An unusual case of cyanosis

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Abstract:
Hepatopulmonary syndrome is a recognised complication of cirrhosis. However there are only few reports of this condition in patients with Non Cirrhotic Portal Fibrosis (NCPF) and Extra-Hepatic Portal Vein Obstruction (EHPVO). Here we present a 34 year old female with biopsy proven Non Cirrhotic portal fibrosis (NCPF) who presented with cyanosis and shortness of breath. She was thoroughly evaluated for all cardiac and pulmonary causes for her symptoms and was finally diagnosed to have Hepatopulmonary syndrome.

Keyword: Hepatopulmonary syndrome, Non Cirrhotic Portal Fibrosis, Orthodeoxia

Case report:
Introduction:
Hepatopulmonary syndrome is characterized by hypoxemia and intrapulmonary vascular dilatations. This syndrome most commonly occurs in cirrhosis patients and is found to affect as many as 15-20% of patients with cirrhosis. Intrapulmonary vascular dilations can be detected through contrast Echocardiography or by lung perfusion scanning with technetium-99m microaggregated albumin ($^{99m}$Tc-MAA). We present a case of Non cirrhotic portal fibrosis complicated by Hepatopulmonary syndrome.

Case history: A 34 year old female presented with complaints of shortness of breath and bluish discolouration of her lips, tongue and finger tips of two months duration. She did not have orthopnea. On the contrary she felt more comfortable lying down.

Pan digital clubbing Cyanosis
An Initiative of The Tamil Nadu Dr. M.G.R. Medical University
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Table 1 ABG analysis

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<thead>
<tr>
<th></th>
<th>Supine</th>
<th>Standing</th>
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<tr>
<td>PO2</td>
<td>54.2 mmHg</td>
<td>43.9 mmHg</td>
</tr>
<tr>
<td>pH</td>
<td>7.440</td>
<td>7.426</td>
</tr>
<tr>
<td>PCO2</td>
<td>12.7 mmHg</td>
<td>15.0 mmHg</td>
</tr>
<tr>
<td>HCO3</td>
<td>13.1 mEq/l</td>
<td>12.2 mEq/l</td>
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She was a known case of Non Cirrhotic Portal Fibrosis (NCPF), diagnosed 16 years back. She had recurrent episodes of variceal upper gastro-intestinal bleed, for which banding was done repeatedly. She underwent splenectomy 5 years back and was vaccinated against capsulated organisms. Over the past three years, she developed two episodes of Extra-pulmonary tuberculosis, for which Anti-Tuberculous Therapy (ATT) was given.

Baseline investigations were normal. An ultrasonogram of the abdomen confirmed the previous diagnosis. Liver function tests were normal. A recent liver biopsy report of the patient showed periportal fibrosis and ductular proliferation with preserved lobular architecture, suggestive of NCPF. An Echocardiogram and a CT chest were ordered to seek cardiac and pulmonary causes of dyspnoea and cyanosis. Both the reports were normal. Pulse oximetry in room air showed significant hypoxemia (SPO2 90%), with significant difference between lying and erect posture (>10%). An arterial blood gas analysis was performed with the patient in lying and standing posture. The results are shown in Table 1. Contrast Echocardiogram was performed suspecting hepatopulmonary syndrome. There was significant crossover of contrast material after five cardiac cycles, which was suggestive of intra-pulmonary shunting.

CT pulmonary angiogram was done to detect any treatable pulmonary AV malformation as the cause for her symptoms. However the report was normal suggesting that there were no significant pulmonary AV fistulas. MR angiogram was done, which showed significant crossover of contrast from the pulmonary arteries into the veins especially in the lower lobes (right > left).
Final diagnosis of Hepatopulmonary syndrome, secondary to Non cirrhotic portal fibrosis was made and the patient has been enrolled in the liver transplant list of our gastroenterology department.

**Discussion** Pulmonary complications of cirrhosis include Hepatopulmonary Syndrome (HPS) and Portopulmonary Hypertension (PPH). It is estimated that around one third of the patients evaluated for liver transplant have pulmonary complications. There are only few reports linking hepatopulmonary syndrome with Non Cirrhotic Portal Fibrosis and normal liver function. HPS is also reported to occur in patients with ischemic hepatitis, post hepatic portal hypertension and chronic hepatitis without cirrhosis. A syndrome similar to HPS has been described in children with congenital abnormalities that divert hepatic blood from the pulmonary circulation. Recent experimental and clinical data has shown that Nitric oxide plays a key role in the pathogenesis of Hepatopulmonary syndrome. Microscopic examination shows dilated intrapulmonary arterioles and capillaries and dilated vascular channels between pulmonary arteries and veins. The dilated intrapulmonary capillaries results in ineffective oxygenation of RBCs in the centre of the capillary while breathing in room air. These dilated capillaries thereby produce a functional right to left shunt. These dilatations are particularly common in the lower lobes. The clinical features are progressive shortness of breath, cyanosis, clubbing, cutaneous telangiectasias, spider naevi. Orthodeoxia is a characteristic finding in HPS. In upright posture the lower lobes get maximum blood flow which results in hypoxemia, as most of the intra-pulmonary capillary dilatations are located in the lower lobes. Hypoxemia is a prerequisite for the diagnosis of hepatopulmonary syndrome. Every diagnostic approach should begin with the documentation of hypoxemia at rest by means of arterial blood gas analysis. An arterial partial pressure of oxygen lower than 8.65 kPa (65mmHg) is a good cut off to show a decreased value.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Diagnostic criteria for Hepatopulmonary syndrome[1]</th>
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<tbody>
<tr>
<td>Oxygenation defect</td>
<td>Partial pressure of oxygen &lt; 8.65 kPa or abnormally arterial oxygen gradient = 15 while breathing room air</td>
</tr>
<tr>
<td>Pulmonary vascular disease</td>
<td>Positive findings on contrast-enhanced echocardiography or abnormal uptake in the brain (&gt;5%) with radioactive lung perfusion scanning. PORTAL HYPERTENSION (most common) with or without cirrhosis</td>
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<td>Liver disease</td>
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**Diagnositic criteria**

Contrast Echocardiography is the most sensitive method to diagnose HPS. The appearance of contrast material in the left atrium, within three to six cardiac cycles of its appearance in right atrium, is highly suggestive of intrapulmonary shunting. When the materials appear before three cycles, it denotes intracardiac shunting. An alternative to contrast echocardiography is scintigraphic perfusion scanning with technetium-99m microaggregated albumin (99mTc–MAA).
Normally the macroaggregates that exceed 20µm in diameter are almost completely trapped in the pulmonary circulation. In the presence of a cardiac right-to-left shunt or intrapulmonary vascular dilatation the uptake of 99mTc macroaggregated albumin can be documented in other organs such as the brain or the spleen. Pulmonary angiography is not a standard diagnostic tool in HPS. It may be used to demonstrate large pulmonary AV shunts. Very limited options are available for treatment of patients with hepatopulmonary syndrome. Currently there is no established medical therapy for the treatment of HPS. Few case reports have shown that some drugs may improve oxygenation. In one small study garlic preparation was able to reduce the oxygen desaturation. Other agents which have been tried are pentoxifylline, aspirin, N-acetyl cysteine, glucocorticoids, norfloxacin, Somatostatin and almitrine. However none of them are of significant benefit. Oxygen supplementation has been employed in those with severe disease; however there is no long term clinical study to determine its efficacy. Most patients on oxygen therapy report some improvement in their symptoms. TIPS (Trans-Jugular Intra-hepatic Porto-systemic Shunt) have been used in HPS to reduce portal pressure in some case reports. Some have employed pulmonary angiography with embolization of intrapulmonary shunts. Both these invasive techniques should be studied further before being recommended. Liver transplant is the only definitive treatment shown to reverse HPS in as many as 80% of the patients. Patients with severe HPS (PaO2<60mmHg) are prioritized for liver transplant giving exception points to MELD scoring. Those with severe HPS may have increased post operative mortality compared to those without HPS.

References: