the presentation as 'a young male admitted with hypokalemic quadriparesis, who rapidly improved with KCl correction.' The patient was subsequently referred for Schirmer's test, CPK total, and ANA profile to investigate an underlying autoimmune etiology. The evaluating physician identified the presentation as 'hypokalemic paraparesis likely Sjögren's syndrome' with ANA positive (Jo-1 positive) and referred the patient to our institute for minor salivary gland biopsy.

Clinical Examination

General physical examination revealed a young male of average build with no pallor, icterus, or clubbing. Extraoral examination showed no visible salivary gland swelling and no cervical lymphadenopathy. Intraoral examination revealed significantly reduced salivary pooling with frothy, thick saliva and dry, mildly erythematous oral mucosa. (Figure 1) Examination of the dentition revealed grossly carious tooth 16, with prominent staining (++) and calculus (++) consistent with xerostomia-associated caries susceptibility and poor oral hygiene. No oral candidiasis or mucosal ulcerations were noted at the time of examination.

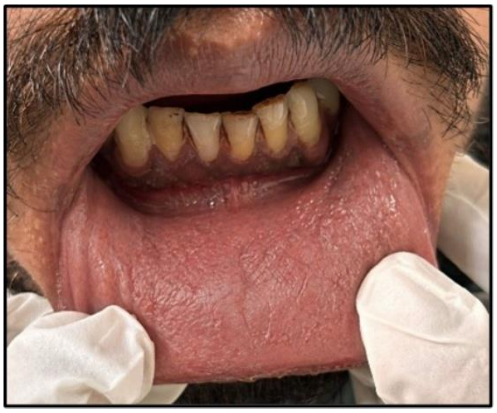

Fig. 1: Reduced salivary pooling with dry labial mucosa.

Ophthalmological Assessment

Ophthalmological evaluation confirmed severe bilateral keratoconjunctivitis sicca. Visual acuity was 6/12 (right eye) and 6/6 (left eye). Lids, conjunctiva, cornea, anterior chamber, and fundus were within normal limits bilaterally. Schirmer's test yielded values of <5 mm/5 min in both eyes, indicating severely impaired basal tear secretion. The ophthalmologist diagnosed bilateral severe dry eye and prescribed lubricant (hydroxypropyl methylcellulose-based) eye drops twice daily for 30 days along with spectacle correction for the right eye.[6]

Laboratory and Serological Investigations

Comprehensive serological and biochemical investigations were performed at a diagnostic centre (Table 1). Creatine kinase (CK) was within normal limits at 61 U/L (reference: 46–171 U/L). ANA/ENA qualitative profiling by line immunoassay (LIA) demonstrated isolated Anti-Jo-1 positivity, with all other autoantibodies including Anti-Ro/SSA, Anti-La/SSB, Scl-70, PM-Scl, CENP-B, PCNA, ds-DNA, nucleosomes, histones, Rib-P, and AMA-M2, returning negative results. Pre-operative haematological parameters were within safe limits (Haemoglobin: 12.25 g/dL.[5,9]

Table 1: Serological and Biochemical Profile.

Test	Result	Reference Range
CK – Creatine Kinase, Serum (IFCC)	61 U/L (Normal)	46–171 U/L
ANA / ENA Qualitative Profile (LIA)		
U1-nRNP/Sm	Negative	-

Sm	Negative	-
SS-A (Ro-60)	Negative	-
Ro-52	Negative	-
SS-B / La	Negative	-
Scl-70	Negative	-
PM-Scl	Negative	-
Jo-1	**POSITIVE (+)**	-
CENP-B, PCNA, ds-DNA, Nucleosomes, Histones, Rib-P, AMA-M2	All Negative	-
Haemoglobin (pre-biopsy)	12.25 g/dL	13–17 g/dL (male)
Bleeding Time (BT)	2 min 30 sec	1–3 min
Clotting Time (CT)	4 min 30 sec	3–8 min

Minor Salivary Gland Biopsy

Incisional biopsy of the labial minor salivary glands was performed under local anaesthesia using standard technique. A minimum of five minor salivary gland lobules were excised from the lower labial mucosa, lateral to the midline, avoiding the frenulum. The specimen was fixed in 10% neutral buffered formalin and submitted for histopathological examination. Pre-operative fitness was confirmed with CBC. Suture removal was performed at seven days, with post-operative wound care using chlorhexidine-based antiseptic gel (Rexidine, 1-1-1).[7,8]

Histopathological Examination

Haematoxylin and eosin (H&E) stained sections of the minor salivary gland biopsy showed multiple salivary gland lobules exhibiting characteristic features of focal lymphocytic sialadenitis (FLS). Dense, well-circumscribed periductal aggregates of mononuclear inflammatory cells, predominantly small lymphocytes and plasma cells were identified forming discrete foci. (Figure 2).

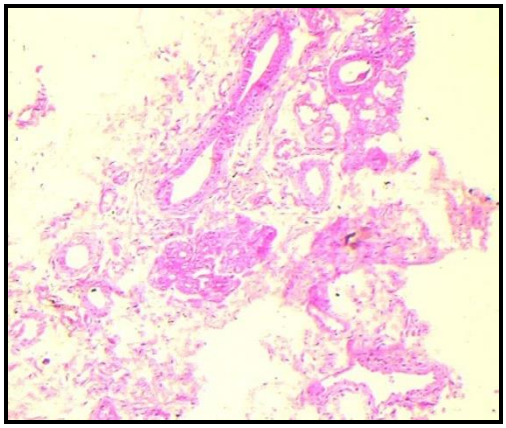

Fig. 2: Periductal aggregates of inflammatory cells (10x magnification).

Each focus consisted of a closely aggregated cluster of ≥50 mononuclear cells in the vicinity of normal-appearing acini, consistent with the Greenspan criterion.[7] The focus score was ≥1 per 4 mm² of evaluable glandular tissue. Acinar cells showed variable degrees of atrophy with reduction in zymogen granule content. (Figure 3) Periductal fibrosis and mild ductal ectasia were noted. (Figure 4).

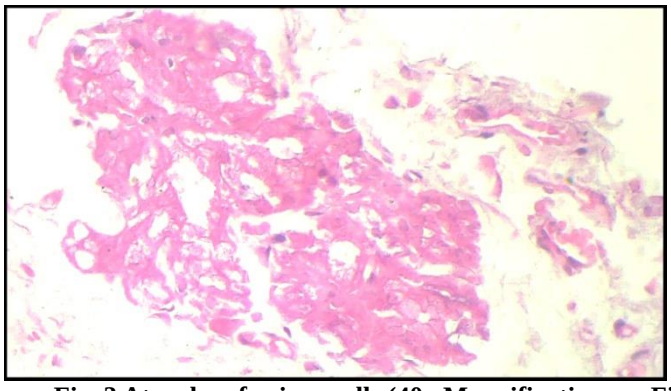

Fig. 3 Atrophy of acinar cells (40x Magnification

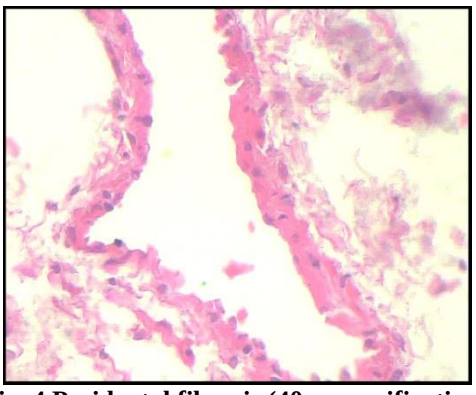

Fig. 4 Periductal fibrosis (40x magnification)

No epimyoepithelial islands, granulomatous inflammation, neoplastic changes, or features of IgG4-related disease were identified. These findings are consistent with the diagnosis of focal lymphocytic sialadenitis associated with Sjögren's syndrome.[6,8]

ACR/EULAR 2016 Diagnostic Scoring and Final Diagnosis

The 2016 ACR/EULAR classification criteria scoring for this patient is summarized in Table 2. A total score of ≥5 was achieved, well above the diagnostic threshold of ≥4, based on biopsy-confirmed FLS (3 points), positive Schirmer's test (1 point), and clinically reduced unstimulated salivary flow and severe dry eye (1 point each, pending formal documentation).[6]

Table 2: ACR/EULAR 2016 Classification Criteria Scoring.

Criterion	Patient Status	Score
Lip biopsy: FLS with focus score ≥1 per 4 mm²	Positive (confirmed)	3
Anti-Ro/SSA antibody positivity	Negative	0
Schirmer's test ≤5 mm/5 min (≥1 eye)	<5 mm bilateral	1
Unstimulated salivary flow ≤0.1 mL/min	Clinically reduced	1*
Ocular staining score ≥5 (van Bijsterveld ≥4)	Severe dry eye (pending formal staining)	1*
TOTAL SCORE		**≥5 (threshold ≥4)**

**Formal ocular staining score and salivary flow rate to be documented. Minimum score of 4 (biopsy + Schirmer's alone) fulfils SS classification criteria.*

The final diagnosis was Primary Sjögren's Syndrome (pSS), seronegative (Anti-Ro/SSA and Anti-La/SSB negative) with biopsy-confirmed focal lymphocytic sialadenitis, severe bilateral keratoconjunctivitis sicca, and a prior episode of hypokalemic quadriplegia likely mediated by distal renal tubular acidosis type 1. Concurrent Anti-Jo-1 positivity raises the possibility of an overlap with Anti-Synthetase Syndrome, warranting rheumatological follow-up.

Management and Follow-Up

The patient was referred to the Department of Rheumatology for systemic management of pSS and evaluation of Anti-Jo-1 positivity, including pulmonary function testing and high-resolution CT chest to exclude interstitial lung disease. Ophthalmic management with lubricant eye drops was initiated. Oral management included intensive oral hygiene instruction, prescription fluoride therapy for caries prevention, chlorhexidine gel post-biopsy, and regular 3-monthly dental recalls. Monitoring for lymphoma development and electrolyte surveillance (serum potassium) were recommended. The patient was counselled regarding kharra (smokeless tobacco) cessation given its compounding effect on salivary gland function and oral carcinogenesis risk.

DISCUSSION

The present case is notable for three clinically distinctive features that collectively render it a rare and instructive contribution to the Sjögren's syndrome literature: the young male demographic, hypokalemic quadriplegia as the index event, and isolated Anti-Jo-1 positivity in the absence of classical Anti-Ro/SSA and Anti-La/SSB antibodies.

Atypical Demographics: Young Male Presentation

Sjögren's syndrome is the second most prevalent systemic autoimmune disease worldwide, with an overwhelming female predilection (female-to-male ratio 9:1 to 20:1) and peak incidence in the fourth to fifth decade.[1,2] Male SS, constituting approximately 58% of cases, is associated with distinct clinical features including more severe extraglandular disease, a higher rate of seronegativity, and a potentially greater risk of lymphomatous transformation.[10] Cases in individuals under 30 years of age frequently present with extraglandular features including renal involvement, neuropathy, and haematological abnormalities, sometimes preceding or overshadowing classic sicca symptoms.[4] This atypical presentation in a 27-year-old male is therefore particularly uncommon and diagnostically challenging.

Hypokalemic Paralysis as a Presenting Manifestation

Hypokalemic paralysis as the presenting manifestation of SS is rare but well-documented, primarily mediated through distal renal tubular acidosis (dRTA) type 1. In pSS, autoimmune lymphocytic infiltration of the renal tubular epithelium impairs the H+/K+-ATPase pump, resulting in urinary potassium wasting, metabolic acidosis, and severe hypokalemia.[4,11] Distal RTA occurs in approximately 5–10% of pSS patients and may precede the classic sicca diagnosis. The acute reversal of quadriplegia with intravenous potassium chloride correction, as observed in our patient, is the hallmark therapeutic response confirming hypokalemia as the primary mechanism.

Without identifying and treating the underlying autoimmune disease, episodes of hypokalemic paralysis may recur, posing a life-threatening risk. A systematic diagnostic workup including Schirmer's test, salivary flow measurement, serological profiling, and minor salivary gland biopsy is therefore mandatory in any case of unexplained hypokalemic paralysis where an autoimmune etiology is suspected.[6]

Seronegative Sjögren's Syndrome and the Role of Biopsy

Anti-Ro/SSA and Anti-La/SSB antibodies carry the highest weight (3 points) in the 2016 ACR/EULAR criteria and are considered the serological hallmarks of SS. However, approximately 30–50% of histologically confirmed SS patients are seronegative for both antibodies.[9] Seronegative pSS represents a distinct clinical subtype with potentially more prominent extraglandular manifestations including renal tubular acidosis, peripheral neuropathy, and vasculitis, while glandular disease may appear milder on serological assessment.[12]

In seronegative cases, the minor salivary gland biopsy assumes diagnostic primacy as the only objective histopathological evidence for SS classification. This case exemplifies seronegative pSS: the combination of positive Schirmer's test (bilateral <5 mm), biopsy-confirmed FLS with a focus score ≥1 per 4 mm², and clinical sicca features fulfils the ACR/EULAR 2016 criteria with a score of ≥5, firmly demonstrating that seronegativity does not exclude SS in the presence of positive histopathology and objective sicca tests.[6,7] For the oral pathologist, accurate interpretation and quantification of the focus score on labial minor salivary gland biopsy is a direct and decisive contribution to patient diagnosis in such cases.

Anti-Jo-1 Positivity and Autoimmune Overlap

Anti-Jo-1 (anti-histidyl-tRNA synthetase) is detected in approximately 25–30% of patients with idiopathic inflammatory myopathies and in up to 75% of patients with Anti-Synthetase Syndrome (ASS).[5] The ASS encompasses inflammatory myopathy, interstitial lung disease, mechanic's hands, Raynaud's phenomenon, arthritis, fever, and notably sicca features including xerostomia and keratoconjunctivitis sicca blurring the clinical boundary with primary SS.[13]

In our patient, three diagnostic possibilities exist: (1) pSS with incidental Anti-Jo-1 positivity; (2) ASS presenting with prominent sicca features and FLS on biopsy; or (3) a true overlap autoimmune syndrome. The normal CK (61 U/L) at the time of testing argues against active myositis currently, though this does not exclude prior episodic myositis in the context of the hypokalemic quadriplegia episode. Definitive classification requires dedicated rheumatological evaluation, pulmonary function testing, high-resolution CT chest to exclude interstitial lung disease, and serial muscle enzyme monitoring.[5,13]

Oral Manifestations and Dental Implications

Xerostomia and salivary hypofunction in SS create a cascade of oral complications including rampant cervical and smooth-surface dental caries, oral candidiasis, dysgeusia, and mucosal atrophy.[14] In this patient, grossly carious tooth 16 with prominent staining and calculus was consistent with xerostomia-associated caries susceptibility. The concurrent kharra (smokeless tobacco) habit compounds oral risk by introducing fermentable sugars and altering the oral microbiome, making tobacco cessation counselling a mandatory management adjunct.

Dentists and oral medicine specialists are frequently the first clinicians to encounter undiagnosed SS patients presenting with unexplained xerostomia or rampant caries, highlighting the front-line diagnostic responsibility of the dental profession. Oral management in line with established guidelines[14] included intensive oral hygiene instruction, topical fluoride therapy, chlorhexidine gel, and regular 3-monthly recalls.

Multidisciplinary Approach

This case was managed through a comprehensive multidisciplinary framework involving neurology, ophthalmology, rheumatology, and oral pathology exemplifying best practice in the management of a systemic autoimmune disease with multiorgan involvement. Early diagnosis, prompt multidisciplinary referral, and regular long-term follow-up are fundamental to optimizing outcomes in pSS and preventing potentially life-threatening extraglandular complications, including recurrent hypokalemic paralysis and lymphoma development.

CONCLUSION

This case report presents a rare presentation of primary Sjögren's syndrome; seronegative and biopsy-confirmed in a 27-year-old male whose index event was hypokalemic quadriplegia, mediated through distal renal tubular acidosis type 1. The concurrent Anti-Jo-1 positivity introduces an additional diagnostic dimension requiring rheumatological evaluation for Anti-Synthetase Syndrome overlap.

Three key clinical lessons emerge: first, SS can occur in young males and must be included in the differential diagnosis of unexplained hypokalemic paralysis; second, seronegativity for Anti-Ro/SSA and Anti-La/SSB does not exclude pSS. The minor salivary gland biopsy is diagnostically indispensable in such cases, and the oral pathologist's role in accurately interpreting focal lymphocytic sialadenitis is directly pivotal to patient care; third, the oral manifestations of SS: xerostomia, salivary hypofunction, and rampant caries are frequently the most accessible early features in dental practice, placing the dental team at the frontline of diagnosis and referral. This case contributes to the growing literature on atypical SS presentations and reinforces the critical diagnostic role of the oral pathologist.

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