Case Report

Hepatopulmonary syndrome - An unusual complication of chronic liver cell disease

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Abstract

Intrapulmonary vascular dilatations in the presence of chronic liver cell disease (CLCD), portal hypertension or congenital portosystemic shunts result in hepatopulmonary syndrome (HPS). Cyanosis, platypnoea and orthodeoxia are the main clinical features and contrast echocardiography is used for its diagnosis. The only available curative therapy is liver transplantation. Here we report a case of 62-year-old lady with CLCD and portal hypertension, who was investigated for hypoxia, clubbing and cyanosis. The diagnosis of HPS was made with the aid of arterial blood gas analysis, saline bubble contrast echocardiography and computer tomographic pulmonary angiography.

Keywords: Chronic liver disease, Hepatopulmonary syndrome, Bubble contrast echocardiography, Computer tomographic pulmonary angiography

Funding: None

Competing interest: None

Received: 20.12.2022 **Accepted revised version:** 03.06.2023 **Published:**25.07.2023

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Cite this article as: Senadeera N.*et al*, Hepatopulmonary syndrome - An unusual complication of chronic liver cell disease: a case report Anuradhapura Medical Journal 2023; 17 (2): 40-42, DOI: http://doi.org/10.4038/amj.v17i2.7753

Introduction

Among the complications of chronic liver disease, HPS has a prevalence ranging from 4-47% depending on diagnostic criteria, methods used and population studied. On average the prevalence is 25% [1,2]. It presents with exertional dyspnoea, platypnoea, orthodeoxia, cyanosis and digital clubbing [1-3]. The pathogenesis of HPS has not been clearly understood. Studies suggest increased levels of nitric oxide (NO) and endothelin-1in the setting of CLCD with portal hypertension play a role in intrapulmonary vasodilatations. Failure of cirrhotic liver to clear the circulating pulmonary vasodilators may be a contributing factor. This leads to ventilation-perfusion mismatch in the lung, giving rise to the pulmonary symptoms[1,3]. The prognosis is poor when CLCD is complicated with HPS [1,3].

Case presentation

A 62-year-old female, known to have CLCD and portal hypertension for the past 5 years, defaulted to follow up, transferred from local hospital to a tertiary care unit

due to unexplained desaturation detected following admission with an acute diarrheal illness for two days. She denied progressive shortness of breath on exertion in the past. During physical examination, there was grade III pan digital clubbing, central cyanosis and hepato-splenomegaly. Lung and heart auscultation were unremarkable and she was not in respiratory distress. She had no cornel Kayser Fleischer rings. She had an oxygen saturation of 88% when in the supine position and 79% when upright (orthodeoxia). Her arterial blood gas (analysis while in lying down position showed partial pressure of arterial oxygen of 53 mmHg. In upright position, partial pressure of arterial oxygen dropped to 45 mmHg. Transthoracic echocardiography with intravenous agitated saline revealed microbubbles appearing in left atrium after 3 cardiac cycles which is suggestive of abnormal extracardiac shunting (likely pulmonary) (Figure 1)

Table 1: Haematological and biochemical parameters of the patient

Investigation	Results
Random blood sugar	83 mg/dl
Full blood count	
WBC	9 x10^9/L (4.5 -11 x 10^9)
Hb	13.2g/dL (12-15g dL)
Platelets	114 x 10^9/L (150-450 x 10^9)
Blood urea	8.1mmol/L (2.8-7.7)
Serum creatinine	73 µmol/L (60-120)
Aspartate aminotransferase	47 U/L (10-35)
Alanine aminotransferase	23 U/L (13-40)
Alkaline phosphatase	45 IU/L (35-130 IU/L)
Total bilirubin	27 µmol/L (5-21)
International normalize ratio (INR)	1.3
Total proteins	72g/L (64-80)
Serum Albumin	30g/L (35-52)
Serum Globulins	41g/L (20-35)
Antinuclear antibodies (ANA)	Negative
Serum Ferritin	102 ng/mL (20-400)
Serum ceruloplasmin	41.5 mg/dL (15-60)
Hepatitis B surface antigen (Hep B sAg)	Negative
Hepatitis C antibodies (IgM, IgG)	Negative

There was no atrial septal defect, ventricular septal defect or patent foramen ovale. Her ejection fraction was 60% with good left ventricular systolic function. Her spirometry was normal with normal lung volume measurements. Computer tomographic pulmonary angiogram (CTPA) showed dilated peripheral arterioles and veins in bilateral lower lobes (right>left) with arterio-venous malformations noted in right lower lobe (Figure 2). There were no filling defects suggestive of pulmonary embolism. These findings were consistent with a diagnosis of hepatopulmonary syndrome. Her investigation results are in the table 1.

Her ultrasound scan abdomen showed liver span of 16.2cm with coarse echo texture and enlarged spleen up to 15cm. There were no focal liver lesions. Gastro-duodenoscopy showed large esophageal varices with red sign and endoscopic banding was done. She was managed with diuretics, laxatives and beta blockers (carvedilol) and referred for liver transplantation. But it was decided by the transplant surgeon to manage her conservatively considering her age.

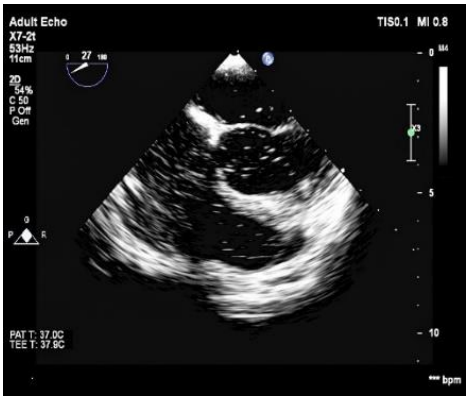

Figure 1 – Contrast echocardiography with agitated saline showing bubbles appearing in left atrium and left ventricle after 3rd cardiac cycle

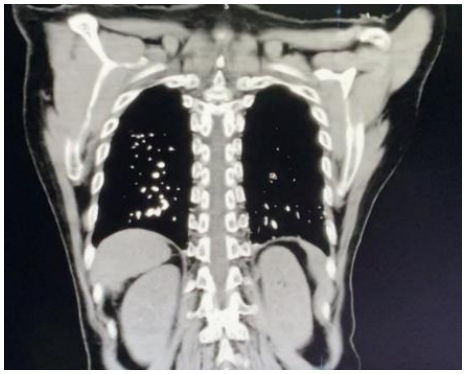

Figure 2 – CT pulmonary angiogram showing dilated peripheral arterioles and veins in bilateral lower lobes (Right>Left).

Discussion

This case report highlights the classical presentation of an uncommon complication (hepatopulmonary syndrome) related to CLCD and the high index of suspicion with eliciting the key physical signs (platypnea-orthodeoxia) leads to the correct diagnosis. Hepatopulmonary syndrome is caused by accumulation of pulmonary vasodilators like prostaglandins, intestinal endotoxins, TNF-alpha and NO in a patient with CLCD [1,3,5]. For the diagnosis of HPS, there should be evidence of CLCD and / or portal hypertension, hypoxia (PaO_2 of <80 mmHg), vascular dilatations in the lung bases and the absence of other cardiopulmonary disease [3]. Diagnosis can be made with the help of contrast enhanced echocardiography, pulse oximetry, ABGs and macro aggregated albumin lung perfusion scan (99mTc-MAA) [1,3,4]. Though we had no facilities for 99mTc-MAA, other diagnostic tests confirmed the presence of HPS in our patient. Her normal pulmonary functions with normal lung volumes excluded chronic parenchymal lung disease and CT pulmonary angiogram confirmed the presence of dilated pulmonary vessels at lung bases. After variceal banding, we arranged trans oesophageal echocardiography with bubble contrast study to confirm the absence of functional intra-cardiac shunts and to get better images of bubble crossing after three cardiac cycles. There is no correlation between the development of HPS and the severity of cirrhosis [2,3]. Our patient was in Child-Pugh class A when HPS is diagnosed. We could not identify an aetiology for the CLCD. Her diagnosis was delayed most probably due to defaulted follow up for five years from initial diagnosis of CLCD. There are medical and surgical options in the management and liver transplantation is curative. Some may need long term oxygen therapy [1,2,4]. Her MELD (Model for end-stage liver disease) score was 11 and she was referred to liver transplant surgeon for further management. However, as she was more than 60 years of age a decision was taken for conservative management.

Conclusion

HPS is a rare complication of CLCD with poor prognosis. The diagnosis of HPS is complicated as it is often asymptomatic and when symptoms do appear, they are not specific and are easily correlated with other more prevalent medical illnesses. Therefore, we should always consider this condition in the differential diagnosis of unexplained hypoxemia, cyanosis and digital clubbing in a patient with CLCD beyond traditional cardiopulmonary causes. Bed-side assessment for orthodeoxia is a very sensitive test to detect HPS.

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