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Case Report

Severe Hypoxemia in a Young Patient: Unusual Presentation of Cryptogenic Cirrhosis with Hepatopulmonary Syndrome

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Abstract

Cirrhosis can cause changes in micro-vasculature of any bodily system; when it involves pulmonary arteries, impaired gas exchange takes place due to increased production of vasodilatory substances like nitric oxide, vessel remodeling and angiogenesis, resulting in hypoxemia. We are reporting a case of a 35-year-old woman who presented to emergency department with bluish discoloration of her fingertips and exertional dyspnea, with no known prior liver disease. Examination revealed SpO_2 levels of 60% via pulse oximetry at room air, palmar erythema, digital clubbing and splenomegaly. Further evaluation revealed an A-a gradient of 66mmHg and contrast echocardiography confirmed intra-pulmonary shunt, but no etiology of chronic liver disease was identified. Imaging confirmed cirrhosis, which was labelled cryptogenic, along with evidence for portal hypertension. She was diagnosed with Hepatopulmonary Syndrome (HPS) and was referred to liver transplant medicine based on MELD exception criteria. This case signifies the importance of considering HPS in any patient with unexplained hypoxemia and suspected chronic liver disease. Importance of MELD exception criteria is also highlighted for this patient as liver transplant remains the only treatment for HPS at the moment.

Keywords: Hepatopulmonary Syndrome, Cirrhosis, Hypoxemia, Contrast Echocardiography, MELD Exception, Liver Transplantation, Cryptogenic cirrhosis

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Introduction

Hepatopulmonary Syndrome (HPS) is a significant but often underrecognized complication of chronic liver disease.[1] One study found 48.96% prevalence in advanced cirrhosis.[2] In Pakistan, HPS has been found in 26% to 29% of cirrhotic patients. It results from intrapulmonary vascular dilatations leading to right-to-left shunting and impaired oxygenation.[3] It often presents with clubbing, cyanosis, platypnea, and dyspnea.[4] The diagnosis is clinical, radiological, and echocardiographic - often requiring a high index of suspicion.[5] HPS incidence correlate with Child-Pugh score and MELD score. A previous study revealed no significant relationship between mortality and HPS when adjustments were made for the severity of liver disease.[4] However, other studies have found out increased mortality related to HPS and stressed the use of MELD exception points for such patients.[3,6] HPS was also identified as an independent predictor of mortality; in addition to age, Child-Pugh scoring and renal dysfunction. Liver transplantation is currently the only curative option and complete resolution of symptoms is seen in all patients after 1 year.[1,7] Despite several challenges, outcomes of liver transplant are improving in Pakistan.[8] Cryptogenic cirrhosis is a diagnosis of exclusion and also contributes to morbidity and mortality. We present a case of HPS in a young woman with no known history of liver disease who presented primarily with respiratory complaints.

Case Presentation

A 35-year-old married woman having two kids, no abortions, presented with bluish discoloration of her fingertips for two weeks. She had also reported progressive exertional dyspnea and fatigue upon inquiry. She denied all other respiratory and cardiac symptoms, including orthopnea, PND, cough, and chest tightness. She had no significant past medical

and surgical history. She was neither known for chronic liver disease, use of drugs/alcohol, nor blood transfusion. There was no history of liver disease in the family.

Upon examination, she had a pulse rate of 98 bpm, respiratory rate 22 per minute, blood pressure 110/70mmHg and SpO_2 of 60% at room air, without positional changes. Her hands were warm with cyanosis of the fingertips, that improved with oxygen therapy. She also had grade-II digital clubbing, palmar erythema, and an enlarged spleen. Conjunctival pallor, jaundice, ascites, and signs of encephalopathy were absent. Her BMI was within the normal range.

Investigations

Table 1: *Summary of Laboratory Investigations*

Test	Result	Reference Range
Hemoglobin	12.9 g/dL	11.5–15.0 g/dL
WBC Count	2.7 × 10^9/L	4.0–10.0 × 10^9/L
Platelets	81 × 10^9/L	150–450 × 10^9/L
Total Bilirubin	1.8 mg/dL	0.3–1.2 mg/dL
ALT / AST	24 / 49 U/L	< 35 / < 45 U/L
ALP	213 U/L	35–104 U/L
Albumin	2.8 g/dL	3.4–5.4 g/dL
PT / INR	17 sec / 1.24	11–15 sec / < 1.2
Creatinine	0.7 mg/dL	0.6–1.2 mg/dL
A–a Gradient	66 mmHg	< 15 mmHg
PaO_2	60 mmHg	> 80 mmHg (room air)
HBsAg / Anti-HCV	Negative	
ANA / Autoimmune Profile	Negative	

Contrast Echocardiography: Normal RV and LV function and structure. Delayed contrast appearance in the left heart chamber suggesting intrapulmonary shunting. No intracardiac shunts were observed. Pulmonary artery systolic pressure was measured as 30 mmHg.

HRCT Chest: No parenchymal lung disease. Liver visualized with an irregular margin. Splenomegaly noted.

CT Triphasic Liver: Features consistent with cirrhosis and portal hypertension. Segment VI/VIII hypodensity seen; splenomegaly with possible portosystemic collaterals.

Diagnosis

Hepatopulmonary Syndrome (HPS) secondary to likely cryptogenic cirrhosis. Based on:

- Chronic liver disease with radiological signs of cirrhosis and splenomegaly. Work-up for etiology of it were extensively inconclusive.
- Severe hypoxemia (PaO_2 = 60 mmHg), A–a gradient = 66 mmHg
- Positive contrast echocardiography indicating intrapulmonary shunting
- No primary pulmonary or cardiac pathology

Scoring and Transplant Evaluation Child-Pugh Score

- Bilirubin: 1.8 → 1 point
- Albumin: 2.8 → 2 points
- INR: 1.24 → 1 point
- No Ascites → 1 point
- No Encephalopathy → 1 point

Total = 6 (Class A)

MELD Score Calculation:

MELD = 3.78 × ln(1.8) + 11.2 × ln(1.24) + 9.57 × ln(1.0) + 6.43 = 11

Although the lab MELD is low, marked hypoxia qualifies her for MELD Exception under standard transplant criteria.

***Management and Outcome*:** This patient was put on oxygen therapy and was referred to the transplant hepatology team, and given her PaO_2 levels equal to 60 mmHg, she qualifies for MELD exception criteria and was listed for liver transplant. Treatment regimen related to chronic liver disease was also commenced.

Discussion

Hepatopulmonary syndrome (HPS) is an underdiagnosed but curable condition. It involves pulmonary microvascular dilatations and right-to-left shunting of the blood flow.[1,3] Patients with HPS present most commonly with respiratory complaints in the setting of chronic liver disease. Classic clinical manifestations of HPS include platypnea (dyspnea worsened by an erect position and improved by a supine position) and orthodeoxia (exacerbation of hypoxia and hypoxemia in an upright position), both of which are relatively uncommon, and the insidious onset and progression of dyspnea, clubbing, and central cyanosis. Occasionally, HPS may be the initial manifestation of cirrhosis. Clubbing and hypoxemia in patients with liver disease and in the absence of intrinsic cardiopulmonary disease must be investigated for HPS.[3,5] Many patients, particularly those with early HPS, are asymptomatic or have symptoms only on exertion.[3] The diagnosis of HPS requires a high degree of clinical suspicion,

measurement of the A-a gradient, evidence of intrapulmonary shunting, and ruling out of intrinsic cardiopulmonary disease as the cause of hypoxemia.[3] The most sensitive test for the diagnosis of intrapulmonary shunting is contrast echocardiography and also the gold standard.[3,5] This case spotlights the significance of simple clinical signs, such as central cyanosis, when correlated with hypoxemia and echocardiographic findings, leading to the early diagnosis of HPS without the need for establishment of decompensated liver disease features. MELD scoring may not correlate with the presence of HPS and high mortality, prompting transplant centers to adopt MELD exception criteria to prioritize these patients.[3,5] Although our patient exhibited compensated liver disease (Child-Pugh A), the presence of moderate to severe hypoxemia (PaO_2 = 60 mmHg; A-a gradient 66 mmHg) significantly elevated her mortality risk, underscoring the necessity for policy level inclusion of HPS as a priority indication. The natural progression of HPS without transplantation is poor, establishing the role of liver transplantation as both a corrective and curative intervention.[3,6] Current studies targeting nitric oxide and angiogenesis pathways have yet to demonstrate curative outcomes.[1,3] This case also highlights that hepatopulmonary syndrome can manifest independently of advanced liver dysfunction and necessitates early identification to facilitate timely consideration for liver transplantation. Liver transplantation reverses HPS in most affected patients and improves survival.[6] Recent advancement and better care of such patients has also resulted in favorable outcomes.[8]

Conclusion

Hepatopulmonary Syndrome (HPS) is a severe and less acknowledged complication of chronic liver disease. The presence of HPS significantly increases mortality in patients with cirrhosis. Its clinical significance lies not only in the mortality but also in the fact that conventional liver scoring systems, such as the Model for End-Stage Liver Disease (MELD), often undervalue its impact. Early evaluation of subtle signs like unexplained dyspnea, cyanosis, or clubbing, combined with investigations like contrast echocardiography, is essential for timely diagnosis of HPS. As there are no effective medical treatments for HPS at the moment, liver transplantation remains the only definitive treatment, often resulting in resolution of hypoxemia and favorable long-term outcomes. It is also highlighted that HPS can be the first clinical presentation of cirrhosis and can present without classical orthodeoxia-platypnea syndrome. Our patient also had slightly decreased hemoglobin levels, which were related to anemia of chronic illness. HPS does not necessarily correlate with the presence of significant decompensation of liver disease and can be present in the early course of disease. Enhanced awareness, early diagnostic suspicion, and structured transplant referral pathways, including MELD exception policies, are essential to improve prognosis in affected patients.

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Authors' Contribution

HA: Conception

WQ: Design of the work

MNM,H: Data acquisition, analysis, or interpretation

HA,MNM,H: Draft the work

WQ: Review critically for important intellectual content

All authors approve the version to be published

All authors agree to be accountable for all aspects of the work

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