

November 2015 Critical Care Case of the Month

Samir Sultan, DO

Banner University Medical Center Phoenix
Phoenix, AZ

History of Present Illness

A 39-year-old Caucasian woman was admitted to the ICU with worsening dyspnea and increasing oxygen requirements. Her lips turned blue with minimal activity. She was admitted to another hospital 5 months earlier with pneumonia. At discharge she was placed on oxygen. At follow-up with her pulmonologist, she was diagnosed with sleep apnea.

Past Medical History, Family History, Social History

- She has a history of an optic glioma at age 7 with resection followed by radiation therapy and development of panhypopituitarism.
- Liver cirrhosis diagnosed in 2014 with presentation of hematemesis.
- Type 2 diabetes mellitus
- Denies tobacco, ethanol, or illicit drug use.
- There is a family history of diabetes and liver cirrhosis

Physical Examination

- Vital signs: 110 / 86, HR 97, RR 16, 88% on 6 liter O₂
- General: obese female (BMI 35) in no apparent distress
- Chest: Clear to auscultation bilaterally
- Cardiovascular: regular rate without murmur or rub
- The remainder of the physical exam was normal

Radiography

A chest x-ray was interpreted as normal.

Laboratory

- CBC: hemoglobin 13.8 gm/dL, WBC 7 X 10³ cells/microliter with a normal differential
- Basic metabolic panel: Na⁺ 132 mEq/L, K⁺ 4 mEq/L, Cl⁻ 100 mEq/L, HCO₃⁻ 22 mEq/L, glucose 150 mg/dL.
- Arterial blood gases (ABGs): PaO₂ 35 mm Hg, PaCO₂ 37 mm Hg, pH 7.43

Which of the following is/are **not** possible cause(s) of hypoxemia **in this patient?**

1. Decreased diffusion (alveolar capillary block)
2. Ventilation-perfusion mismatch
3. Hypoventilation
4. 1 and 3
5. All of the above

Correct!
3. Hypoventilation

There are multiple causes of hypoxemia (Table 1).

Table 1. Causes of hypoxemia.

- Ventilation-perfusion mismatch (vascular anomaly or obstruction, alveolar filling anomalies)
- Right to left shunting (congenital heart, pulmonary arteriovenous malformations, lobar lung collapse)
- Hypoventilation (drugs, neuromuscular, myopathic, obesity, chronic lung disease)
- Decreased diffusion (interstitial lung disease, pulmonary hypertension)
- Low FiO_2 (higher altitudes)
- Low mixed venous O_2 (shock)

Of these ventilation-perfusion mismatch, where blood flows to poorly ventilated areas in the lung, is the most common. Some debate the existence of decreased diffusion at least in interstitial lung disease. Hypoventilation is incorrect because the alveolar-arterial gradient (A-a gradient) is not normal as indicated by hypoxemia with a normal of low pCO_2 .

The patient was placed on 100% oxygen and the ABGs were repeated. There was minimal change.

Based on this observation, which of the following is the **most likely cause** of the patient's hypoxemia?

1. Low FiO_2
2. Right to left shunting
3. Shock
4. Ventilation-perfusion mismatch
5. None of the above

Correct!

2. Right to left shunting

Although not 100% diagnostic, inhalation of 100% oxygen raises the PaO₂ minimally in right to left shunting because the venous blood shunted to the arterial circulation is not or only modestly oxygenated.

Shunt fraction is calculated by the following formula:

$$Q_s/Q_t = (C_cO_2 - C_aO_2) / (C_cO_2 - C_vO_2)$$

Where

- Q_s=blood flow through the shunt
- Q_t=total cardiac output
- C_cO₂=pulmonary end-capillary O₂ content. Generally held to be the same as the alveolar O₂ content
- C_aO₂=arterial oxygen content
- C_vO₂=mixed venous O₂ content
- v=venous

Normally there is 4-10% shunt due to Thebesian and bronchial veins which drain deoxygenated blood into the arterial circulation.

Which of the following would be the **next most appropriate step** in the patient's evaluation?

1. Chest CT scan
2. Complete pulmonary function testing
3. Echocardiogram
4. Pulmonary angiogram
5. Ventilation-perfusion lung scan

Correct!
3. Echocardiogram

None are totally incorrect. However, of the choices listed an echocardiogram is probably most appropriate because of the frequency of congenital heart disease as a cause of a right to left shunt. The patient's transesophageal echocardiogram (TEE) showed normal right ventricular size and function, a tricuspid valve with mild tricuspid regurgitation. no mitral regurgitation, normal left ventricular function and size with normal systolic function and an ejection fraction of 60-65% and an interatrial septum intact with no obvious defect demonstrated on color flow doppler.

Based on the patient's overall clinical picture which of the following is the **most likely diagnosis?**

1. Hepatopulmonary syndrome
2. Interventricular septal defect
3. Patent ductus arteriosus
4. Pulmonary arteriovenous malformation
5. Recurrent pulmonary emboli

Correct!

1. Hepatopulmonary syndrome

Given the patient's history of cirrhosis with an apparent non-cardiac right to left shunt, hepatopulmonary syndrome is the most likely cause of her hypoxemia. A ventilation-perfusion scan and a pulmonary angiogram were performed and showed only early detection of tracer or dye in the arterial circulation. An attempt to balloon occlude the pulmonary lobar branches showed no improvement in oxygenation.

Although first described by Fluckiger in 1884, the term hepatopulmonary syndrome (HPS) was coined by Kennedy and Knudson (2) while at the University of Arizona in Tucson. They observed a syndrome characterized by hypoxemia aggravated by exercise, orthodeoxia (fall in arterial blood oxygen on assuming the upright posture), hypocapnia, and evidence of hyperdynamic circulation, but otherwise normal indices of pulmonary air flow, volume, and distribution of ventilation as an infrequent complication of hepatic cirrhosis. An illustrative case was described, supporting the presence of a shunt or shunt-like mechanism consisting of low-resistance vascular communications within the lung. Although the cause of HPS is not entirely clear it may be a pulmonary manifestation of spider angiomas. There is also evidence of excessive NO production which may result in excessive pulmonary artery vasodilatation (3).

Which of the following have been proposed as **treatments for hepatopulmonary syndrome?**

1. Garlic
2. Liver transplantation
3. Methylene blue
4. 1 and 3
5. All of the above

Correct!
5. All of the above

Liver transplantation is the only well-recognized treatment for HPS. The degree of arterial hypoxemia appears to influence survival after liver transplantation. Swanson and colleagues (4) at the Mayo Clinic demonstrated in a case-control study involving 61 HPS patients that long-term survival for HPS patients is worse in the subgroup with lower baseline PaO₂ (50 mmHg). Since not all patients are appropriate for immediate liver transplantation, interest has surfaced for other therapies. Both methylene blue and garlic have been proposed (5,6).

Our patient was begun on garlic 500 mg twice a day while being evaluated for liver transplantation. Her PaO₂ improved marginally to 47 mm Hg.

References

1. Montgomery H, Zinsser HF, Howwitz O. Oxygen tension of tissues by the polarographic method. II Detection of right to left shunts by changes in skin oxygen tension resulting from inhalation of oxygen. *Circulation*. 1950;2(6):845-9. [\[PubMed\]](#)
2. Kennedy TC, Knudson RJ. Exercise-aggravated hypoxemia and orthodeoxia in cirrhosis. *Chest*. 1977;72(3):305-9. [\[PubMed\]](#)
3. Grace JA, Angus PW. Hepatopulmonary syndrome: update on recent advances in pathophysiology, investigation, and treatment. *J Gastroenterol Hepatol*. 2013;28(2):213-9. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Swanson KL, Wiesner RH, Krowka MJ. Natural history of hepatopulmonary syndrome: Impact of liver transplantation. *Hepatology*. 2005;41(5):1122-9. [\[CrossRef\]](#) [\[PubMed\]](#)
5. Schenk P, Madl C, Rezaie-Majd S, Lehr S, Müller C. Methylene blue improves the hepatopulmonary syndrome. *Ann Intern Med*. 2000;133(9):701-6. [\[CrossRef\]](#) [\[PubMed\]](#)
6. De BK, Dutta D, Pal SK, Gangopadhyay S, Das Baksi S, Pani A. The role of garlic in hepatopulmonary syndrome: a randomized controlled trial. *Can J Gastroenterol*. 2010;24(3):183-8. [\[PubMed\]](#)