ID: 14-0100; June 2015
DOI: 10.1530/ERP-14-0100

CASE REPORT

A case of hepatopulmonary syndrome

James Offer, Lawrence Green, Andrew R Houghton and Jim Campbell

Grantham and District Hospital, Lincolnshire, UK

Correspondence should be addressed to J Offer
Email
James.offer@nhs.net

Summary

This report presents the case of a 42-year-old man with liver cirrhosis who presents with breathlessness. Initial investigations are unable to explain his persistent hypoxia and a diagnosis of hepatopulmonary syndrome is considered. Saline contrast echocardiography is utilised in confirming the diagnosis. Details of this case as well as practicalities in performing and interpreting saline contrast echocardiography are reviewed.

Learning points:

- Key features of hepatopulmonary syndrome are liver disease, hypoxia and pulmonary vascular dilatations.
- Saline contrast echocardiography is a simple inexpensive procedure to perform and key to confirming the diagnosis of hepatopulmonary syndrome. Detection can be improved by performing the scan in the stand-up position.
- Agitated saline contrast studies are more commonly performed to identify intra-cardiac shunts. Timing of contrast arrival in the left heart chambers is key to differentiating intra-cardiac shunting from extra-cardiac pulmonary transit.

Background

The prevalence of hepatopulmonary syndrome in end-stage liver disease is reported to be between 4 and 47% (1, 2, 3, 4). Satisfaction of three criteria is usually required for a diagnosis to be made; liver disease, hypoxia and evidence of intrapulmonary vascular dilatations (1, 2, 3, 4, 5, 6). The hypoxaemia results from a combination of mechanisms. There is ventilation–perfusion mismatching with the vascular dilatations causing increased perfusion of the alveolar capillary bed. Dilated capillaries surrounding alveoli lead to reduced oxygenation of red blood cells by increasing the distance that oxygen must travel to them. Both mechanisms are further exacerbated when the dilatations result in increased perfusion to poorly oxygenated areas of the lung. Physical shunting via direct arterio-venous connections bypassing the alveoli can also occur, although this is less common than pulmonary vascular dilatations (1, 3). Liver transplantation is currently the only effective treatment and prognosis is poor without this (1, 4). Saline contrast echocardiography has been shown to be a practical, highly sensitive test in confirming intrapulmonary vascular dilatations (1, 2, 3, 4, 6, 7).

Case presentation

A 42-year-old male with known alcoholic liver cirrhosis was admitted to his local District General Hospital with abdominal distension, jaundice, breathlessness and lethargy. On examination, the patient appeared cyanotic with clubbing of the fingers and toes. He was noted to be hypoxic (SpO_2 88% on air, 92% with 28% inspired O_2) and tachycardic with a pulse rate of 109 b.p.m. In addition to this mild pitting peripheral oedema, hepato-splenomegaly and florid spider naevi were also present. Routine blood tests showed a mild normocytic anaemia (100 g/l), evidence of thrombocytopenia, abnormal liver function and clotting in keeping with his liver disease. The ECG was unremarkable and ambulatory blood gas analysis demonstrated type 1

respiratory failure (pO_2 6.5 kPa on air). A routine chest X-ray did not reveal any cause for the hypoxia. To exclude pulmonary embolism, a computed tomography (CT) pulmonary angiogram was performed but no abnormalities were found. Including no evidence of arterio-venous malformations. A subsequent overnight oximetry was not suggestive of obstructive sleep apnoea and routine lung function tests were also normal. Transthoracic echocardiography showed borderline left ventricular dilatation with normal systolic function, normal right ventricular size and function. There was mild bi-atrial dilatation, but no evidence of an atrial septal defect. In view of his persistent and unexplained hypoxia, the patient was referred to the Consultant Respiratory Physician who felt that the patient may have developed hepatopulmonary syndrome and referred the patient for an agitated saline contrast echocardiogram to confirm the diagnosis (Fig. 1). Contrast can be observed arriving in the left heart chambers six beats after entering the right, with maximum opacification achieved eight to ten beats after initial contrast appearance. In conjunction with this patient's presentation and the medical history of alcoholic liver disease, this confirmed a diagnosis of hepatopulmonary syndrome. Computed tomography pulmonary angiography (CTPA) can detect arterio-venous malformations; however, it does have limitations as to the size of malformations it can detect and obviously will only identify those within the regions scanned (7, 8). Therefore, the delayed appearance of agitated saline appearing in the left heart helps confirm the diagnosis but cannot differentiate between passage via dilated capillaries and arterio-venous shunts.

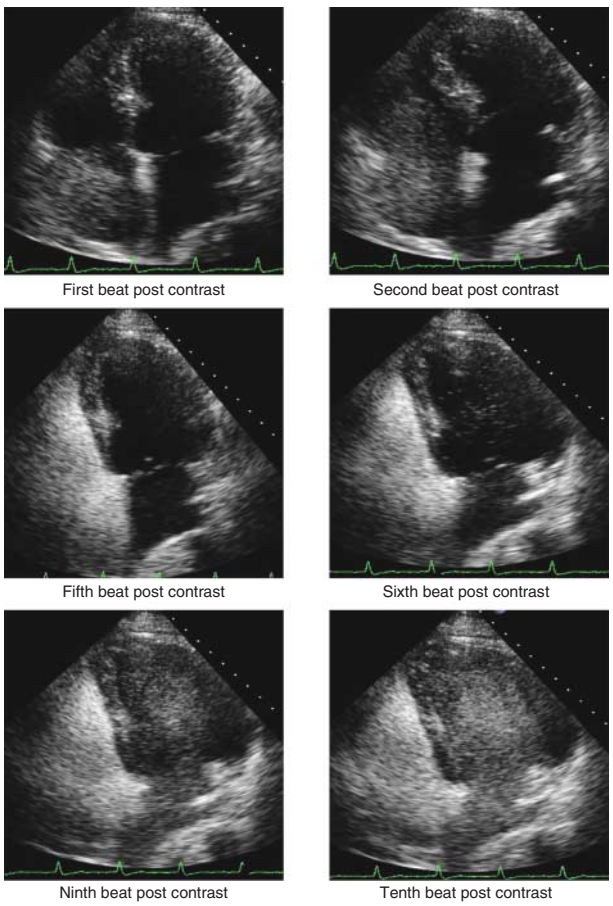

Figure 1
Agitated saline contrast echocardiography images. Contrast can be observed arriving in the left heart chambers six beats after entering the right.

Treatment and outcome

Following the diagnosis of hepatopulmonary syndrome, the patient has now been referred to a tertiary centre for consideration of a liver transplant.

Discussion

Lung perfusion scans using macroaggregated albumin are an alternative to saline contrast echocardiography; however, they are more invasive, less sensitive and cannot distinguish whether right-to-left flow is a result of intra-cardiac or extra-cardiac pathology (1). The frequent presence of oesophageal varices in patients with cirrhosis also promotes the use of transthoracic echocardiography first line in preference to transoesophageal echocardiography. Agitated saline microbubbles are usually prevented from entering the left side of the heart due to their size (up to 10 μm diameter) being too large to pass through normal capillaries (mean pulmonary capillary diameter 8 μm) (3, 4, 5). Pulmonary vascular dilatations or arterio-venous malformations allow passage and thus opacification of the left-sided chambers (3). Intra-cardiac shunts (atrial septal defect (ASD); ventricular septal defect (VSD); patent foramen ovale (PFO)) with right-to-left flow also result in a positive study. However, timing of the number of cycles from appearance of bubbles in right-sided chambers to appearance in the left enables for differentiation between the two. Left-sided bubbles appearing within three beats are consistent with an intra-cardiac shunt and four to eight beats with a extra-cardiac, i.e. pulmonary, cause (1, 2, 4, 5, 9). The degree of passage through the lungs can be quantified from the number of bubbles seen on the left side: <5, small; 5–20, moderate and >20, large (2). Pulmonary vascular dilatations tend to be more prevalent in lower zones and therefore detection can be improved by performing the

saline contrast study in the supine and standing positions due to gravitational forces increasing blood flow to these zones in the upright position (2). This is also the basis for orthodeoxia (decreased saturations on supine to upright), which can also be observed in hepatopulmonary syndrome (2). In addition to scanning in these postures, performing with and without a valsalva manoeuvre/cough is also recommended during saline contrast echocardiography. The use of a provocation manoeuvre induces a transient rise in right atrial pressure and can help unmask intra-cardiac shunts (2, 9). When performing a valsalva manoeuvre, a patient should be asked to strain as injection takes place and then release once bubbles were seen entering the right atrium (9). False positives for extra-cardiac shunting are possible either due to a delayed intra-cardiac shunt or PFO's resulting in a platypnea–orthodeoxia syndrome (10). It is also possible for large pulmonary vascular dilatations to result in quicker passage of bubbles appearing within three beats and making distinction between intra- and extra-cardiac shunting more difficult (1, 5).

In our Echocardiography Department, agitated saline studies are performed using 8.5 ml normal saline, 1 ml patient's blood (used to increase stability of microbubbles) and 0.5 ml air; this is consistent with other laboratories (2). Once drawn up, the mixture is agitated by passing between two 10 ml Leur lock syringes via a three-way tap. Some authors do not recommend the use of patient's blood and suggest that the effect on bubble stability is not sufficient when balanced against the risk of blood product spraying/spillage when mixing. However, the use of Leur lock syringes minimises this risk (2, 9). The left antecubital vein is commonly used as the site of injection (2, 3). There is evidence that injection via the femoral vein can increase diagnosis for intra-cardiac shunts; however, this is impractical to perform (9).

Declaration of interest
The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the case report.

Funding
This case report did not receive any specific grant from any funding agency in the public, commercial or not-for-profit sector.

Patient consent
Written consent was obtained.

Author contribution statement
L Green and Dr J Offer wrote the manuscript and performed the saline contrast echocardiography. Dr A R Houghton reviewed the article before submission and advised on performing the specialised scan. Dr J Campbell was consulted during the case and he first proposed hepatopulmonary syndrome as the diagnosis. He also reviewed the article before submission.

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Received in final form 2 March 2015
Accepted 9 March 2015