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CASE REPORT

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Hepatopulmonary Syndrome: Clinical Case and Literature Review

Síndrome hepatopulmonar: Caso clínico y revisión de la literatura

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ABSTRACT

Hepatopulmonary syndrome is a pulmonary vascular disease that presents with hypoxemia caused by liver disease (usually cirrhosis with portal hypertension), which mainly affects middle-aged adults, although it has also been observed in children, with no significant difference between sexes. The prevalence varies widely (4-44%) depending on diagnostic criteria and population under study, being approximately 15% in patients with cirrhosis, and depending on the criteria used to define hypoxemia and/or the PA-aO (alveolar-arterial oxygen) gradient.
Two case reports are presented with different initial presentation and without a history of liver disease as diagnostic challenge.

Key words: Hepatopulmonary syndrome; Portal hypertension; Hypoxemia

RESUMEN

El síndrome hepatopulmonar es una enfermedad vascular pulmonar que cursa con hipoxemia causada por una enfermedad hepática (usualmente cirrosis con hipertensión portal), que afecta principalmente a adultos de mediana edad, aunque también se ha observado en niños, sin diferencia significativa entre sexos. La prevalencia varía ampliamente (4 %-44 %) según los criterios de diagnóstico y población estudiada; siendo de aproximadamente el 15 % en pacientes con cirrosis, de acuerdo con los criterios utilizados para definir la hipoxemia o el gradiente PA-aO.
Se tratan dos casos clínicos con distinta presentación inicial sin antecedentes de enfermedad hepática como desafío diagnóstico.

Palabras clave: Síndrome hepatopulmonar; Hipertensión portal; Hipoxemia

CASE REPORT 1

41-year-old woman from Peru, non-smoker, with a history of rheumatoid arthritis diagnosed in 2015 (she was previously treated with methotrexate but discontinued the medication and stopped her follow-ups). She presents with clinical symptoms lasting for 6 months, characterized by asthenia, adynamia, and dyspnea classified as mMRC II. She was admitted requiring low-flow supplemental oxygen. The following complementary studies were performed: acid-base status: pH 7.39, pCO_2: 40 mmHg, pO_2: 64 mmHg, HCO_3 25 mEq/L, oxygen saturation (SaO_2): 92%, alveolar-arterial gradient: 31.98 mmHg (elevated), chest CT scan: no evidence of pulmonary infiltrates, abdominal CT scan: evidence of splenomegaly. A Doppler ultrasound of the portal system was performed, revealing portal hypertension (a permeable portal vein with a diameter of 13 mm and hepatopetal flow with a velocity of 15 cm/s). Given the suspicion of hepatopulmonary syndrome, a Doppler echocardiogram was requested, which showed the pre-

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sence of bubble passage starting at the fourth heartbeat, confirming the diagnosis.

CASE REPORT 2

62-year-old woman from Buenos Aires, non-smoker, administrative worker, with a medical history of hypothyroidism and vitiligo. She presents with clinical symptoms lasting for 2 months, characterized by dyspnea classified as mMRC II associated with dry cough. She was admitted requiring low-flow supplemental oxygen and displayed platypnea and orthodeoxia. In this context, laboratory tests were performed, including liver function tests showing a cytolytic pattern, and arterial blood gas analysis with the following results: pH: 7.50, pCO_2: 28 mmHg, pO_2: 52 mmHg, HCO_3: 22 mEq/L, oxygen saturation: 90%, A-a gradient: 62.7 mmHg (elevated). As part of further investigation, an abdominal ultrasound was conducted, diagnosing portal hypertension (with findings of a permeable portal vein measuring 14 mm in diameter and hepatopetal flow at a velocity of 17 cm/s). Given the high suspicion of hepatopulmonary syndrome, an echocardiogram was performed, which revealed bubble passage starting at the fifth heartbeat, confirming the diagnosis.

DISCUSSION

Pulmonary shunting represents the extreme of the V/Q (ventilation/perfusion) mismatch, where venous blood perfuses non-ventilated areas of the lung, resulting in a venous admixture that depletes arterial oxygen content. This leads to hypoxemia, hypocapnia, and an increase in the alveolar-arterial oxygen gradient ($A\text{-}aO_2$).[1]

The hepatopulmonary syndrome (HPS) is a pulmonary vascular disease associated with hypoxemia caused by liver disease (usually cirrhosis with portal hypertension), characterized by the proliferation and dilation of pulmonary capillaries. In severe cases, intrapulmonary arteriovenous fistulas may form, further disrupting gas exchange.

Significant dilation of capillaries and precapillaries, up to 100 μm in diameter is observed, contributing to V/Q mismatch, diffusion limitation, and anatomical shunts that result in hypoxemia. In experimental studies of HPS, mediators such as TNF-α, nitric oxide, endothelin-1, and vascular endothelial growth factor generated by intravascular monocytes induce microvascular alterations.[2]

This syndrome primarily affects middle-aged adults, although it has also been observed in children, with no significant difference between sexes. The prevalence varies widely (4-44%) depending on diagnostic criteria and population under study, being approximately 15% in patients with cirrhosis, depending on the criteria used to define hypoxemia and/or the PA-aO (alveolar-arterial oxygen) gradient.[3]

Patients with HPS typically present with platypnea, defined as difficulty breathing that worsens in the upright position (standing or sitting) and improves when lying down, associated with portal hypertension. Additionally, patients may present with orthodeoxia: a ≥5% drop in PaO^2 when moving from the supine to upright position, reflecting a ventilation-perfusion mismatch.[4]

The diagnosis of HPS is based on three pillars: confirmation of liver disease, with or without portal hypertension; presence of oxygenation abnormalities; and a positive echocardiogram with passage of bubbles after the third heartbeat.[5] In the echocardiogram with passage of bubbles using agitated saline, microbubbles larger than 10 μm in diameter are observed. These microbubbles normally do not pass through the pulmonary capillary bed. The delayed detection of microbubbles injected intravenously into the left side of the heart, occurring 3 or more cardiac cycles after visualization in the right side of the heart indicates abnormal vascular dilation in the intrapulmonary capillary bed.

A chest X-ray may reveal bibasal nodular or reticulonodular opacities, although most patients show normal findings. Pulmonary function tests frequently demonstrate a decreased diffusing capacity of the lungs for carbon monoxide (DLCO).

The severity of the HPS is classified based on hypoxemia: mild ($PaO^2 \geq 80$ mmHg), moderate (PaO^2 = 60-79 mmHg), severe (PaO_2 = 50-59 mmHg), and very severe ($PaO^2 < 50$ mmHg).[2]

The presence of HPS significantly worsens the prognosis and quality of life for affected patients. Those with HPS have double the risk of death compared to patients with similarly severe cirrhosis but without HPS.[6]

Treatment for HPS is supportive. Supplemental oxygen is recommended to maintain oxygen saturations above 88%.

The definitive treatment for HPS is liver transplantation, which can reverse pulmonary vascular dilations and improve survival, showing 5-year post-liver transplant survival rates of 76–87%.[3]

In conclusion, two case reports highlight the lack of a direct correlation between the development of hepatopulmonary syndrome and the severity of the cirrhosis, underscoring the importance of maintaining a high index of clinical suspicion

in patients with dyspnea and liver disease. The echocardiogram with passage of bubbles emerges as the most accessible and sensitive modality for detecting intrapulmonary shunting, providing crucial diagnostic confirmation.

Conflict of interest

Authors have no conflicts of interest to declare.

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