Yong *et al. Egyptian Liver Journal* (2023) 13:43
https://doi.org/10.1186/s43066-023-00280-w

Egyptian Liver Journal

CASE REPORT

Open Access

Dyspnoea in liver cirrhosis: beyond the ordinary cardiopulmonary cause

Yun Xiu Yong[1], Lee Yee Lim[2*] and Kuan Yee Lim[3]

Abstract

Background Dyspnoea is a common presentation to the casualties, attributed mostly to cardiopulmonary diseases. Approach to dyspnoea consists of initial acute management to ensure airway patency, respiratory support, and hemodynamic stability, followed by identification of the underlying disease for a definite management to reduce short-term inpatient morbidity and mortality, and rehospitalization in long term. Awareness of the patient's pre-existing medical conditions is a crucial clue to guide the attending doctor to the primary cause. Dyspnea in chronic liver disease can be due to concomitant cardiopulmonary diseases as well as pulmonary vascular congestion or abnormality associated with portal hypertension such as hepatopulmonary syndrome.

Case presentation A 59-year-old man presented with a syncopal attack associated with breathlessness after physical exertion. He had alcohol associated liver cirrhosis for 2 years with a 6-month duration of platypnea and reduced effort tolerance. His physical examination revealed a cyanosed man with normal blood pressure and heart rate, without evidence of systemic and pulmonary fluid congestions. Chest radiography and computed tomography showed no evidence of pulmonary embolism and parenchymal disease and a normal echocardiography ruled out any cardiogenic cause. A diagnosis of hepatopulmonary syndrome was made after the appearance of microbubbles over left atrium at fourth to fifth cardiac cycle demonstrated by a transthoracic contrast-enhanced echocardiography to suggest an extracardiac intrapulmonary shunt.

Conclusions HPS is not an uncommon complication of chronic liver disease. Usual manifestation of HPS is platypnea which needs to be differentiated from orthopnoea associated with cardiopulmonary disease. Nevertheless, there is no effective therapeutic approach of HPS besides liver transplantation.

Keywords Platypnea, Chronic liver disease, Breathlessness

Background

Liver cirrhosis is a consequence of chronic liver inflammation, that is followed by diffuse hepatic fibrosis, which eventually leads to liver failure. Its common aetiologies are viral hepatitis infection, alcohol-related hepatitis and metabolic associated fatty liver disease. It has high global prevalence with significant morbidity and mortality which is associated with various complications such as hepatic encephalopathy, ascites, variceal bleeding, bacterial infections and kidney dysfunction leading to frequent hospital admission and impaired quality of life [1].

Dyspnea is one of the common complaints of patients with liver cirrhosis, reported up to 70% among those undergoing evaluation for liver transplant. It can happen as a result of intrinsic cardiopulmonary diseases which is not related to liver disease such as obstructive airway diseases, interstitial lung diseases and congestive heart failure. On the other hand, dyspnoea may be attributed to

*Correspondence:
Lee Yee Lim
limleeyee88@gmail.com
[1] Department of Medicine, Hospital Keningau, Keningau, Sabah, Malaysia
[2] Department of Internal Medicine, Queen Elizabeth Hospital II, Lorong Bersatu, Off, Jalan Damai, Luyang Commercial Centre, 88300 Kota Kinabalu, Sabah, Malaysia
[3] Department of Medicine, Hospital Canselor Tuanku Muhriz, Jalan Yaacob Latif, Bandar Tun Razak, Kuala Lumpur, Malaysia

© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

complications of liver cirrhosis with portal hypertension resulting in fluid retention in cases of ascites and hepatic hydrothorax. Intrapulmonary vascular abnormalities associated with portal hypertension such as hepatopulmonary syndrome (HPS) and portopulmonary hypertension may lead to dyspnoea as well [2].

Case presentation

A 59-year-old man presented with a syncopal attack after walking for a short distance at home. The event was precipitated by breathlessness, in which further history revealed he had platypnea and reduced effort tolerance for the past 6 months. There was no fitting episode observed. He was diagnosed with alcoholic associated liver cirrhosis two years ago which was complicated with multiple episodes of oesophageal variceal bleed. Otherwise, he did not have any other medical illnesses particularly pulmonary and cardiac diseases.

Upon arrival, he was cyanosed centrally and peripherally with an oxygen saturation of 80% under room air recorded on pulse oximetry. He was conscious with full Glasgow Coma Scale and his hemodynamic was normal with a blood pressure of 140/80 mmHg and a heart rate of 54 beats per minute. There were visible dilated veins over his anterior chest wall and he had stage four fingers and toes clubbing. Other systemic examination was unremarkable and there were no signs of liver decompensation such as jaundice and ascites.

His arterial blood gas obtained at sitting position under room air showed hypoxemia with partial pressure oxygen of 44.9 mmHg. He also had thrombocytopenia with a platelet count of $126 \times 10^3/\mu L$. Other routine blood investigations including renal profile, liver function test and coagulation profile were normal. His computed tomography of thorax and pulmonary artery excluded pulmonary embolism and there was no significant lung parenchymal pathology seen. His echocardiogram showed good left ventricular systolic function with an ejection fraction of 67% and there was no evidence of pulmonary hypertension as well as intracardiac shunt.

A transthoracic contrast-enhanced echocardiography was performed with infusion of agitated saline through right cubital vein which demonstrated the appearance of microbubbles over left atrium at fourth to fifth cardiac cycle, suggesting of an extracardiac intrapulmonary shunt or dilatation (Fig. 1). A diagnosis of hepatopulmonary syndrome was made and he was managed with oxygen supplementation. Unfortunately, due to resources limitation, he was prescribed with long-term oxygen therapy at home until a liver transplant is available.

Discussion

Hypoxemia is commonly associated with pathology of respiratory and cardiovascular systems with ventilation/perfusion mismatch as the most common underlying mechanism. The relation of arterial hypoxemia and chronic liver disease was first reported in nineteenth century and the term "hepatopulmonary syndrome" was first used in 1988, which is characterized by the triad of liver disease, arterial hypoxemia and intrapulmonary vascular dilatation [3]. Intrapulmonary vascular dilatation is the main pathophysiology of HPS with unclear mechanism. It was postulated to be associated with nitric oxide with evidence of increased level of exhaled nitric oxide in cirrhotic patients which normalise after liver transplantation, as well as an increased activity of both endothelial nitric oxide synthase and inducible nitric oxide synthase found in the pulmonary microvasculature in experimental animal model with chronic common bile duct ligation [4].

The diagnostic criteria of HPS includes partial pressure of oxygen less than 80 mmHg while breathing under room air in a sitting position and at rest, or alveolar-arterial oxygen gradient of more than 15 mmHg while breathing room air, pulmonary vascular dilatation as shown by positive contrast-enhanced echocardiography or by radioactive lung perfusion scan, and portal hypertension

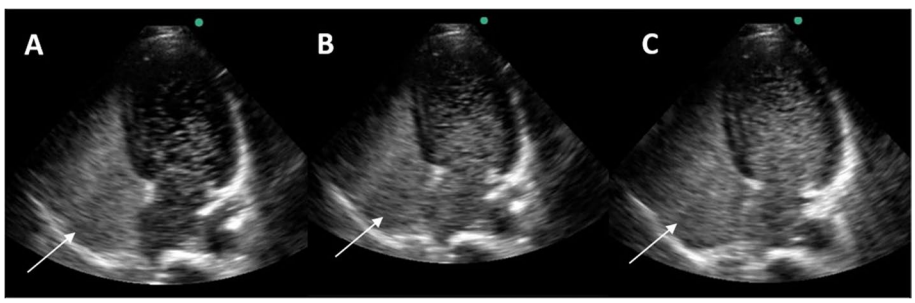

Fig. 1 Transthoracic contrast-enhanced echocardiography with apical four chamber view shows microbubbles appearing over left heart at **A** fourth cardiac cycle, **B** fifth cardiac cycle, and **C** sixth cardiac cycle. White arrow: right atrium

with or without cirrhosis [5]. It is crucial to consider HPS in liver cirrhotic patient with portal hypertension who has unexplained hypoxemia after ruling out lung and heart pathology as shown in our case where a computed tomography of thorax and pulmonary artery as well as an echocardiography did not show any significant pathology. The gold standard for diagnosing a pulmonary vascular dilatation is by a contrast-enhanced echocardiography with agitated saline which was well demonstrated in our patient where the microbubbles seen in the left atrium at fourth to fifth cardiac cycle which confirmed an intrapulmonary vascular shunt or dilatation. In normal condition, the microbubbles should not appear in the left heart as it will be trapped in the pulmonary circulation and absorbed by the alveoli, and if the microbubbles appear in the left atrium before the third cardiac cycle indicates an intracardiac shunt. Transoesophageal echocardiography is superior than transthoracic echocardiography in diagnosis; however, it is invasive and higher risk as oesophageal varices are common in portal hypertensive patient. A radioactive lung perfusion scan is another option to establish pulmonary vessels dilatation but it is not as sensitive as echocardiography because it does not distinguish between intrapulmonary and intracardiac shunting [5].

Oxygen supplementation is indicated for patients with hypoxemia and liver transplantation is the only established treatment to improve survival and clinical outcomes in patients with HPS. There is no approved medical therapy for HPS as many medications such as pentoxifylline, mycophenolate mofetil, aspirin, methylene blue, nitric oxide inhibitors, somatostatin, and oral garlic consumption had been tried but did not show a conclusive benefit [5].

Conclusion

HPS is not an uncommon complication of chronic liver disease. Usual manifestation of HPS is platypnea which needs to be differentiated from orthopnoea associated with cardiopulmonary disease. Nevertheless, there is no effective therapeutic approach of HPS besides liver transplantation.

Acknowledgements
Not applicable.

Authors' contributions
All authors contributed equally in design and write up of the manuscript. All authors read and approved the final manuscript.

Funding
None.

Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
Not applicable. Patient's written consent was obtained.

Competing interests
The authors declare that they have no competing interests.

Received: 29 May 2023 Accepted: 26 August 2023
Published online: 01 September 2023

References

1. Ginès P, Krag A, Abraldes JG, Solà E, Fabrellas N, Kamath PS (2021) Liver cirrhosis. Lancet 398(10308):1359–1376
2. Fallon MB, Abrams GA (2000) Pulmonary dysfunction in chronic liver disease. Hepatology 32(4):859–865
3. Sarkar M, Niranjan N, Banyal PK (2017) Mechanisms of hypoxemia. Lung India 34(1):47
4. Machicao VI, Fallon MB (2012) Hepatopulmonary syndrome. Semin Respir Crit Care Med 33(1):11–16
5. Bansal K, Gore M, Mittal S (2023) Hepatopulmonary syndrome. In: StatPearls. StatPearls Publishing, Treasure Island. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562169/. [Updated 6 Dec 2022]

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Submit your manuscript to a SpringerOpen journal and benefit from:

- ► Convenient online submission
- ► Rigorous peer review
- ► Open access: articles freely available online
- ► High visibility within the field
- ► Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com