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Overlap Syndrome: Primary Sclerosing Cholangitis with Sjogren's Syndrome

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Abstract: ***The co - occurrence of Small Duct Primary Sclerosing Cholangitis (PSC) and Sjögren's Syndrome presents a clinical puzzle that demands a refined lens for diagnosis. This case study of a 22 - year - old female, who presented with vague and overlapping symptoms like fatigue, jaundice, pruritus, and xerostomia, sheds light on a truly rare autoimmune overlap. Despite initial normal imaging and non - specific lab results, a strong clinical suspicion prompted a liver biopsy, which confirmed small duct PSC—an entity less aggressive yet elusive in presentation. The concurrent positivity for anti - Ro and anti - La antibodies, alongside signs of glandular dysfunction, established the presence of Sjögren's Syndrome. What makes this case particularly meaningful is not just its rarity, but the way it illustrates how traditional diagnostic paths may fall short in detecting such overlap syndromes. It is evident that when faced with autoimmune ambiguity, a multidisciplinary approach anchored in persistence can make all the difference. The patient's partial response to immunosuppressive and symptomatic therapy further emphasizes the need for vigilant long - term management and consideration for transplant in refractory cases. This suggests that while small duct PSC and Sjögren's may seem like distant clinical cousins, their intersection—especially in the Indian context—invites both curiosity and caution. Ultimately, this report does more than add to the literature; it underscores the necessity for broader awareness and nuanced protocols in handling rare autoimmune intersections.***

Keywords: Small duct PSC, Sjögren's syndrome, autoimmune overlap, liver biopsy diagnosis

1. Introduction

PSC is a disease where inflammation and scarring (fibrosis) cause narrowing and blockage of the bile ducts, both inside (intrahepatic) and outside (extrahepatic) the liver. In classic (large duct) PSC, both intrahepatic (inside the liver) and extrahepatic (outside the liver) bile ducts are affected and typically show abnormalities on imaging like MRCP (magnetic resonance cholangiopancreatography) or ERCP. In small duct PSC, the larger bile ducts appear normal on imaging, but liver biopsy shows PSC - like changes. Small duct PSC accounts for about 5%–15% of all PSC.

Sjögren's syndrome is a chronic autoimmune disease in which the body's immune system mistakenly attacks its own moisture - producing glands, primarily affecting the salivary and lacrimal (tear) glands. This results in the two most common symptoms: dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca). It can present as Primary Sjogren's Syndrome or in combination with other autoimmune conditions as Secondary Sjogren's syndrome

The overlap of Primary Sclerosing Cholangitis (PSC) and Sjögren's Syndrome is extremely rare. While both are autoimmune diseases, their concurrent occurrence is not well - documented in the medical literature. Small duct PSC an even rarer condition though less aggressive as compared to classical PSC is a challenging diagnosis and requires high degree of suspicion. The case unravels the diagnostic challenges, therapeutic interventions, and the multidisciplinary approach essential for managing this extremely rare presentation of overlap syndrome.

2. Case Report

A 22 year female came with chief complain of fatigue, abdominal pain, loss of appetite and yellowish discolouration of eyes. Patient also complained of dry skin associated with severe nocturnal itching and discomfort in swallowing food. No c/o arthralgia, arthritis, haematemesis, malena or altered sensorium were noted.

On examination patient had icterus and was vitally stable with

orientation to time place and person. No evidence of liver cell failure or signs of liver cirrhosis were noted on initial examination. Initial labs were s/o direct hyperbilirubinemia and grossly elevated ALP levels as the only significant finding.

USG A+P was done and no evidence of cirrhosis, hepatomegaly, splenomegaly or portal hypertensive were found. MRCP was done and revealed normal biliary tree.

Further blood investigations were done

ANA - positive 1: 1000, Speckled pattern; ANA profile - anti Ro and anti La positive

Anti Smooth Muscle antibody - Negative; Anti LKM antibody negatively; Total IgG levels and serum ceruloplasmin levels were normal. Hepatitis B C markers were negative.

On further probing a past history of similar episode was elicited for which patient took treatment, details of which are not known.

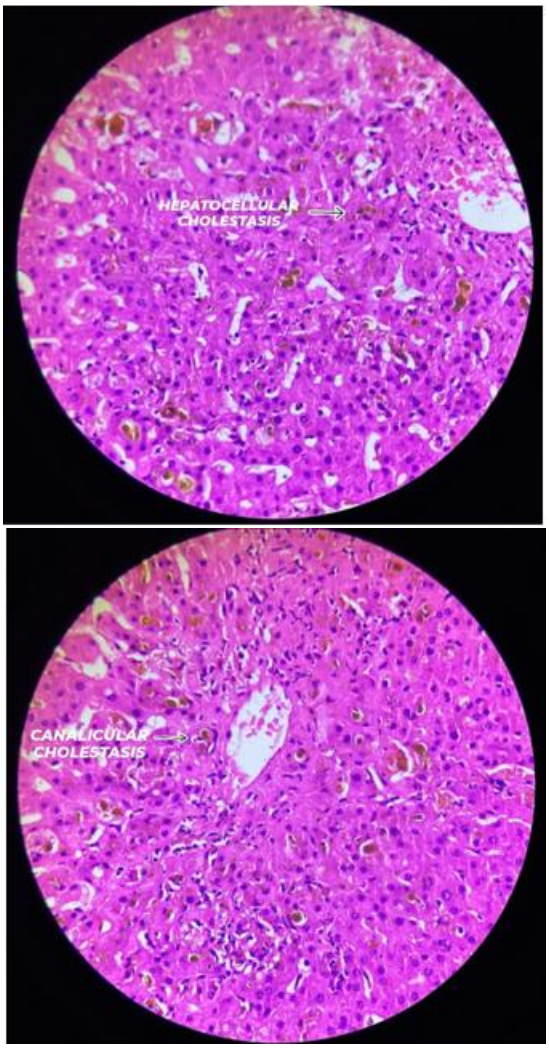
A probable diagnosis of Autoimmune Hepatitis with Sjogren's Syndrome was made and patient was treated with high dose corticosteroids in the form of Inj Methyprednisone 1gm IV OD for 5 days. Symptomatic treatment for puritis, xerophthalmia and cholestasis was initiated.

Labs were repeated on Day 3 of pulse therapy and direct hyperbilirubinemia was persistent. Complains of loss of appetite, fatigue and severe itching were persistent. MRCP was repeated and was within normal limit. AMA antibody were done and were negative. Patient was posted for liver biopsy. Biopsy was suggestive of small duct Primary Sclerosing Cholangitis.

Prothrombin time, Total Vit D levels and Lipid profile was done to look for complications. Colonoscopy screening was done for inflamatory Bowel Disease and no evidence was found.

Lab investigations

Anti nuclear antibodies - Positive 1: 1000, Speckled pattern.
Anti Smooth Muscle antibody - Negative
Anti Liver Kidney Microsomal antibody I and II - Negative
Anti Mitochondrial antibody - Negative
ANA profile - Anti Ro and Anti La positive. Total IgG levels - 800 mg/dl Ceruloplasmin levels - 25 mg/dl
Total Vit D levels - 100 mg/dl Prothrombin time/INR - 12/1.5



Liver Biopsy

	On admission	D1 of Pulse	D3 of Pulse	On discharge
HB	11.3			11.7
TLC	13310			6920
PLT	472000			317000
PCV	36.2			39.1
MCV	85.9			86.6
TB	20.9	13.3	14.5	0.4
DB	19.1	11.6	12.9	0.3
IB	1.8	1.7	1.6	0.1
SGOT	85	81	80	13
SGPT	128	101	73	14
ALP	498	337	262	57

Treatment given:

Patient was given the following treatment once the diagnosis of Sjogren's Syndrome and Primary Sclerosing Cholangitis was confirmed.

Tab Omnacortil 20 mg OD

Tab Urodeoxycholic acid 300 mg BD Cholestyramine sachet TDS Carboxymethycellulose eye drops TDS Uprise D sachet once a week

Patient had significant relief in symptoms with the above treatment though complete resolution of symptoms was not achieved.

Patient was counselled for liver transplant and regular follow up was advised.

3. Conclusion

Patients presented with extremely vague symptoms and hence the diagnosis of Sjogren's Syndrome was challenging. Indirect hyperbilirubinemia with a normal MRCP finding necessitated the need for biopsy for the diagnosis of PSC. The prognosis of small duct PSC though better than classical PSC will eventually require a liver transplantation as patient had only partial symptomatic relief with medical management. Sjogren's Syndrome is usually associated with Primary Billary Cirrhosis and it's association with PSC is hardly ever reported. This extremely rare overlap syndrome highlights the complex ways in which connective tissue disorders can present in patients.

4. Discussion

This case of a young female sheds lights on the complexities inherent in the diagnosis and treatment of overlap syndrome, a rare phenomenon encompassing the coexistence of Sjogren's Syndrome and Primary Sclerosing Cholangitis. Case reports of this overlap syndrome are not common in literature. Figueroa R, Attanasio F reported a case of 30 year old woman suffering from Primary sclerosing cholangitis associated with Sjögren's syndrome, retroperitoneal fibrosis and chronic pancreatitis. Waldram R, Kopelman H, Tsantoulas D, Williams R. reported another case of chronic pancreatitis, sclerosing cholangitis, and sicca complex in two siblings in Lancet in 1975 March.

Primary Sclerosing Cholangitis is in itself a rare condition accounting for 1 - 2/k1, 00, 000 cases in Asia which may also be accounted to the fact that it remains a pretty under diagnosed condition given its vague presentations. Since classic PSC is already rare small duct PSC is even rarer, with an estimated prevalence of roughly 0.1 to 2 per 1, 00, 000 population (5 - 15% of all PSC cases).

Studies from India have reported PSC as a rare condition. A retrospective study from a tertiary care center in western India identified 28 patients with PSC between 2008 and 2017. It is strongly associated with inflammation bowel disease especially ulcerative colitis. About 70 - 80% of patients with primary Sclerosing Cholangitis have ulcerative colitis, however only 2 - 7% of patients with ulcerative colitis have Primary Sclerosing Cholangitis. Hence colonoscopy and screening is must in patients of primary Sclerosing Cholangitis.

Sjögren's syndrome is another autoimmune disorder which is considered rare in India though it may be under diagnosed given its varied and vague symptoms. SS is more prevalent in women and typically presents in middle age, affecting approximately 0.7% of the population. A study from northern India assessed the prevalence of secondary SS in patients with Rheumatoid Arthritis (RA). Among 199 RA patients, 5.5% had secondary SS. A separate study from a tertiary care center in south India analyzed 332 patients with primary SS. This cohort exhibited unique clinical features, including a higher female - to - male ratio.

In India, the prevalence of PSC is low, and there is no substantial evidence to suggest a higher occurrence of SS in patients with PSC. Therefore, the co - existence of PSC and SS in Indian patients is an exceptional case, and there is no established data or clinical guidelines addressing this overlap within the Indian context. Given the scarcity of cases, there is a need for further research and clinical observation to understand the potential relationship between these two conditions in the Indian population.

Starting the patient on low dose systemic glucocorticoids for treatment of Sjögren's Syndrome is in concurrence with the EULAR 2020 guidelines and which mention he use of pulse therapy followed by low dose maintenance therapy. While current treatment options for PSC are limited, ongoing research offers hope for more effective therapies in the future. UDCA has been widely used to improve liver biochemistry in PSC patients. However, studies have shown that while it may improve liver enzymes at low - to - moderate doses (15–23 mg/kg/day), it does not significantly alter transplant - free survival or liver - related outcomes. Liver transplantation remains the only curative treatment for advanced PSC. Long - term survival post - transplant is relatively favorable, with 5 - year survival rates ranging from 79% to 85%.

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