Clinical note

Platypnea-orthodeoxia syndrome: Importance of patient position for correct diagnosis at the time of $^{99m}$Tc-MAA injection

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A B S T R A C T

A 65-year-old male presented with unexplained hypoxia that became exacerbated by an upright posture (platypnea-orthodeoxia syndrome) secondary to hepatopulmonary syndrome (HPS). A $^{99m}$Tc-macroaggregated albumin pulmonary perfusion scan revealed a right to left shunt of 29% in the sitting position, which had not been previously detected when the radiotracer injection was performed with the patient in supine position, nor was it diagnosed using another non-invasive imaging method (transthoracic contrast echocardiography and angio-CT). A transeosophageal echocardiography was contraindicated due to the presence of esophageal varices. The administration of the radiopharmaceutical in sitting position for the study of the pulmonary perfusion allowed us to confirm the presence of the shunt and consider the patient a candidate for liver transplantation.

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Síndrome platipnea-ortodeoxia: importancia de la posición del paciente en el momento de la inyección de $^{99m}$Tc-MAA para un correcto diagnóstico

R E S U M E N

Varón de 65 años de edad que presentó hipoxia sin explicación que se exacerbaba en sedestación (síndrome platipnea-ortodeoxia) secundaria a un síndrome hepatopulmonar (SHP). Una gammagrafía de perfusión pulmonar con macroagregados de albúmina $^{99m}$Tc- reveló un cortocircuito derecha a izquierda, de 29% en la posición sentada que no se había detectado previamente cuando la inyección del radiotrazador se realizó con el paciente en posición supina, ni fue diagnosticado por otros métodos de imagen no invasivo (ecocardiografía transtorácica de contraste y angio-CT). Una ecocardiografía transesofágica estaba contraindicada debido a la presencia de varices esofágicas. La administración del radiotrazador en sedestación nos permitió confirmar la presencia del cortocircuito y considerar al paciente candidato para trasplante hepático.

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Introduction

Platypnea-orthodeoxia syndrome (POS) is characterized by dyspnea and hypoxemia in an upright posture that improves in supine, being hepatopulmonary syndrome (HPS) one of the most frequent causes. HPS is characterized by the presence of liver disease, with or without portal hypertension, associated with intrapulmonary vasodilation and abnormal arterial oxygenation.1

We report the case of a patient with chronic cirrhosis of enditic etiology with severe portal hypertension and little hepatocellular involvement that showed a clinically severe syndrome of platypnea-orthodeoxia secondary to HPS, in which lung perfusion scan with $^{99m}$Tc-macroaggregated albumin ($^{99m}$Tc-MAA) performed by injecting the radiotracer in sitting position was key to detect the existence of a right-left shunt, which had not been previously detected when the radiotracer injection was performed with the patient in supine position.

Case report

We report the case of a 65-year-old male with a medical history of endotic cirrhosis with esophageal varices (Child–Pugh A6), without episodes of decompensation or any other relevant history. He came to the hospital for an episode of hemoptysis and tachypnea, confirming severe hypoxemia with pO2 of 45.1 mmHg, pH 7.43, pCO2 45 mmHg and an oxygen saturation of 82% (alveolar–arterial gradient 48.3 mmHg). Suspecting a pulmonary embolism, angio-CT was performed showing no filling defects in the pulmonary arteries, or other findings that could explain the patient’s clinical status. One week after admission, there was a spontaneous remission of
hemoptysis. Incidentally we noticed a platypnea-orthodeoxia syndrome with hypoxemia by raising the patient’s head of the bed, lowering his O₂ saturations down to 65% in this case and increasing them to 92% in supine position. Suspecting HPS was responsible for the problem we performed transthoracic echocardiography with bubble-agitated serum, but right-left shunt was not diagnosed. Transeophageal echocardiography was not performed by the presence of esophageal varices.

Looking at the results obtained, a perfusion lung scan was performed with 5 mCi (185MBq) ⁹⁹mTc-MAA (according to standard protocol radiotracer injection with the patient in supine position), demonstrating no extrapulmonary uptake (% shunt <6%, within a range of physiological shunt) (Fig. 1A).

Excluding other causes of POS and persisting suspicion of HPS a pulmonary perfusion study was repeated with ⁹⁹mTc-MAA, but this time doing the radiotracer injection with the patient seated, confirming extrapulmonary activity at brain and kidney uptake with a percentage of 29%. These findings are consistent with a pathological right-left shunt (Fig. 1B).

We can not only demonstrate the presence of shunt image, but also perform the quantification of extrapulmonary activity by determining areas of interest by this formula:

\[
\% \text{Shunt} = \left( \frac{\text{Total body count} - \text{Total lung count}}{\text{Total body count}} \right) \times 100
\]

As these results confirm the suspected diagnosis, liver transplantation was considered as the ideal treatment for the patient and he was included on the waiting list.

Discussion

It is common that lung function is impaired in patients with advanced liver disease. There are several mechanisms that produce alterations in gas exchange, among which are: ventilation-perfusion imbalance, intrapulmonary vasodilation, pulmonary vaso-occlusive disease and intrapulmonary vasodilatation.

Hepatopulmonary syndrome is characterized by liver disease, pulmonary vasodilation and oxygenation deficiency. The vascular component abnormalities include dilated pulmonary capillaries and less commonly lung and pleural arteriovenous communications. Vasodilation can result in capillary diameters greater than 100 µm producing a direct transit of erythrocytes comprising venous blood from the pulmonary artery to the systemic circulation, thus failing in its oxygenation.

It is believed that the vasodilatation present in the HPS is the result of increased production of vasodilators, being nitric oxide (NO) the most involved. It has been observed that exhaled levels of NO increase in patients with HPS and that these are normalized after transplantation. It is still uncertain the exact mechanisms of increased endogenous NO production and its relationship with the presence of portal hypertension and the degree of liver injury.

The clinical of HPS include symptoms and signs associated with chronic liver disease and respiratory complications. The most common symptom found is dyspnea although this is non-specific. Other findings would be spider veins, cyanosis, clubbing and orthodeoxia platypnea. Both platypnea – defined as the worsening of dyspnea when the patient moves from the supine to standing position – and orthodeoxia – understood as the exacerbation of hypoxemia in standing position – are the result of increased blood flow by gravity into the dilated vessels of the lung bases.

Orthodeoxia has a relatively low sensitivity for HPS although it increases in severe cases. In cirrhotic patients it is highly specific for HPS but it has been observed in a variety of processes (Table 1).

In our case it was a cirrhotic patient with O₂ saturation decreased to 65% in a sitting position, with an increase of up to 95% in the supine position, so we suspected HPS.

Measuring pressure at different levels of pO₂ in the cardiopulmonary system we would get confirmation and locations of the

Table 1

Causes of platypnea-orthodeoxia syndrome.

<table>
<thead>
<tr>
<th>Cardiac disease</th>
<th>Associated with atrial septal defect (ASD)</th>
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<tr>
<td></td>
<td>- Interatrial septum aneurisma</td>
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<tr>
<td></td>
<td>- Severe hypoxia</td>
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<td></td>
<td>- Atrial myxoma</td>
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<td></td>
<td>- Aneurysms of the ascending aorta</td>
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<td>- After to pneumonectomy</td>
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<td>Pulmonary disease</td>
<td>- Constrictive pericarditis/pericardial effusion</td>
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<tr>
<td></td>
<td>- Hepatopulmonary syndrome (HPS):</td>
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<tr>
<td></td>
<td>- Liver cirrhosis</td>
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<td></td>
<td>- Portal hypertension non cirrhosis</td>
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<td></td>
<td>- Fulminant hepatitis</td>
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<td></td>
<td>- Rejection after liver transplantation</td>
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<tr>
<td></td>
<td>- Pulmonary arteriovenous malformations</td>
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<tr>
<td></td>
<td>- Parenchymal lung diseases</td>
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<td></td>
<td>- Pulmonary emphysema</td>
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<td></td>
<td>- Interstitial lung disease (ILD)</td>
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<td></td>
<td>- Respiratory distress syndrome</td>
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<td></td>
<td>- Obstructive</td>
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<tr>
<td></td>
<td>- Larynx cancer</td>
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<tr>
<td></td>
<td>- Lung cancer</td>
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</tbody>
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[Modified from Lopez Gaston O D. Platypnea-orthodeoxia syndrome].
shunt, but at the cost of invasive procedures. Therefore, it was very important to be able to diagnose the shunt using non-invasive imaging methods.\(^5\)

Two non-invasive methods, contrast echocardiography and lung perfusion scan are used to diagnose HPS.\(^6\)

The contrast transesophageal echocardiography is the method of election and can detect shunts under 4%.\(^7\) In normal conditions, the bubbles (air and serum injected in a peripheral vein) are trapped in the lung, so their visualization in the left atrium (LA) give the diagnosis of shunt, while the time of arrival (number of heartbeats) from the right atrium (RA) tells whether it is from the heart or the lung.\(^8\) In our patient it was contraindicated to do a transesophageal echocardiography due to the presence of esophageal varices. We performed transthoracic echocardiographies in supine and standing position. The presence of shunt was not detected.

Then, a lung perfusion scintigraphy with \(^99\)mTc-MAA was performed by injecting the radiotracer in supine position. Peripheral vein injection of albumin macroaggregated labeled with \(^99\)mTc (\(^99\)mTc-MAA), leads to their entrapment in the pulmonary vascular bed (arterioles and capillaries) with peripheral distribution proportional to the regional pulmonary blood flow. This makes it possible to obtain imaging that reflects pulmonary perfusion. The average arteriolar diameter is between 20 and 25 \(\mu\)m while the capillary is 8 \(\mu\)m therefore the diameter of the macroaggregated should fall between 10 and 40 \(\mu\)m to achieve a homogeneous distribution.\(^9\) The test poses an acceptable level of risk, since particles are biodegradable and the blocking is transitory. Under normal conditions, approximately 90% of the particles are retained in the vascular bed in the 5 min following injection, progressively being released after fragmentation and being trapped by the reticuloendothelial system. There should be a limitation on the maximum number of injected particles: the number of arterioles in the lungs of a healthy adult falls between 200 and 300 million. Thus, the administration for diagnostic purposes of 300,000 macroaggregated particles with a similar size to its diameter obstructs one in every thousand arterioles, this being within safe ranges.

If suspicion exists of right-left shunt, a situation in which the capillaries have diameters greater than 100 \(\mu\)m, the administration should consist of the lowest numbers of particles that can produce an acceptable image (not more than 150,000) since the particles may reach the systemic circulation and embolize in organs such as the kidney and brain.\(^8\)

Usually the administration of \(^99\)mTc-MAA is performed with the patient in supine position to minimize the apico-caudal gradient and obtain a perfusion image with a homogeneous distribution of the radiotracer. The image should be obtained before the first minute of injection and not after 5–10 min, so as not to increase the physiological shunt. Perfusion lung scan with \(^99\)mTc-MAA establishes the diagnosis of shunt if the radiotracer shows distribution in extrapulmonary organs such as the kidney, brain or spleen.\(^1\)

In our patient, the study with the radiotracer injection in supine position detected no activity in the systemic territory, presenting a shunt quantification in the upper limits of normality (5.8%).

Following a clinical suspicion of HPS without imaging confirmation, and taking into account that the vascular dilations occur more frequently in the basal lung segments, we decided to administer the radiotracer (\(^99\)mTc-MAA) with the patient seated, with the aim of increasing the apico-caudal gradient. Once the study was performed under these conditions, we could identify radiotracer activity in systemic territories (kidney and brain) obtaining a shunt quantification value of 29%, all of which established the diagnosis of right-left shunt.

The most important point to note from our case is that the administration of the radiopharmaceutical in sitting position for the study of the pulmonary perfusion allowed us to confirm the presence of the shunt (which had not been shown by other diagnostic methods) and to be able to consider the patient a candidate for liver transplantation, that is de only causal therapy.\(^5\)

References