Liver disease masquerading as primary cardiopulmonary disease: Hepatopulmonary syndrome as a result of idiopathic cirrhosis

Bartholameuz Nuwan Aravinda, Ratnatilaka Asoka, Sadikeen Aflah

ABSTRACT

Introduction: Liver disease and portal hypertension can be associated with pulmonary vascular complications including hepatopulmonary syndrome and portopulmonary hypertension. Hepatopulmonary syndrome is characterized by arterial hypoxemia and pulmonary vascular dilatations. Exertional dyspnea, platypnea-orthodeoxia, cyanosis and digital clubbing are commonly found symptoms and signs in hepatopulmonary syndrome.

Case Report: Here we discuss a patient with chronic liver disease whose initial presentation was hepatopulmonary syndrome with progressive exertional dyspnea, cyanosis and clubbing. Diagnosis of hepatopulmonary syndrome was made through a constellation of findings in blood gas analysis, contrast echocardiography with biochemical and ultrasound evidence of liver disease applied to standard criteria; having excluded other possible causes.

Conclusion: Hepatopulmonary syndrome should be suspected in any patient with liver disease and hypoxia. It should also be formulated in the differential diagnosis of a patient with otherwise unexplained exertional dyspnea and cyanosis with digital clubbing.

International Journal of Case Reports and Images (IJCRI)

International Journal of Case Reports and Images (IJCRI) is an international, peer reviewed, monthly, open access, online journal, publishing high-quality, articles in all areas of basic medical sciences and clinical specialties.

Aim of IJCRI is to encourage the publication of new information by providing a platform for reporting of unique, unusual and rare cases which enhance understanding of disease process, its diagnosis, management and clinico-pathologic correlations.

IJCRI publishes Review Articles, Case Series, Case Reports, Case in Images, Clinical Images and Letters to Editor.

Website: www.ijcasereportsandimages.com

CASE REPORT

PEER REVIEWED | OPEN ACCESS

Liver disease masquerading as primary cardiopulmonary disease: Hepatopulmonary syndrome as a result of idiopathic cirrhosis

Bartholameuz Nuwan Aravinda, Ratnatilaka Asoka, Sadikeen Aflah

ABSTRACT

Introduction: Liver disease and portal hypertension can be associated with pulmonary vascular complications including hepatopulmonary syndrome and portopulmonary hypertension. Hepatopulmonary syndrome is characterized by arterial hypoxemia and pulmonary vascular dilatations. Exertional dyspnea, platypnea-orthodeoxia, cyanosis and digital clubbing are commonly found symptoms and signs in hepatopulmonary syndrome. **Case Report:** Here we discuss a patient with chronic liver disease whose initial presentation was hepatopulmonary syndrome with progressive exertional dyspnea, cyanosis and clubbing. **Diagnosis of hepatopulmonary syndrome was made through a constellation of findings in blood gas analysis, contrast echocardiography with biochemical and ultrasound evidence of liver disease applied to standard criteria; having excluded other possible causes.** **Conclusion:** Hepatopulmonary syndrome should be suspected in any patient with liver disease and hypoxia. It should also be formulated in the differential diagnosis of a patient with otherwise unexplained exertional dyspnea and cyanosis with digital clubbing.

Bartholameuz Nuwan Aravinda¹, Ratnatilaka Asoka², Sadikeen Aflah³

Affiliations: ¹MBBS, Registrar-Medicine, National Hospital, Colombo, Sri Lanka; ²MBBS, MD, Consultant Physician, National Hospital, Colombo, Sri Lanka; ³MBBS, MD, Consultant Chest Physician, Central Chest Clinic, Colombo, Sri Lanka.

Corresponding Author: Nuwan Aravinda Bartholameuz Ward 42/56A, National Hospital, Colombo 10, Sri Lanka, City- Colombo, Colombo 01000; E-mail: nbaravinda@gmail.com

Received: 04 September 2016

Accepted: 01 November 2016

Published: 01 February 2017

Keywords: Cirrhosis, Cyanosis, Digital clubbing, Hepatopulmonary syndrome

How to cite this article

Bartholameuz NA, Ratnatilaka A, Sadikeen A. Liver disease masquerading as primary cardiopulmonary disease: Hepatopulmonary syndrome as a result of idiopathic cirrhosis. Int J Case Rep Images 2017;8(2):116–119.

Article ID: Z01201702CR10759BA

doi:10.5348/ijcri-201720-CR-10759

INTRODUCTION

Cyanosis indicates the presence of deoxygenated haemoglobin of ≥ 5 g/dL in arterial blood. Causes of cyanosis include intracardiac right-left shunts, lung diseases and pulmonary arteriovenous malformation (AVM). Clubbing is due to fibrovascular proliferation in nail beds, mediated by platelet derived growth factor released from megakaryocytes or platelet emboli which do not reach nail bed unless there is pulmonary capillary damage or intracardiac shunts [1]. Here we discuss a rare cause of dyspnea, cyanosis and clubbing associated with cirrhosis which mimicked primary cardiopulmonary disease.

CASE REPORT

A 56-year-old female was admitted with a history of progressive shortness of breath on exertion for 6 months duration. She had severe central cyanosis with gross clubbing. Mild icterus, palmar erythema and prominent

peripheral pulses were also noted. Respiratory rate was 24/min. Systemic examination was normal. Arterial oxygen saturation (SpO_2) lying supine was 80% and on standing was 76%. Investigations revealed leucopenia ($4.31 \times 10^3/\mu\text{L}$), thrombocytopenia ($31 \times 10^3/\mu\text{L}$), and hemoglobin 15.6 g/dL with macrocytosis in peripheral blood smear. Arterial blood gas (ABG) analysis in supine position showed pH 7.43, PCO_2 28.6 mmHg, PaO_2 56 mmHg, HCO_3^- 19.4 mmol/L and Alveolar-arterial oxygen gradient of 58 mmHg. PaO_2 dropped to 50.2 mmHg upon standing.

Total serum protein was normal (67 g/dL) with reversed serum albumin: globulin ratio (0.6). Serum bilirubin was elevated ($42.8 \mu\text{mol/L}$). PT was 17.4 s (INR 1.26) and APTT was 46 s (26 s–40 s). Liver enzymes were normal (AST 40 U/L, ALT 22 U/L, and ALP 107 U/L). Abdominal ultrasound detected coarse echo texture in a normal size liver, splenomegaly (12.5 cm; normal <12 cm), portal vein diameter of 1.4 cm (<1.3 cm) without ascites or pleural effusion. Esophagogastroduodenoscopy showed mild portal hypertensive gastropathy and no varices. Hepatitis B and C serology were negative. Serum ferritin was 172 ng/mL. Serum ceruloplasmin levels were normal and there were no Kayser-Fleischer rings. ANA and anti-mitochondrial antibodies were negative. Lipid profile was normal. TSH, Free T4, and HbA1c were normal.

High resolution computed tomography of the chest (HRCT) revealed normal lung parenchyma (Figure 1). Contrast-enhanced computed tomography (CECT) of the chest and pulmonary angiogram detected pulmonary venous congestion and dilated venous collaterals without evidence of pulmonary hypertension or AVM. Gross splenorenal collaterals were noted (Figure 2). No evidence of portal vein thrombosis was found.

Transthoracic echocardiogram was normal. Transesophageal echocardiography detected a small patent foramen ovale (PFO) but bubble contrast study excluded functional PFO. There was indirect evidence of pulmonary capillary dilatation by detecting micro-bubbles in left atrium after three cardiac cycles following the appearance of bubbles in the right atrium.

Her lung function tests were normal (FEV1 94.1%; FVC 99.5%; FEV1: FVC 94.6%, VC 88.1%) except for low DLCO (44%) reflecting a diffusion-perfusion defect due to pulmonary vascular dilatation and hyperdynamic circulation.

This is a case with hypoxia, clubbing, cirrhosis and portal hypertension with evidence of intra-pulmonary vascular dilatation (IPVD) confirming the diagnosis of hepatopulmonary syndrome (HPS).

DISCUSSION

In this case, cyanosis was due to dilatation of pulmonary vessels leading to ventilation perfusion mismatch causing hypoxia. Aetiology of pulmonary vascular dilatation in cirrhosis is thought to relate to an

Figure 1: High resolution computed tomography of the chest showing normal lung parenchyma and dilated pulmonary vasculature extending up to pleural surface.

Figure 2: Contrast-enhanced computed tomography showing gross splenorenal collaterals (arrow).

increase in pulmonary NO by means of both endothelial and inducible NO synthase (eNOS and iNOS) [2–4].

An increased hepatic production of vasoconstrictor Endothelin-1 (ET-1) stimulates the production of ETB receptors in pulmonary microcirculation. ETA causes vasoconstriction while ETB causes vasodilatation through increase in eNOS activity [2–4].

Portal hypertension weakens intestinal mucosal barrier due to impaired drainage. It allows increased enteral translocation of bacteria and endotoxins which stimulate release of vasoactive substances like TNF- α . This leads to increased pulmonary sequestration of macrophages and local production of pro-inflammatory mediators causing an increase in iNOS activity and NO production [2–4].

Normal pulmonary functions and HRCT of the chest excluded chronic parenchymal lung disease.

Transesophageal echocardiography with bubble contrast study could not reveal any functional intra-cardiac shunts but indicated presence of pulmonary vascular dilatation in the absence of AVM. These micro-bubbles are larger than normal pulmonary capillary diameter (8–15 μm) and cannot pass through normal pulmonary capillaries [2]. Evidence of pulmonary vascular dilatation was also apparent in HRCT and CT pulmonary angiogram. The dilatation of small peripheral pulmonary vessels is the hallmark of HPS [5, 6].

This patient has orthodeoxia which is defined as a fall in $\text{PaO}_2 \geq 5\%$ when upright, or 4 mmHg [2]. PaO_2 decreases in upright position as blood flow increases through already dilated vessels in basal segments of lungs, due to gravity. This increases ventilation-perfusion mismatch and hypoxia worsens [7].

Triad of liver disease (portal hypertension and/or cirrhosis), IPVD (positive findings in contrast echocardiography or abnormal uptake in the brain ($>6\%$) with radioactive lung perfusion scanning) and arterial hypoxemia ($\text{PaO}_2 < 80$ mmHg or alveolar arterial oxygen gradient > 15 mmHg while breathing ambient air) is diagnostic of HPS [2]. SpO_2 improved to 96% (PaO_2 99.9 mmHg) with oxygen (4 L/min via face mask). MELD (Model for end-stage liver disease) score was 12. Since only proven treatment for HPS is liver transplantation [3], patient was referred to transplant surgeon for further management.

Domiciliary oxygen was arranged as supportive therapy. The patient was a teetotaler and aetiology of cirrhosis and portal hypertension was not identified. Time taken from initial presentation to diagnosis approximates twenty months emphasized the importance of increased awareness of HPS among clinicians across different subspecialties [8].

CONCLUSION

Hepatopulmonary syndrome (HPS) should be suspected in any patient with established liver disease and hypoxia. It can also be the initial presentation of liver disease mimicking primary pulmonary disease such as interstitial lung disease or primary cyanotic heart disease with secondary cardiogenic cirrhosis. Identifying primary underlying pathology helps institution of appropriate care to patients. Therefore, HPS should also be entertained in differential diagnosis of a patient presenting with exertional dyspnea, cyanosis and digital clubbing beyond traditional cardiopulmonary causes.

Author Contributions

Bartholameuz Nuwan Aravinda – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the

article, Revising it critically for important intellectual content, Final approval of the version to be published
Ratnatilaka Asoka – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Sadikeen Aflah – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Revising it critically for important intellectual content Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

Copyright

© 2017 Bartholameuz Nuwan Aravinda et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

REFERENCES

1. Spicknall KE, Zirwas MJ, English JC 3rd. Clubbing: An update on diagnosis, differential diagnosis, pathophysiology, and clinical relevance. *J Am Acad Dermatol* 2005 Jun;52(6):1020–8.
2. Rodríguez-Roisin R, Krowka MJ. Hepatopulmonary syndrome: A liver-induced lung vascular disorder. *N Engl J Med* 2008 May 29;358(22):2378–87.
3. Tumgor G. Cirrhosis and hepatopulmonary syndrome. *World J Gastroenterol* 2014 Mar 14;20(10):2586–94.
4. Porres-Aguilar M, Altamirano JT, Torre-Delgadillo A, Charlton MR, Duarte-Rojo A. Portopulmonary hypertension and hepatopulmonary syndrome: A clinician-oriented overview. *Eur Respir Rev* 2012 Sep 1;21(125):223–33.
5. McAdams HP, Erasmus J, Crockett R, Mitchell J, Godwin JD, McDermott VG. The hepatopulmonary syndrome: Radiologic findings in 10 patients. *AJR Am J Roentgenol* 1996 Jun;166(6):1379–85.
6. Chawla A, Gaikwad V, Dubey N, Bosco J. CT Pulmonary Angiography Features of a Hepatopulmonary Syndrome. *Korean J Radiol* 2015 Jul-Aug;16(4):951–2.
7. Naeije R. Hepatopulmonary syndrome and portopulmonary hypertension. *Swiss Med Wkly* 2003 Mar 22;133(11-12):163–9.
8. Dhoble C, Saoji N, Jeswani J, Rios R. A 45-Year-Old Undiagnosed Cirrhotic Patient with Hepatopulmonary Syndrome as First Presentation: A Case Report. *Am J Case Rep* 2015 Oct 22;16:751–5.

Access full text article on
other devices

Access PDF of article on
other devices

Edorium Journals: An introduction

Edorium Journals Team

About Edorium Journals

Edorium Journals is a publisher of high-quality, open access, international scholarly journals covering subjects in basic sciences and clinical specialties and subspecialties.

Invitation for article submission

We sincerely invite you to submit your valuable research for publication to Edorium Journals.

But why should you publish with Edorium Journals?

In less than 10 words - we give you what no one does.

Vision of being the best

We have the vision of making our journals the best and the most authoritative journals in their respective specialties. We are working towards this goal every day of every week of every month of every year.

Exceptional services

We care for you, your work and your time. Our efficient, personalized and courteous services are a testimony to this.

Editorial Review

All manuscripts submitted to Edorium Journals undergo pre-processing review, first editorial review, peer review, second editorial review and finally third editorial review.

Peer Review

All manuscripts submitted to Edorium Journals undergo anonymous, double-blind, external peer review.

Early View version

Early View version of your manuscript will be published in the journal within 72 hours of final acceptance.

Manuscript status

From submission to publication of your article you will get regular updates (minimum six times) about status of your manuscripts directly in your email.

Our Commitment

Six weeks

You will get first decision on your manuscript within six weeks (42 days) of submission. If we fail to honor this by even one day, we will publish your manuscript free of charge.*

Four weeks

After we receive page proofs, your manuscript will be published in the journal within four weeks (31 days). If we fail to honor this by even one day, we will publish your manuscript free of charge and refund you the full article publication charges you paid for your manuscript.*

Favored Author program

One email is all it takes to become our favored author. You will not only get fee waivers but also get information and insights about scholarly publishing.

Institutional Membership program

Join our Institutional Memberships program and help scholars from your institute make their research accessible to all and save thousands of dollars in fees make their research accessible to all.

Our presence

We have some of the best designed publication formats. Our websites are very user friendly and enable you to do your work very easily with no hassle.

Something more...

We request you to have a look at our website to know more about us and our services.

* Terms and condition apply. Please see Edorium Journals website for more information.

We welcome you to interact with us, share with us, join us and of course publish with us.

Edorium Journals: On Web

Browse Journals

CONNECT WITH US