ORIGINAL RESEARCH PAPER

Pulmonary Medicine

KEY WORDS:
Hepatopulmonary Syndrome, Liver Cirrhosis, Liver Transplantation, Portal Hypertention, Contrast Echocardiography.

HEPATOPULMONARY SYNDROME : A RARE CASE REPORT

Dr Urjita J. Parmar — 3rd Year Resident, Department of Pulmonary Medicine, B.J. Medical College, Ahmedabad.

Dr Rahul Kumar Rohit* — 3rd Year Resident, Department of Pulmonary Medicine, B.J. Medical College, Ahmedabad .*Corresponding Author

Dr Rajesh N. Solanki — Head of Department, Department of Pulmonary Medicine, B.J Medical College, Ahmedabad.

ABSTRACT

Hepatopulmonary Syndrome(HPS) is a liver-induced pulmonary vascular disorder characterised by a widened alveolar-arterial oxygen gradient. The prevalence of HPS is reported as 4% to 32% in cohorts of cirrhotic patients undergoing liver transplant evaluation. Here in we report a 14 year old male patient who presented with gradual onset of breathing difficulty with peripheral cyanosis and digital clubbing as initial symptoms. The diagnosis of HPS was confirmed by contrast-enhanced TTE. His respiratory symptoms was improved following pentoxifylline treatment.

INTRODUCTION

"Hepatopulmonary Syndrome" is defined as the triad of liver disease, pulmonary gas exchange abnormalities leading to arterial deoxygenation and widespread intrapulmonary vascular dilatation(IPVD).When cirrhotic patients have no sign of any cardiovascular disease, severe hypoxemia (PO2<60 mmHg) strongly indicates HPS. A diagnosis is established when patients present with liver disease associated with IPVD and arterial gas exchange abnormalities (arterial-alveolar oxygen gradients A-a) O2 >15mmHg or PaO2<80mmHg.

Here in we present a known case of cirrhosis presented as hepatopulmonary Syndrome.

CASE REPORT

A 14-year old hindu male patient was admitted to our hospital for gradual onset of breathlessness with peripheral cyanosis and digital clubbing since 2 years, which was progressively increased since past 2 months. He had no complaint of fever, cough, chest pain, pedal edema and hemoptysis. He had no past history of hypertension, diabetes mellitus, tuberculosis and was not having any addiction. He didn't had similar illness in his family. He had chronic history of hyperbilirubinemia since birth and he admitted in his nearby hospital for the same and never diagnosed in detail.

At the time of admission general condition was poorly built, afebrile, vitaly stable, temperature was 36.8^{0}C, pulse was 106/min, respiratory rate was 24/min, blood pressure was 110/70mmHg, Spo2 60 on room air. There was presence of peripheral cyanosis and digital clubbing noted on physical examination.

There was presence of platypnea (dyspnea with standing) and orthedeoxia (decrease of PaO_2 of 5% or 4mmHg upon standing) which was confirmed with ABGA in supine and standing position.

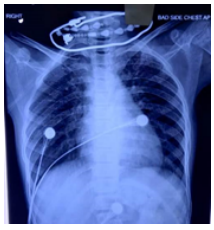
On inspection bilaterally equal chest movement present.
On auscultation bilateral equal air entry present.

ABGA showed PaO_2:60, $PaCO_2$:28,
pH:7.52, HCO_3:22, SpO_2:85% in standing position

CBC, RFT, PT/INR, RBS were within normal limit, LFT was altered (Total bilirubin:5.2, Direct bilirubin:0.4).

Sputum for AFB was negative.

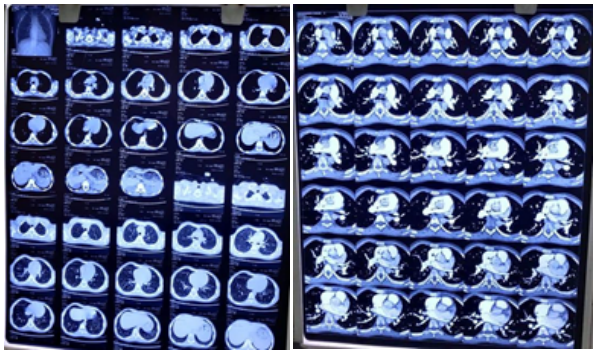
Chest radiography PA view:



Ultrasonography of abdomen:- suggestive of changes of liver cirrhosis along with minimally raised periGB and peri portal echogenicity with multiple dilated splenorenal collaterals are noted.

2D-ECHO(Without Contrast) and **dopplar study** was normal.

HRCT Thorax suggestive of :
Relatively smaller left lung volume, mild smooth inter lobular septal thickening in left upper lobar region-? Edema, patchy subpleural atelectetic changes in right upper lobe.



CT Pulmonary Angiography was normal with no evidence of pulmonary thromboembolism.

Gastromedicine and Cardiologist opinion was taken and advice for **Contrast-enhanced transthoracic echocardiogram (TTE).**

Bubble contrast-enhanced TTE was done which showed presence of **Intrapulmonary vasodilatation(IPVD)** which was later on confirmed as **Hepatopulmonary Syndrome (HPS).** Patient significantly improved after 3months of **Pentoxifylline [**PDE-4 inhibitor**]** treatment and patient was successfully discharged with long term supplemention oxygen therapy(LTOT) at home and was on regular follow up.

DISCUSSION:

Hepatopulmonary Syndrome(HPS) is a liver induced pulmonary vascular disorder characterised by a widened alveolar-arterial oxygen gradient. The widened gradient is the result of intrapulmonary vasodilation(IPVD) in the presence of hepatic disease or portal hypertension. It consists triad of liver dysfunction, unexplained hypoxemia, intrapulmonary vasodilation(IPVD).

The most common liver disease responsible for HPS is liver cirrhosis. Other liver diseases may contribute;

- Non cirrhotic portal hypertension
- Extrahepatic portal vein obstruction
- Chronic active hepatitis
- Fulminant hepatic failure
- Congenital hepatic fibrosis
- Biliary atresia
- Budd chiari syndrome
- Wilson's disease
- a1-antitrypsin deficiency

HISTORY OF HPS:

A relationship between cirrhotic liver and lung was first described by Fluckiger in 1884 and later on the term "Hepatopulmonary Syndrome" was coined by Kennedy and Knudson in 1977.

The prevalence is reported to be between 9-29% of patients with liver disease.

Pathophysiology:

1) Vasodilatation: Persistent pulmonary and systemic vasodilatation is mostly explained by the imbalance of vasodilator and vasoconstrictor agents favoring vasodilators. This could be due to a-overproduction of the vasodilators from injured hepatobiliary system.

b-decrease in their clearance by the liver.
c-production of a vasoconstrictor inhibitor.
d-normal sensitivity of the pulmonary vessels to vasoconstrictors in response to hypoxemia is blunted in HPS.

2) Hypoxemia : Widespread pulmonary precapillary and capillary vasodilatation.

- Pulmonary capillary diameter is normally about 8-15 micrometer(μm)and this could rise upto 500 micrometer (μm) in HPS.
- Distinct arterio-venous (AV)malformations and direct AV communications.
- Pleural spider angiomas may also form.

CLINICAL FEATURES:

More than 80% of patients present with symptoms and signs of liver disease. In less than 20%, the presenting symtoms and sign are related to lung disease. These include Dyspnea, Clubbing, Cyanosis, Platypnea and Orthodeoxia .

DIFFERENTIAL DIAGNOSIS:

1)Portopulmonary hypertension(PPH) and
2)Hereditary hemorrhagic telangiectasia (HHT).

DIAGNOSIS:

Diagnostic criteria for HPS are:

1) cirrhosis or portal hypertension
2) a widened age-corrected alveolar-arterial oxygen gradient(>15mmHg)
3) demonstration of IVPD on bubble contrast-enhanced transthoracic echocardiogram(TTE)

Bubble contrast-enhanced TTE is most sensitive test for the detection of IPVD.

HPS-Severity Classification

Mild: Pao_2 >80mmHg
Moderate: Pao_2 60 to 80mmHg
Severe: Pao_2 50 to 60mmHg
Very Severe: Pao_2 <50mmHg

MANAGEMENT:-

No medical has been shown to improve patients with HPS but many agents have been tried unsuccessfully. Out of those Pentoxifylline, a phosphodiesterase-4 inhibitor that interferes with tumor necrosis factor(TNF-α) synthesis when used with a duration of over 3months has a high success rate.

In severe or very severe HPS, Long term oxygen therapy(LTOT) is the most frequently recommended therapy. However Liver transplantation is the only therapy proved so far to resolve HPS. Other therapies includes

1) Transjugular intrahepatic portosystemic shunt(TIPS),
2) Embolisation of AVM,
3) Garlic which decreases the NO synthesis.

CONCLUSION:

No known medical treatment for HPS exists, and patients with HPS have a poorer prognosis than for patients with liver disease without HPS. HPS is an indication for, and is curable by, liver transplantation.

REFERENCES:

1. Kennedy TC ,knudson RJ.Exercise-aggravated hypoxemia and orthodeoxia in cirrhosis.chest.1977;72:305-309.[pubMed]
2. Berthelot P,Walker JG,Sherlock S,Ried L,Arterial changes in the lungs in cirrhosis of the liver-lung spider nevi.N Engl J Med.1966;274:291-298.[pub Med] [DOI].
3. Fussner LA, Krowka MJ.Current Approach to the Diagnosis and Management of Portopulmonary Hypertention Curr Gastroenterol Rep. 2016; 18:29. [pubMed] [DOI]
4. Rodriguez-Roisin R,Krowka MJ.Hepatopulmonary syndrome-a-liver-induced lung vascular disorder.N Engl J Med.2008;358:2378-2387. [pubMed] [DOI]
5. Krowka MJ.Hepatopulmonary syndrome:recent literature(1997 to 1999) and implications for liver transplantation.Liver Transpl.2000;6:S31-S35. [pubMed]
6. Elias N,Scirica CV,Hertl M.Liver transplantation for the Abernathy malformation.N Engl J Med.2008;358:858. [pubMed] [DOI]
7. Stoller JK, Lange PA, Westveer MK Carey WD, vogt D, Handerson JM. Prevalance and reversibility of the hepatopulmonary syndrome after liver transplantation. The cleveland clinic experience. West J Med. 1995; 163: 133-138 .[pubMed]