Case Report

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Intersection of Coeliac Disease and Sjögren's Syndrome: A Report of Two Cases

Internal Medicine Section

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ABSTRACT

Coeliac Disease (CD) and Sjögren's Syndrome (SS), both autoimmune disorders, are gaining attention for their complex interaction when occurring together. CD involves gluten intolerance and can present with gastrointestinal symptoms, while SS affects various organs, primarily causing dryness of the eyes and mouth. Diagnosis for each relies on specific criteria including serologic testing and histopathology. When these conditions overlap, they create unique clinical challenges, highlighting the need for a thorough understanding of their combined effects on health. This exploration aimed to uncover the intricacies of their relationship, including clinical manifestations and implications for diagnosis and management when dealing with both simultaneously. In both cases (58-year-old female and 47-year-old female), there was gastrointestinal villous atrophy as a manifestation of CD, which improved with simple dietary modification.

Keywords: Anti-tissue transglutaminase, Autoantibodies, Immunoglobulin A, Villous atrophy

CASE REPORT

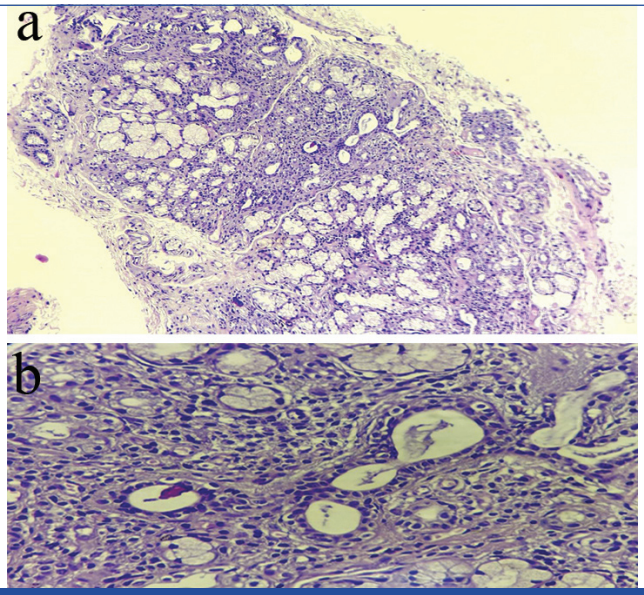
Case 1

A 58-year-old female presented with complaints of dry mouth for five months, fever persisting for one month, documented to be 100-101°F, mainly occurring at night and relieved with medication. The patient also complained of vomiting for one month consisting of food particles, accompanied by a burning sensation in the epigastric region. She had a known history of hypertension for two years on T.Amlodipine 5 mg OD, asthma for the last 10 years on Metered Dose Inhaler (MDI) Foracort 2 puffs BD, osteoarthritis for five years, and an anxiety disorder for the last year on T.Clonazepam 0.5 mg OD at bedtime.

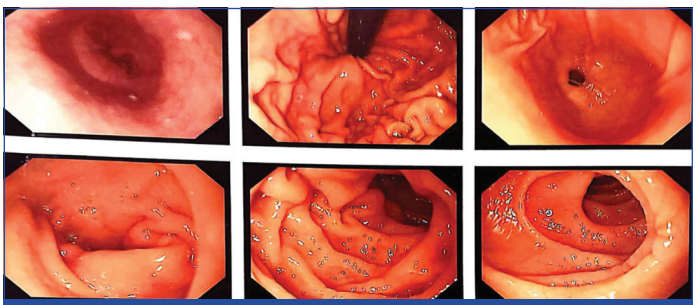
During the general physical examination, the patient was conscious, oriented to time, place, and person, with a blood pressure of 106/70 mmHg, pulse rate of 90/min, SpO_2 of 98% on room air and blood sugar level of 136 mg/dL. Pallor was present with poor oral hygiene and a dry tongue. Systemic examination of the patient was normal.

The patient underwent a series of diagnostic assessments, revealing the following results: Haemoglobin levels were measured at 10.8 grams per decilitre, with a total leukocyte count of 5400 per microlitre and a platelet count of 200,000 per microlitre. The Mean Corpuscular Volume (MCV) was determined to be 85.3 femtolitres, while total protein levels were recorded at 5.6 grams per decilitre, with albumin at 3.1 grams per decilitre. Additionally, alkaline phosphatase was 87 U/L, calcium was 8.8 mg/dL, chloride was 116 mol/dL, Creatine Kinase-MB was 6 U/L, Creatine Kinase was 49 U/L, creatinine was 1.1 mg/dL, direct bilirubin was 0.1 mg/dL, indirect bilirubin was 0.2 mg/dL, lactate dehydrogenase was 208 U/L, sodium was 134 mmol/L, potassium was 4.4 mmol/L, Parathormone was 25 pg/mL, aspartate transaminase was 37 U/L, alanine transaminase was 17 U/L, quantitative C-Reactive Protein (CRP) was 3.0 mg/dL, Total Iron Binding Capacity (TIBC) was 222 ug/dL, total iron was 59 ug/dL, urea was 11 mg/dL, uric acid was 8.5 mg/dL. The Coronavirus Disease-2019 (COVID-19) Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) was negative, C-Reactive Protein (CRP) was positive (>10 mg/dL), Rheumatic factor and anti-Cyclic Citrullinated Peptide (CCP) were negative, and urine routine was normal.

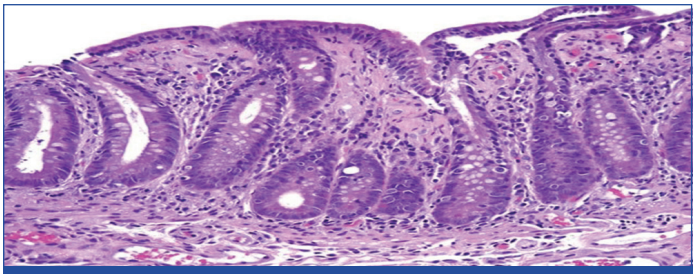
An autoimmune profile was sent for further evaluation, which was found to be strongly positive for SSA/Ro60, SSA/R052, and SSB/La. The patient also tested positive for Immunoglobulin A (IgA)-Anti-Tissue Transglutaminase (TTG). The Schirmer test was positive, and a labial biopsy [Table/Fig-1a,b] showed chronic inflammatory cell infiltrate with acinar atrophy. The upper gastrointestinal endoscopy [Table/Fig-2] revealed a 4 cm hiatus hernia and D2 scalloping, with a biopsy [Table/Fig-3] suggestive of villous atrophy.



[Table/Fig-1]: Haematoxylin and Eosin (H&E) stain of labial biopsy: (a) Low power (10x); b) High power (100x) sample showing chronic inflammatory cell infiltrate compromising of lymphocyte and plasma cell (more than 50) with acinar atrophy of the salivary glands.



[Table/Fig-2]: Upper gastrointestinal endoscopy showing normal oesophageal mucosa with hiatus hernia- 4 cm with normal stomach mucosa with duodenal scalloping in D2.



[Table/Fig-3]: Duodenal biopsy suggestive of villous atrophy with flattening of villi and crypts (H&E, 40x).

Based on European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) criteria, the patient was classified as SS, and based on IgA-TTG with gut biopsy was also classified as CD [1]. The patient was advised to follow a gluten-free diet and receive nutritional therapy. Upon follow-up after six months, the patient's symptoms had improved.

Case 2

A 47-year-old female presented with complaints of decreased appetite, loose stools for the last 2 months, and associated generalised weakness. She had a known case of SS for the past eight years and was taking oral cevimeline and methylcellulose eye drops from the Department of Rheumatology. The patient had been hypertensive for the last 10 years on tablet telmisartan 40 mg OD.

During a general physical examination, the patient was conscious, oriented to time, place, and person, with a blood pressure of 138/88 mmHg, a pulse rate of 74/min, SpO_2 of 98% on room air, and a blood sugar level of 186 mg/dL. Mild pallor and a dry tongue were noted. Systemic examination of the patient was normal.

Following a series of investigations, the following results were obtained: Haemoglobin levels measured at 9.8 grams per decilitre (gm/dL), total leukocyte count recorded at 10,400 per microlitre (ul), and platelet count observed at 1.9 lac per microlitre (U/L). The MCV was determined to be 90.6 femtolitres (fL). Additionally, the total protein level was found to be 5.4 grams per decilitre (g/dL), with an albumin concentration of 3.2 g/dL. Alkaline phosphatase activity was measured at 60 units per liter (U/L), calcium was 9.8 mg/dL, chloride was 106 mol/dL, creatinine was 1.0 mg/dL, direct bilirubin was 0.25 mg/dL, indirect bilirubin was 0.18 mg/dL, lactate dehydrogenase was 198 U/L, sodium was 129 mmol/L, potassium was 4.6 mmol/L, aspartate transaminase was 45 U/L, alanine transaminase was 40 U/L, quantitative CRP was 3.4 mg/dL, TIBC was 282 ug/dL, total iron was 58 ug/dL, urea was 5.6 mg/dL, uric acid was 3.5 mg/dL. The COVID-19 RT-PCR was negative, CRP was positive (>10 mg/dL), Rheumatic factor and anti-CCP were negative, and urine routine was normal. The retroviral test was also negative. The patient was positive for IgA-anti-Tissue Transglutaminase (TTG). The patient's symptoms improved after starting a gluten-free diet and nutritional therapy. On further follow-up after six months, the patient's symptoms settled.

DISCUSSION

The CD is a chronic autoimmune enteropathy in individuals with genetic susceptibility to gluten in the diet. It can be asymptomatic or may present as chronic diarrhoea with features of malabsorption. Diagnosis is based on serologic testing, genetic susceptibility testing, and histopathology of duodenal mucosal biopsy. On the other hand, SS is a systemic autoimmune disorder causing inflammation of the lacrimal and salivary glands. It can also involve organs such as the joints, skin, lungs, gastrointestinal tract, nervous system, and kidneys. CD and SS are both autoimmune diseases with a related genetic background and also occur in association with type 1 diabetes mellitus, autoimmune thyroid disease, and primary biliary cholangitis [2].

In the cases presented, authors encountered patients exhibiting features characteristic of both SS and CD simultaneously. In both cases, the patients presented with gastrointestinal symptoms as manifestations of CD, which was confirmed by being positive for IgA-anti-TTG. Biopsies were performed to further assess the condition, showing villous atrophy. The authors first case was also simultaneously diagnosed with SS using the American College of Rheumatology/European League against Rheumatism (EULAR/ACR) guideline, and the second case was already a known case of the same which later developed the symptoms. This convergence of symptoms prompted a closer examination, leading to the diagnosis of co-existing autoimmune conditions. The present case report underscores the importance of comprehensive assessment in patients with autoimmune disorders, especially when overlapping symptoms are present. By recognising the co-occurrence of these conditions, clinicians can implement appropriate management strategies to improve patient outcomes and quality of life.

There are consistent observations regarding the association between SS and CD. In the present case report, the presence of CD was found to be more common with SS. A study by Iltanen S et al., suggested the prevalence of CD in 34 SS patients ranges from 14.7% compared to the general population, which is only 1% [3]. Another study by Luft LM et al., reported a seroprevalence of 12% in a cohort of 50 SS patients, with five out of the six positives being biopsy-confirmed CD (10%) [4]. Additionally, in a study by Bartoloni E et al., 25 CD cases were reported in 354 SS patients (prevalence 7.1%), out of which 24 were biopsy-proven cases, and one was subclinical CD detected on screening [5]. Another study by Caglar E et al., reported a prevalence of SS-A/SS-B antibody positivity of 6.5% in 31 CD patients [6]. According to a study, 15% of patients with SS also have biopsy-proven CDs, meaning the prevalence of CD is much higher in Sjogren patients than in the general population [7].

Furthermore, insights into the potential mechanisms underlying the co-existence of these autoimmune disorders have been explored. The proposed mechanisms include increased intestinal permeability leading to a "leaky gut," post-translational modifications of luminal proteins, and dysregulation of immune responses [8]. The presence of anti-TTG antibodies in various organs, including saliva, suggests a systemic autoimmune process linking both conditions [9,10]. The case reported by Balaban DV et al., further illustrates the diagnostic challenges posed by the atypical presentation of autoimmune disorders. In their study, iron deficiency was incidentally discovered in a patient with SS, leading to the subsequent diagnosis of CD [11]. This underscores the importance of vigilant clinical evaluation and consideration of underlying autoimmune aetiologies, even in the absence of overt gastrointestinal symptoms.

The presented cases highlight the clinical significance of recognising the co-occurrence of SS and CD. By integrating findings from the present case with those from existing studies, the authors underscore the importance of early detection, comprehensive evaluation, and multidisciplinary management approaches in optimising patient care for individuals with overlapping autoimmune conditions.

CONCLUSION(S)

The present case report has illuminated the significant correlation between SS and CD, elucidating their prevalence rates and mutual implications. The prevalence of CD among SS patients underscores the necessity of robust screening protocols to identify and manage these concurrent autoimmune conditions effectively. Conversely, the presence of SS in CD patients highlights the bidirectional nature of their association, urging clinicians to maintain a high index of suspicion for autoimmune co-morbidities. By understanding the shared pathogenic mechanisms, such as dysregulated immune responses and genetic predispositions, healthcare providers can adopt a multidisciplinary approach to optimise patient care. Moving

forward, continued research efforts are warranted to explore novel diagnostic and therapeutic strategies tailored to address the complex interplay between SS and CD, ultimately enhancing the management and quality of life for individuals affected by these autoimmune disorders.

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REFERENCES

[1] Shiboski CH, Shiboski SC, Seror R, Criswell LA, Labetoulle M, Lietman TM, et al. American College of Rheumatology/European league against rheumatism classification criteria for primary Sjögren's Syndrome: A consensus and data-driven methodology involving three international patient cohorts. Arthritis Rheumatol. 2017;69(1):35-45. Doi: 10.1002/art.39859. Epub 2016 Oct 26. PMID: 27785888; PMCID: PMC5650478.

[2] Lauret E, Rodrigo L. Celiac disease and autoimmune-associated conditions. Biomed Res Int. 2013;2013:127589. Doi: 10.1155/2013/127589. Epub 2013 Jul 24. PMID: 23984314; PMCID: PMC3741914.

[3] Iltanen S, Collin P, Korpela M, Holm K, Partanen J, Polvi A, et al. Celiac disease and markers of celiac disease latency in patients with primary Sjögren's syndrome. Am J Gastroenterol. 1999;94(4):1042-46.

[4] Luft LM, Barr SG, Martin LO, Chan EK, Fritzler MJ. Autoantibodies to tissue transglutaminase in Sjögren's syndrome and related rheumatic diseases. J Rheumatol. 2003;30(12):2613-19.

[5] Bartoloni E, Bistoni O, Alunno A, Cavagna L, Nalotto L, Baldini C, et al. Celiac disease prevalence is increased in primary Sjögren's Syndrome and diffuse systemic sclerosis: Lessons from a large multi-center study. J Clin Med. 2019;8(4):540.

[6] Caglar E, Ugurlu S, Ozenoglu A, Can G, Kadioglu P, Dobrucali A. Autoantibody frequency in celiac disease. Clinics (Sao Paulo). 2009;64(12):1195-200.

[7] Lidén M, Kristjánsson G, Valtýsdóttir S, Hällgren R. Gluten sensitivity in patients with primary Sjögren's Syndrome. Scand J Gastroenterol. 2007;42(8):962-67.

[8] Lerner A. Matthias T. Autoimmunity in celiac disease: Extra-intestinal manifestations. Autoimm Rev. 2019;18(3):241-46.

[9] Lerner A, Aminov R, Matthias T. Dysbiosis may trigger autoimmune diseases via inappropriate posttranslational modification of host proteins. Front in Microbiol. 2016;7:84.

[10] Hu S, Vissink A, Arellano M. Identification of autoantibody biomarkers for primary Sjogren's syndrome using protein microarrays. Proteomics. 2011;11(8):1499-507.

[11] Balaban DV, Mihai A, Dima A, Popp A, Jinga M, Jurcut C. Celiac disease and Sjögren's syndrome: A case report and review of literature. World J Clin Cases. 2020;8(18):4151-61. Doi: 10.12998/wjcc.v8.i18.4151. PMID: 33024773; PMCID: PMC7520766.

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