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CASE FOR DIAGNOSIS

Dyspnoea and cyanosis in a cirrhotic patient

G. Stratakos*, K. Malagari#, E. Broutzos#, E. Zakynthinos*, C. Roussos*, S. Papiris*

Case history

A 48-yr-old male presented with cyanosis and dyspnoea at minimal exertion. Over the last year he had been complaining of progressively increasing exertional dyspnoea, and during this time was hospitalized twice for pneumonia. His medical problems started 5 yrs ago when after an episode of haematemesis, cryptogenic hepatic cirrhosis with portal hypertension was diagnosed. He subsequently underwent successful sclerotherapy for oesophageal varices. He had a 30 pack-yr smoking history and worked as a technician of electronic devices. One of his sisters has been diagnosed and treated for idiopathic pulmonary fibrosis.

On admission he was cyanotic and complained of nonproductive cough. His temperature was 37°C, pulse rate 98·min^{-1}, respiratory rate was 30·min^{-1} and his blood pressure 160/90 mmHg. Physical examination revealed finger clubbing and two spider nevi on his thorax but absence of ascitic fluid, pleural effusions, peripheral oedemas or lymph node enlargements. The liver was not palpable, but the spleen showed marked enlargement. The chest was clear to auscultation. A 2/6 systolic murmur was heard at the pulmonary artery focus.

Blood analysis showed reduction of both white cells ($3300\times10^6\cdot L^{-1}$) and platelets ($27000\times10^6\cdot L^{-1}$). Blood chemistry was within normal range except for the international normalized ratio (INR) (1. 7) and serum bilirubin (total 63.3 M, indirect 41 M).

Arterial blood gases analysis (while breathing room air) indicated marked hypoxaemia (arterial oyxgen tension (P_{a,O_2}): 4.3 kPa, arterial carbon dioxide tension (P_{a,CO_2}): 3.7 kPa, pH: 7.46, bicarbonate: 20.2 mM). Supplemental 100% oxygen was administered without significant response. Arterial blood gases while breathing 100% oxygen proved to worsen at upright position while improving at supine position (P_{a,O_2}: 4.7 kPa, P_{a,CO_2}: 3.8 kPa, pH: 7.46 *versus* P_{a,O_2}: 7.2 kPa, P_{a,CO_2}: 3.8 kPa, pH: 7.46). The observed "orthodeoxia" was compatible with the clinical improvement noted during supine position (platypnoea).

The chest radiographs (fig. 1a and 1b), computed tomography (CT) of the chest (fig. 2) and the ^{99}Tc albumin macroaggregate body scan (fig. 3), were as shown.

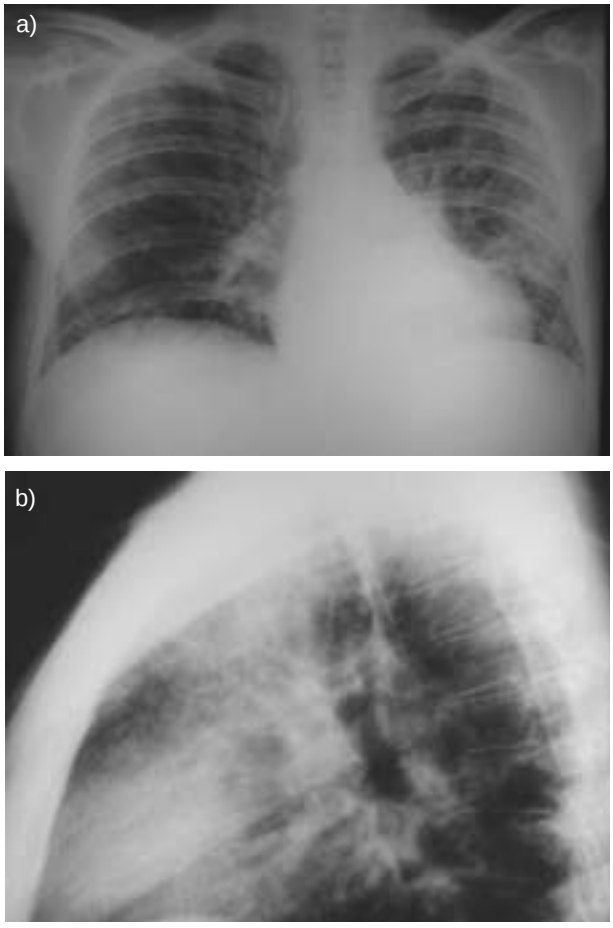

Fig. 1.–Chest radiography a) posteroanterior and b) lateral view.

*Dept of Critical Care and Pulmonary Services, National and Capodistrial University of Athens, Evangelismos Hospital and #2nd Dept of Radiology, National and Capodistrial University of Athens, Eugenidion Hospital, Athens, Greece.

Correspondence: G. Stratakos, Evangelismos General Hospital, Pulmonary and Critical Care Dept, 45–47 Ipsilandou Str, 106 75 Athens, Greece. Fax: 30 0107244941. E-mail: grstrat@otenet.gr

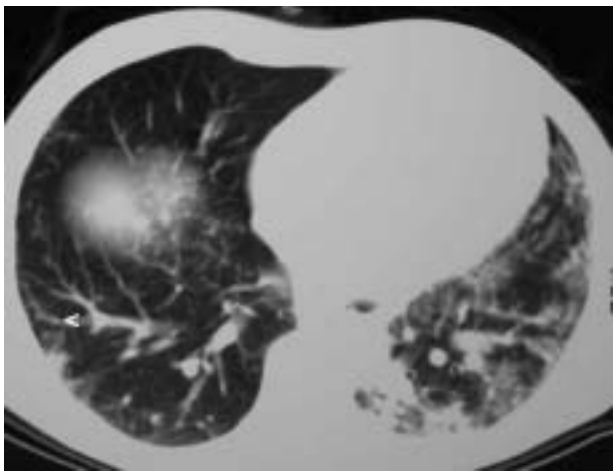

Fig. 2. – Computed tomography of the chest.

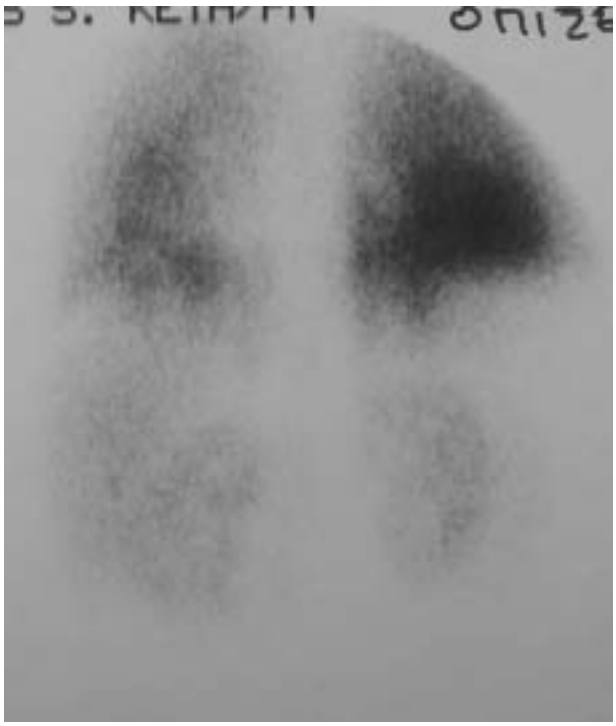

Fig. 3. – ^{99}Tc albumin macroaggregate lung scan (posterior view).

BEFORE TURNING THE PAGE, WRITE DOWN YOUR INTERPRETATION OF THE FIGURES, YOUR DIAGNOSIS, ALTERNATIVE DIAGNOSES AND SUGGESTED TREATMENT.

Interpretation

Chest radiography

Posteroanterior view (fig. 1a) and lateral view (fig. 1b) reveal increased vascular markings and reticular opacities at the peripheral portions of the lungs, mainly in the lower lung zones, more accentuated on the left. There is no mediastinal enlargement, and pulmonary hilae are of normal configuration.

Computed tomography of the chest

Chest CT scan (lung window) shows dilated peripheral pulmonary vessels reaching the subpleural portion of the lungs (fig. 2).

^{99}Tc albumin macroaggregate body scan

Radiolabelled albumin has escaped from the pulmonary vascular bed (fig. 3) and is taken up by kidneys, liver and the brain (not shown in this figure). This indicates the presence of pronounced right-to-left shunt.

Diagnostic considerations and confirming procedure

The above radiological and clinical findings were highly suggestive of either intrapulmonary or intracardiac right-to-left shunt. Hepatopulmonary syndrome on the basis of severe cirrhosis with portal hypertension, patent foramen ovale with increased right ventricle afterload, as well as other forms of arteriovenous communications (*e.g.* congenital cardiopathy with Eisenmenger syndrome) had to be considered. Contrast enhanced echocardiography with agitated saline, showed left atrial microbubble opacification 6 heart beats later than right heart chamber opacification, confirming the presence of intrapulmonary shunt. Normally, microbubbles are filtered by the pulmonary capillary bed and do not appear in the left side of the heart unless there is a right-to-left shunt. Intracardiac shunt (as in patent foramen ovale), causes left heart chamber opacification generally sooner (within 3 heart beats) than intrapulmonary shunt.

A pulmonary arteriography study followed in order to investigate the type and size of the arteriovenous malformations as well as their amenability to embolization therapy. Selective catheterizations revealed dilated and tortuous peripheral pulmonary arteries with clear evidence of arteriovenous shunting at two seconds (fig. 4). Diffuse "spongy" like arteriovenous shunts were seen most numerous in the lower lobe posterior segments of both lungs (left>right).

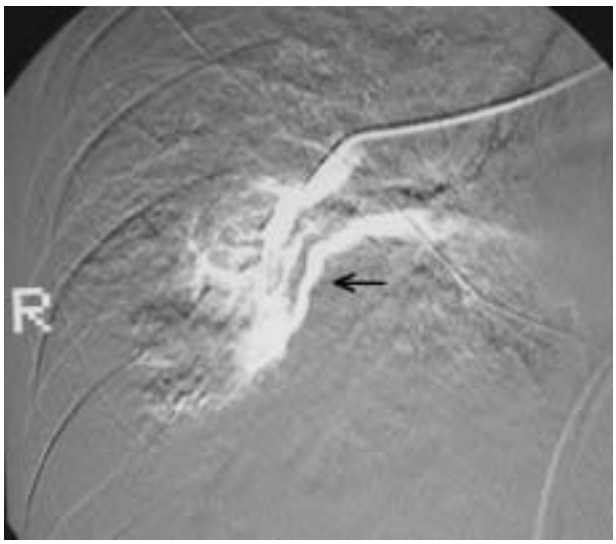

Fig. 4. – Pulmonary angiography. Tortuous peripheral pulmonary arteries are seen with early filling of pulmonary veins (arrow) providing clear evidence of arteriovenous shunting.

Diagnosis: Hepatopulmonary syndrome with diffuse (type I) intrapulmonary vascular dilatations

Treatment

Despite the fact that this type of arteriovenous malformation is not usually associated with significant improvement after embolization, selective embolization was performed in an attempt to reduce shunt before other more definite measures. A total of seven malformations were occluded using Gianturco coils measuring 3–4 mm in diameter. The procedure was totally uneventful and the patient was discharged 2 days later with mild improvement having a P_{a,O_2} value of 8.4 kPa while breathing 100% oxygen. This patient remains under follow-up and has been registered to a waiting list for liver transplantation.

Discussion

The hepatopulmonary syndrome (HPS) is defined as the triad of advanced liver disease, increased alveolar-arterial oxygen gradient (>2.7 kPa while breathing room air), and evidence of intrapulmonary vascular dilatations (IPVDs) [1–3]. Incidence of IPVDs in patients with end-stage liver disease has been reported at a rate of 13–47%, half of them associated with hypoxaemia [2]. It has been suggested that the determining factor for the development of the syndrome might be portal hypertension [3]. Most patients will present with the signs and symptoms of liver disease while pulmonary manifestations include cyanosis, despnoea, platypnoea, orthodeoxia and digital clubbing [1, 4] Spider nevi, another common clinical feature of HPS, has been proposed as a cutaneous marker of intrapulmonary vascular dilatations [1].

Pathological studies have demonstrated two distinct vascular abnormalities: precapillary and/or capillary

vascular dilatations (type I) and discrete direct arteriovenous communications (type II) that may be distant from gas exchange units, causing anatomic shunting and therefore being amenable to embolization [3, 5, 6]. Type I lesions, angiographically range from minimal, localized spiderly dilatations (which may be related with excellent response to 100% inspired oxygen and liver transplantation) to advanced, diffuse spongy appearance dilatations, which are usually related to limited response to 100% oxygen.

Supplemental oxygen would be expected to improve arterial oxygenation in minimal type I lesions but not in the other types [1, 5, 7]. Pulmonary angiography should be reserved for patients with severe hypoxaemia and poor response to 100% inspired oxygen in whom vascular embolotherapy may be an option, although diffuse "spongy" like IPVD's often do not respond to such treatment [4–10].

In the presented case, a typical HPS was considered associated with hepatic cirrhosis, having as leading symptom severe despnoea and hypoxaemia. Clinical suspicion of HPS was supported by ^{99}Tc body scan and most importantly by contrast echocardiography, which demonstrated intrapulmonary vascular shunting. Although highly sensitive, these techniques could not specify the exact type, localization or size of vascular abnormalities.

Furthermore, the excessive hypoxaemia of the patient as well as his nonresponsiveness to 100% oxygen, led to the hypothesis of type II vascular malformations in which embolotherapy is the treatment of choice [4, 9]. In a recent prospective study where 25 cases were reviewed [11], no patient had a P_{a,O_2}<5.4 kPa while breathing room air in supine position and no one had as little response to 100% oxygen as the presented patient.

In the presented patient, embolization did not produce dramatic improvement probably due to the presence of exceptionally large amounts of diffuse, fine, intrapulmonary vascular dilatations which were practically impossible to occlude. These dilatations might be reversed only after successful liver transplantation. However, high mortality rates have been reported for patients with HPS and severe hypoxaemia who underwent liver transplantation. Therefore these patients represent a very difficult group to treat [11].

In conclusion, hepatopulmonary syndrome should be considered in every patient with portal hypertension and hypoxaemia, especially if platypnoea and orthodeoxia is observed. A delayed positive contrast echocardiography and a positive ^{99}Tc scan might confirm diagnosis. Diffuse type I intrapulmonary vascular dilation as observed in the presented patient may present with severe hypoxaemia resistant to 100% inspired oxygen and pose significant therapeutic problems. In such cases, embolotherapy can be applied even if results are often limited, while liver transplantation remaining the last therapeutic choice, has a high mortality.

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