

# When common things aren't so common: A case report of hepatopulmonary syndrome

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## ABSTRACT

A 60-year-old smoker with a history of liver cirrhosis and chronic obstructive pulmonary syndrome (COPD) presented with hypoxic respiratory failure. This was felt secondary to an exacerbation of COPD. Despite treatment, the patient required 10 L of oxygen to achieve saturations of 88% on ambulation. Interstitial lung disease, pulmonary emboli and pulmonary hypertension were excluded as potential aetiologies of hypoxia. Given the history of cirrhosis, hepatopulmonary syndrome was postulated. Contrast echocardiography suggested an extracardiac shunt; a technetium-99m macroaggregated albumin scan confirmed the diagnosis.

**KEYWORDS:** hypoxia, hepatopulmonary syndrome (HPS), shunt, cirrhosis

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## Case presentation

A 60-year-old woman with a 30 pack-year smoking history presented with increasing shortness of breath over 4 weeks. Her past medical history included hypertension, chronic obstructive pulmonary syndrome (COPD) and alcoholic liver disease with cirrhosis. Chest X-ray demonstrated bilateral lower zone infiltrates. Inflammatory indices were normal. The patient remained hypoxic on 15 L oxygen, requiring admission to intensive care for high flow nasal oxygen and ultimately intubation.

A computed tomography pulmonary angiography demonstrated no pulmonary emboli but noted marked emphysema. No growth was seen on blood and sputum cultures. Bronchoalveolar lavage excluded atypical pathogens including mycobacterium. Transthoracic echocardiography showed normal right ventricular and left ventricular function, with no evidence of valvular disease or pulmonary hypertension. Antibiotics and oral steroids were commenced despite normal inflammatory indices.

The patient was extubated after 4 days and discharged to the respiratory ward, where finger clubbing, spider naevi and

fine bibasal crepitations were noted on examination. Oxygen saturations were 87% on room air and 90% on 3 L oxygen. Serum eosinophils, N-terminal pro-brain natriuretic peptide (NT-proBNP) levels, ACE level, extrinsic allergic alveolitis screen, rheumatoid factor, creatine kinase, hepatitis and vasculitic screen were normal. FEV1 was 1.76 L (92% predicted), forced vital capacity (FVC) 2.65 L (103% predicted), with an obstructive ratio of 66%. Repeat chest X-ray raised the possibility of basal reticulonodular change.

## Differential diagnosis

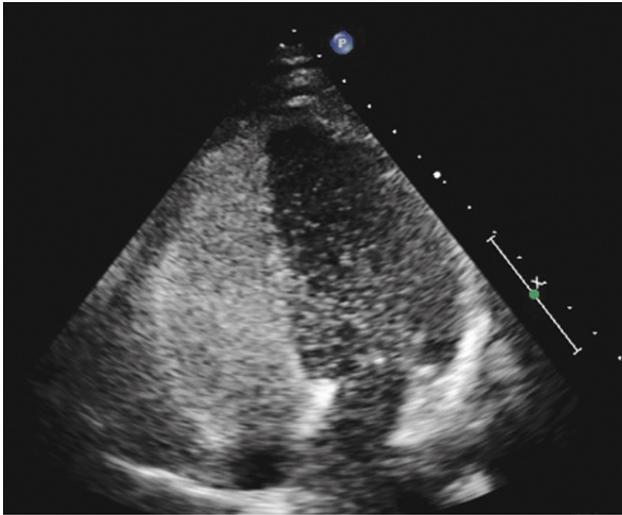
A COPD exacerbation was felt to be the most likely aetiology of the patient's respiratory failure, yet the persistent hypoxia, finger clubbing and reticulonodular changes on X-ray necessitated the exclusion of interstitial lung disease (ILD). High-resolution computed tomography showed no established fibrosis but ground glass opacities in the lower lobes, felt to represent resolving inflammatory change. The ILD multidisciplinary meeting advised empirical treatment with oral steroid and diuretics, yet the patient remained hypoxic and, on ambulatory assessment, walked 30 m before desaturating to SaO<sub>2</sub> 75% on 10 L oxygen.

Although bearing in mind the dictum that 'common things are common', the team was uneasy regarding the patient's diagnosis as the degree of hypoxia appeared out of keeping with the severity of emphysema. This prompted a review of the case and, given the presence of cirrhosis, hepatopulmonary syndrome was postulated. Oxygen saturations were assessed supine and standing, at 90% and 79% on room air, respectively, confirming platypnoea–orthodeoxia syndrome. Contrast echocardiography confirmed an extracardiac shunt with opacification of the left heart chambers after seven cardiac cycles (Fig 1), confirming hepatopulmonary syndrome. A hepatology referral was made for consideration of a liver transplant and the patient was discharged on long-term oxygen (LTOT).

## Outcome and follow-up

During transplant work-up, concern was expressed regarding the extent of the patient's emphysema, with her degree of hypoxaemia considered an unreliable marker of HPS severity. A technetium-99m macroaggregated albumin (TcMAA) study was completed, revealing a shunt fraction of 30.7%. Despite the degree of shunt, our patient was declined for liver transplant.

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**Fig 1. Contrast echocardiography showing extracardiac shunt with opacification of the left heart chambers after seven cardiac cycles, confirming hepatopulmonary syndrome.**

## Discussion

HPS is a rare cause of hypoxaemia, reported in 4–32% of patients with liver disease.<sup>1</sup> Characterised by liver disease, intrapulmonary vascular dilatations (IPVDs) and arterial de-oxygenation in the absence of other cardiorespiratory abnormalities, HPS can be subtyped into type 1 and type 2. Type 1 patients typically display smaller diffuse vascular dilatations while type 2 patients have larger, discrete IPVDs comparable to arteriovenous malformations (AVMs). True AVMs are rare. The driver of pulmonary dilatation has been postulated as nitric oxide; however, the exact cause remains elusive.<sup>2</sup>

When considering a diagnosis of HPS it is useful to assess for orthodeoxia (defined as a  $\text{SpO}_2$  decrease of  $\geq 5\%$  from supine to standing).<sup>3</sup> This decrease in  $\text{SpO}_2$  occurs due to V/Q mismatching from the redirection of blood to the lung bases when standing, an area where IPVDs predominate. Orthodeoxia can also be identified using arterial blood gas analysis with a decrease of  $\geq 0.5$  kPa in  $\text{PaO}_2$  from supine to upright diagnostic. Yet the European Respiratory Society (ERS) caution against using  $\text{PaO}_2$  alone when diagnosing HPS, as this may underestimate oxygen impairment due to reflex hyperventilation.<sup>4</sup> Consequently the A-a oxygen gradient is recommended, with a gradient of  $\geq 2$  kPa when upright on room air (or 2.7 kPa in those aged over 65) the defined cut-off.<sup>4,5</sup>

## Investigations

Patients with suspected HPS should receive chest imaging and pulmonary function testing to exclude other causes of hypoxia. Spirometry is typically normal (unless comorbid respiratory disease exists). TLCO is usually impaired. Chest X-rays are often normal. Transthoracic contrast echocardiography is recommended by the ERS as the first-line investigation.<sup>5</sup> In those with HPS and a right-to-left shunt, agitated saline causes opacification in the left and right heart chambers as the bubbles bypass the pulmonary capillary bed.

For patients with coexistent cardiorespiratory disease, it may be useful to quantify the degree of shunt using radionuclide perfusion scanning with TcMAA. In healthy subjects, the TcMAA is filtered by the

pulmonary capillaries, whereas in HPS the particles bypass the lungs, becoming trapped in the brain and kidneys. The proportion of TcMAA bypassing the lungs is used to quantify the extent of the shunt. The need for invasive pulmonary angiography is rare, as contrast CT often excludes larger IPVDs; as such, it is only advised when attempting to identify type 2 patients with IPVDs amenable to embolisation.<sup>6</sup>

## Treatment

HPS is a progressive disease associated with impaired quality of life. Untreated, mortality is twice that of cirrhotic patients without HPS.

While not a cure, LTOT is the first-line supportive therapy. Liver transplantation remains the only definitive treatment, with 85% of patients demonstrating resolution of vascular dilatations and normalisation of oxygenation at 1 year post-transplant.<sup>7</sup> Severe hypoxaemia and a pre-transplant shunt fraction  $>20\%$  on TcMAA confers greater transplant mortality.<sup>7,8</sup> In light of the poor prognosis with HPS and favourable transplant outcomes, the International Liver Transplant Society recommend expedited transplant referrals in patients with severe HPS.

## Summary

- > Hepatopulmonary syndrome (HPS) is a rare cause of hypoxaemia.
- > The diagnostic difficulty surrounding the condition means it is often diagnosed late in the disease course.
- > When considering a diagnosis of HPS it is useful to assess for orthodeoxia.

It is important for physicians to re-evaluate a patient's diagnosis when the clinical picture does not adequately correlate with the patient's symptoms and signs. ■

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