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Overlap Syndrome: Autoimmune Hepatitis with Primary Biliary Cholangitis - Case Presentation

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Abstract

Overlap syndrome, characterized by the coexistence of autoimmune hepatitis (AIH) and primary biliary cholangitis (PBC), presents a complex and challenging clinical scenario. This case report details the diagnostic journey of a 61-year-old female patient with overlapping AIH and PBC, showcasing clinical features, investigations, and therapeutic interventions. The case emphasizes the importance of multidisciplinary collaboration, tailored treatment approaches, and close follow-up for optimal management of this uncommon but relevant overlap syndrome.

Keywords: ***Overlap syndrome, Autoimmune hepatitis (AIH), Primary biliary cholangitis (PBC), Hepatic encephalopathy, Liver cirrhosis, Corticosteroid therapy, Anti-mitochondrial antibodies, Gastrointestinal symptoms***

INTRODUCTION

Overlap syndrome, a rare medical phenomenon, manifests as the coexistence of two distinct autoimmune liver conditions within an individual. Specifically, the combination of Autoimmune Hepatitis (AIH) and Primary Biliary Cholangitis (PBC) represents a complex and

challenging clinical scenario.[1] Autoimmune Hepatitis is an inflammatory liver disease caused by the body's immune system mistakenly attacking healthy liver cells, leading to inflammation, liver damage, and potentially cirrhosis if left untreated.[2] On the other hand, Primary Biliary Cirrhosis is a chronic, progressive liver disorder characterized by the destruction of small bile ducts within the liver, resulting in impaired bile flow, liver inflammation, and eventual cirrhosis.[3]

The prevalence of PBC and AIH in one study ranged from 2.1% to 19% using the Paris and IAIHG revised criteria, respectively.[4] An important observation regarding AIH-PBC overlap syndrome is that Hispanic patients with PBC had a significantly higher prevalence of overlap syndrome (based on Paris criteria or simplified IAIHG criteria) than non-Hispanic patients (31% vs 13%, respectively).[5]

This case presentation illuminates the intricacies and diagnostic journey of a female patient who exhibited symptoms and laboratory findings suggestive of an overlap syndrome involving these two autoimmune liver diseases. The case unravels the diagnostic challenges, therapeutic interventions, and the multidisciplinary approach essential for managing this uncommon but significant entity in hepatology.

CASE REPORT

A 61-year-old female patient presented with a spectrum of symptoms including abdominal pain, distension, dizziness, reduced appetite, vomiting, and generalized weakness. Medical history indicated a previous diagnosis of autoimmune hepatitis (ANA 1:1000) and portal

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hypertension. Physical examination revealed hepatomegaly, splenomegaly, altered mental status, and ascitic fluid. Initial investigations following admission unveiled heightened ammonia levels, suggestive of hepatic encephalopathy. The patient was promptly initiated on Propranolol and transferred to the female ward for a comprehensive evaluation, encompassing anti-LKM, anti-mitochondrial antibody tests, and liver imaging. Collaborative assessment with a gastroenterologist raised concerns about an overlap syndrome involving autoimmune hepatitis with primary biliary cirrhosis (AIH+PBC), subsequently corroborated by liver reports. Treatment with Prednisolone was instigated while awaiting biopsy results for a nuanced management strategy.

Physical Examination Findings:

Physical examination exhibited signs indicative of severe liver dysfunction, manifesting as hepatomegaly, and splenomegaly. Additionally, displayed a troubling decline in mental state, characterized by disorientation to time, place, and person. Further investigation confirmed esophageal varices, signaling portal vein system pressure elevation. Ascitic fluid, a buildup of fluid in the abdomen, was also detected. Despite hemodynamic stability, the patient's low level of consciousness necessitated immediate admission for further evaluation and treatment.

Lab Investigations:

Test	Result
ANA	1:1000 positive
AMA M2	Positive
Anti LKM	Negative

HIV	Non-reactive
HBsAg	Non-reactive
HCV	Non-reactive
GGTP	18
Plasma Ammonia	103

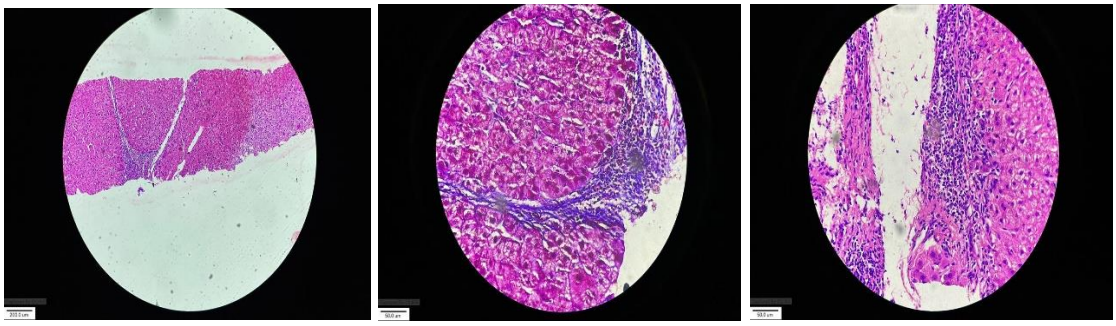
Clinical Course:

Upon admission, comprehensive investigations were promptly initiated, revealing heightened ammonia levels indicative of potential hepatic encephalopathy. Subsequent plans included an array of diagnostic evaluations, notably anti-LKM and anti-mitochondrial antibody tests, aimed at delineating the underlying condition. Propranolol, a selective beta-blocker, was initiated post-stabilization, concurrent with the patient's transfer to the female ward for further management and scheduled liver imaging. A consultation with a gastroenterologist raised suspicion of an overlap syndrome encompassing autoimmune hepatitis with primary biliary cirrhosis, prompting the recommendation for a battery of diagnostic assessments, including ANA, anti-LKM, anti-mitochondrial antibodies, and liver biopsy to ascertain the precise diagnosis. Treatment commenced with Prednisolone, an oral corticosteroid, with a carefully structured dosage tapering plan. Subsequent liver reports validated the suspicion, confirming the presence of overlap syndrome - specifically, the co-occurrence of autoimmune hepatitis with primary biliary cirrhosis (AIH+PBC).

Diagnosis and Management:

- **Diagnosis:** The patient has been diagnosed with overlap syndrome, a complex combination of autoimmune hepatitis (AIH) and primary biliary cirrhosis (PBC).

- **Treatment Approach:** The treatment approach commenced with the initiation of Prednisolone, aimed at immunosuppression to address the autoimmune components involved in the conditions. Additionally, conservative measures were adopted to manage ascites and hepatic encephalopathy, focusing on symptomatic relief and supportive care. Pending confirmation from biopsy results to ascertain and further refine the diagnosis.



A. **B.** **C.**

A. *Scanner view shows bridging fibrosis with ductular reaction in portal tract* **B.** *Masson's trichrome stain showing fibrous septa with bluish infiltration of collagen fibres with ductular reaction of portal tract* **C.** *Lymphocytes invading into hepatic lobules indicating interphase hepatitis which is classic for AIH with hepatocytes showing ballooning degeneration can be seen in AIH and PBC both*

Outcome and Follow-up: The biopsy reports hold significance in confirming the diagnosis and will act as a guiding compass for devising subsequent therapeutic strategies. Pending these crucial results, a meticulous plan for close follow-up and monitoring has been initiated. This vigilant monitoring aims to promptly identify and manage any emerging complications associated with the overlap syndrome of Autoimmune Hepatitis (AIH) and Primary Biliary Cirrhosis (PBC). The emphasis on consistent monitoring reflects the commitment to delivering comprehensive care, ensuring timely interventions and tailored approaches to optimize the patient's well-being and treatment trajectory.

DISCUSSION

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The presented case of a 61-year-old female sheds light on the complexities inherent in diagnosing and managing overlap syndrome, a rare phenomenon encompassing the coexistence of Autoimmune Hepatitis (AIH) and Primary Biliary Cholangitis (PBC) within an individual. According to the literature by **Talwalkar JA et al.,**[6] 83 to 100% of patients with PBC-AIH overlap syndrome are women.

Overlap syndrome represents a unique convergence of autoimmune liver diseases, blending the inflammatory nature of AIH and the destructive progression of PBC.[7] This case exemplifies the complexity of this amalgamation, where distinct autoimmune processes overlap, complicating both diagnosis and treatment pathways. This case reinforces the importance of considering overlap syndrome in patients with known autoimmune liver disease presenting with atypical features or progressive disease despite standard therapy. **Jeong, Sook-Hyang et al.,** suggested that AIH and PBC are rare but mostly treatable diseases if diagnosed in the early stages.[8]

Our treatment initiation with Prednisolone aligns with the standard immunosuppressive approach documented in previous research by **Fan, Xiaoli et al.** for managing AIH-PBC overlap syndrome.[9] This research indicates that patients with decompensated cirrhosis attributed to PBC-AIH, when treated with a combination of UDCA and immunosuppressants, demonstrated elevated rates of biochemical remission and encountered fewer liver-related adverse events. These findings suggest that immunosuppressant therapy could potentially serve as a more efficacious treatment option specifically for well-defined cases of decompensated PBC-AIH overlap syndrome. **Boberg KM, et al** also suggested that immunosuppression stands as the established effective therapy for AIH, while UDCA is advised to decelerate the advancement of PBC.[10]

Beyond specific therapies, our case underlines the crucial role of comprehensive care in managing overlap syndrome. This includes careful monitoring for complications like hepatic encephalopathy and ascitic fluid and providing supportive measures to improve the patient's quality of life. The multidisciplinary approach involving hepatologists, gastroenterologists, and supportive care teams is essential for addressing the complex needs of patients with this rare and challenging condition.

CONCLUSION

In conclusion, this case presentation highlights the diagnostic complexities and multifaceted management of AIH-PBC overlap syndrome. Timely recognition of atypical features, comprehensive investigations, and a collaborative approach are keys to achieving optimal outcomes for patients with this rare but significant entity in hepatology. Further research to optimize diagnostic algorithms and refine treatment strategies remains crucial for improving the long-term prognosis of patients with AIH-PBC overlap syndrome.

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