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The platypnea-orthodeoxia syndrome

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Abstract. **The platypnea orthodeoxia syndrome (POS) is a rare condition characterized by dyspnea and hypoxia in upright position. Pathopysiologic underlying mechanisms are determined by an atrial right-to-left shunt. Coexisting conditions that evolve POS can be of anatomical nature causing interatrial communication or of functional nature producing a deformity of the atrial septum in upright position. Diagnosis is difficult, as it needs to mention about POS. Classically, transthoracic and transesophageal echocardiography in supine and upright position with use of contrast medium and/or Doppler will point the diagnosis. Treatment is predominantly carried out by interventional closure of atrial septal defect that promptly resolves clinical symptoms.**

Key words:
Platypnea, PFO, Occluder, Dyspnea.

Abbreviations

ASA = atrial septal aneurism; ASD = atrial septal defect; PFO = persistent foramen ovale; POS = platypnea orthodeoxia syndrome.

Introduction

Platypnea Orthodeoxia Syndrome (POS) is a relative rare but striking condition with clinically observed dyspnea and hypoxia in upright position. Symptoms resolve typically in lying position. First reported in 1949, a number of cardiopulmonary processes cause the condition due to desoxygenation of blood[1]. The syndrome bases on an atrial right-to-left shunting. A majority of cases are affected by an opening of the interatrial septum, mostly because of a patent foramen ovale (PFO)[2]. Coexisting conditions that evolve POS can be of anatomical nature causing interatrial communication or of functional nature producing a deformity of the atrial septum in upright position. Different underlying conditions are cardiac, pulmonary or hepatic diseases[3,4]. Even though POS isn't common, the incidence is probably underestimated[5]. The syndrome occurs in a variety of clinical settings. Knowledge of epidemiology, clinic, diagnostics and therapy helps clinic practitioners to identify the sometimes initially mysterious appearing disease.

Definition

Platypnea is a breathlessness, which is triggered by orthostatism. Orthodeoxia is recognized as hypoxemia in the upright position. Symptoms are clinical observable as well as a decrease in arterial blood oxygen saturation in a sitting or standing position. Most patients exhibit interatrial communication with and surprisingly without increased right atrium pressures, what could explain right-left-shunting[5,6]. Underlying conditions are a PFO, atrial septal defect (ASD) and atrial septal aneurism (ASA) with septal fenestration (Figures 1, 2). Few other mechanisms can cause a reversal of blood-flow through the interatrial septum. Involved conditions are pericardial effusion or constriction, pulmonary hypertension, pulmonary emphysema, pulmonary arteriovenous malformation, cirrhosis of the liver and aortic aneurysm[5,6-8]. Additional factors are a prominent eustachian valve and alterations of atrial geometry that affects atrial pressures possibly because of right atrial remodeling. Underlying alterations of affected patients may be due to aneurismal expansion and elongation of the ascending aorta[6]. Manifestation of POS can result as a consequence of anatomic changes after pulmonary surgery (pneumoectomy or lobectomy) (Figure 3) as well as development of kyphoscoliosis[9].

Basically three types of causes can lead to POS: cardiac, pulmonary and hepatic causes, namely intracardiac shunts, pulmonary arteriovenous shunts and ventilation/perfusion mismatch (Table I)[5].

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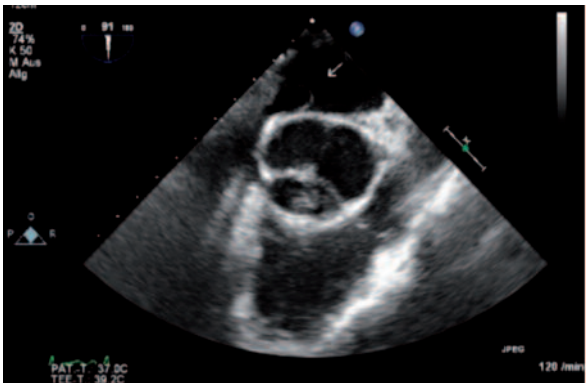

Figure 1. Interatrial septal aneurysm determined by transesophageal echocardiography.

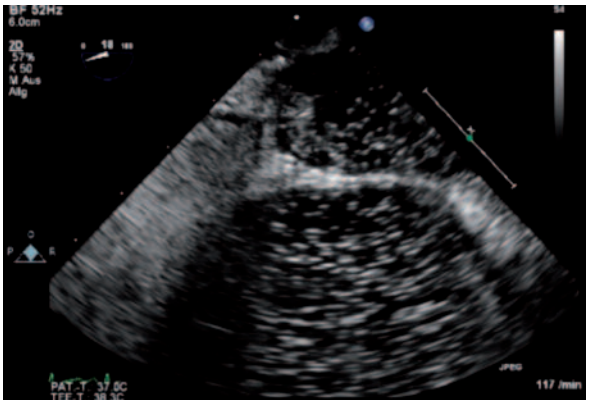

Figure 2. Interatrial shunt due to perforation in septal aneurysm.

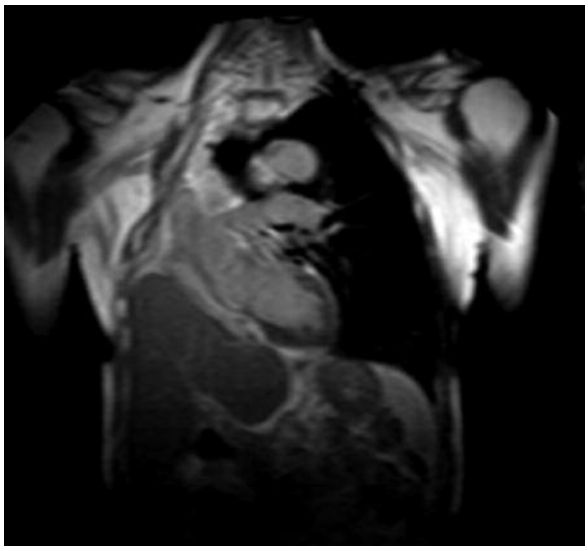

Figure 3. MRI of a patient with right-sided pneumectomy with deformation of heart and vasculature structure.

Pathophysiology

The detailed physiologic mechanism responsible for the positional nature of shunting is not fully understood.

Intracardiac Right-to-Left Shunt

Atrial communication can be a residue of embryonic development, when septa did not fuse until after birth and closure is only functional. The

Table I. Possible causes of platypnea-orthodeoxia syndrome. (Modified according to 2,5).

Intracardiac shunt PFO ASD ASA	R-L shunt without elevated R-L pressure gradient	Compression of RA by aortic dilatation or aneurysm Pericardial effusion or constrictive pericarditis Postpneumectomy[1] Decreased RA compliance (after myocardial infarction) Eosinophilic endomyocardial disease Abnormally lying Eustachian valve or Chiari network Kyphosis RA lipomatosis hypertrophy RA myxoma
	R-L shunt with R-L pressure gradient	Pulmonary thromboembolism Idiopathic pulmonary hypertension Right hydrothorax Long-duration lung diseases causing pulmonary hypertension Postpneumectomy
Pulmonal parenchymal ventilation/perfusion mismatch	Emphysema, COPD, parenchymal lung diseases Other causes of ventilation/perfusion mismatch (autonomic dysfunction, amiodarone toxicity, hepatopulmonary syndrome)	
Pulmonary arteriovenous shunt	Hepatopulmonary syndrome Pulmonary arteriovenous malformations or fistulae Osler-Weber-Rendu syndrome	

R-I = Right-to-left; RA = right atrium; COPD = chronic obstructive pulmonary disease. [1]Postpneumectomy shunt can be present with or without elevated right atrium pressure.

resulting PFO is common and affects at least 25 percent of the general population[5,9]. The rarer ASD with lack of atrial septal tissue is caused by ostium primum, ostium secundum or sinus venous defect. ASA is a result of interatrial septum displacement into the atrium due to enlargement of the mobile septum (Figure 1, 2). There is a coexistence between PFO and ASA in cases with POS[5].

Of course, most people with PFO never develop symptoms of POS, because left atrium pressure is 5-8 mmHg higher than right atrium pressure and atrial septum is functionally closed. Thus, this pressure difference is thought to prohibit right-to-left shunting through a PFO or small ASD. Right-to-left shunt can occur because of a transient pressure elevation in the right atrium (hemodynamic causes) and/or a flow-phenomenon (anatomical distortion)[5,10]. Given the large difference between the prevalence of PFO and POS, it appears that this interatrial defect is itself not sufficient to produce clinically evidence issues in most cases[11,12]. It is suspected that POS is present in patients with an existing PFO in whom there is an additional disease process that increases right heart pressures.

Pulmonary Arteriovenous Shunts and Ventilation/Perfusion Missmatch

Another cause of POS can be a blood-flow of desoxygenated blood through arteriovenous communications mostly in the bases of lungs[13,14]. The increased blood flow in upright position increases the shunt and produces symptoms. This phenomenon is mostly observed in patients with advanced hepatopulmonary syndrome (HPS), when dilated capillary vessels cause ventilation-perfusion mismatch, arteriovenous pulmonary shunt and decreased alveolar-arterial oxygen diffusion. 13 to 47% of these patients are hypoxemic without identifiable lung or heart disease[5,9,15].

Normally in health gravity causes that the blood flow of lung bases is greater than in apical lung regions. However, the alveolar pressure keeps constant in the complete organ. However, increased alveolar pressures can be the result in patients with various lung diseases. In upright position, especially in the apical regions of the lung, the situation aggravates. The pulmonary artery pressure drops and leads to pulmonary capillary compression. This situation can lead to a cessation of blood flow and a respiratory dead space in apical areas of the lungs. A vicious circle begins (diffuse Zone 1 phenomenon): the dead space causes dyspnea and hypoventilation, what increases the dead space and air trapping as well as alveolar pressure[5,9].

Epidemiology

POS is a rare described condition. Ten years ago only 40 cases were published. By 2009 about 130 patients with the disorder were identified. But etiology of POS remained in too many cases unclear. A review of 2012 found 105 articles with a total of 188 patients, each of whom with accepted true platypnea and orthodeoxia[5,11].

Clinical Picture

Affected patients suffer from variable dyspnea or/and hypoxemia dependent on posture. Patients complain of dyspnea in upright position (sitting and standing) with or without cyanosis. The history of symptoms can be short and symptoms can emerge acute, worsen rapidly and be progressive within few days. Flat lying relieves dyspnea and cyanosis, but not in all cases[11]. Patients don't respond to classical therapies of chronic pulmonary disease, ischemic heart disease or left ventricular dysfunction. Case reports show, that affected patients have different additional symptoms: tachycardia, tachypnea, drop of systolic pressure in upright posture[9], drop of oxygen saturation in upright position, even if 100 percent oxygen is applied[10].

Investigations

POS is a differential diagnosis of patients with dyspnea and refractory hypoxemia. Diagnosis of right-to-left shunting is challenging. Initial as-

Table II. Possible criteria for platypnea-orthodeoxia syndrome. (Modified according to 2,5).

- Existence of an interatrial communication
- Right-to-left shunt
- No pulmonary hypertension or elevation of right atrial pressure
- Orthodeoxia ($sPO_2 < 90\%$ or $pO_2 < 60$ mmhg in upright position, normalization in lying position)
- Dyspnea with taking upright position that disappears with lying

POD = Platypnea-orthodeoxia Syndrome; sPO_2 = oxygen saturation; pO_2 = partial pressure of oxygen.

sessment should be the proof of a possible association between breathlessness and upright position. Following oxygen saturation and blood gas analysis (pulse oximetry) in lying and upright position exhibits an orthostatic desaturation[5,9]. In hepatopulmonary syndrome a decrease in the partial atrial pressure of oxygen in upright position of about 5% or at least 4 mmHg was defined[12,15]. One author notes that intracardiac shunting is not in all patients presented with clear postural changes in blood oxygenation. Supplemental oxygen therapy may aid the identification of the disease, because the right-to-left atrial shunt prevents systemic oxygen saturation reaching 100 percent[6,11].

For definitive establishment of diagnosis echocardiography with Doppler mode and conjunct contrast-enhanced echocardiography is important. Both examinations ideally are performed in lying and upright position. These examinations may allow to localize, visualize and semiquantitate the shunt at the atrial level, because of the passage of microbubbles to the left atrium in the first three beats after right-cavity opacification. Another simple and the most sensitive examination is contrast tilt-table transesophageal echocardiography in lying and upright position. Maybe in rare cases the shunt is seen only on Valsava maneuvers[11,16]. In one case of an occult atrial septum defect the shunt could be delineated with IV metaraminol, while transthoracic echocardiography was without a result. Rodrigues et al[5] found in a review of the literature evidence that transthoracic echocardiography can also be sensitive and transthoracic Doppler echocadiography is possibly just as effective as transoesophageal echocardiography[5,6,9,12].

If an intracardiac shunt is not confirmed, an intrapulmonary shunt can exist. Three image techniques can show intrapulmonary vascular dilatations. Contrast-enhanced echocardiography, perfusion scan (scintigraphy) with macroaggregated albumin and pulmonary arteriography[9,15]. Contrast echocardiography is the most sensitive choice and, moreover, less invasive than arteriography. Is direct arteriovenous communication suspected and the response to therapy poor angiography is reasonable. In contrast to intracardiac communication in hepatopulmonary syndrome, the passage of microbubbles during contrast echocardiography through the dilated pulmonary vessels to the left atrium shows a delay of three to six heart beats[5,9,15].

Treatment

Treatment depends on the cause of POS. In cases of intracardiac communication without pulmonary hypertension closure of the defect is a causative therapy with a prompt improvement of symptoms. Closure can be surgical or percutaneous[5,10,17-20]. Nowadays, preferable is the percutaneous approach with cardiac catheterization to close PFO (Figure 4, 5). Coexisting anatomic defects such as aortic elongation, aortic aneurysm, constrictive pericarditis or myxoma, however, require surgical intervention[2,4,7].

Percutaneous closure of PFO or ASD can be performed with a buttoned device, CardioSEAL Septal Occlusion System and Amplatzer Septal Occluder devices or Amplatzer PFO Occluder (Figure 4, 5). After closure, aortic oxygen saturation and systemic blood saturation have to be monitored. Residual shunt can be identified by echocardiography. Anticoagulation with acetylsalicylic acid should last three month following implantation. Transcatheter closure results in immediately enhanced oxygen saturation in upright position after the procedure. Platypnea resolves complete[7,10,12].

In patients with hepatopulmonary syndrome (HPS) advanced liver disease is the cause of POS

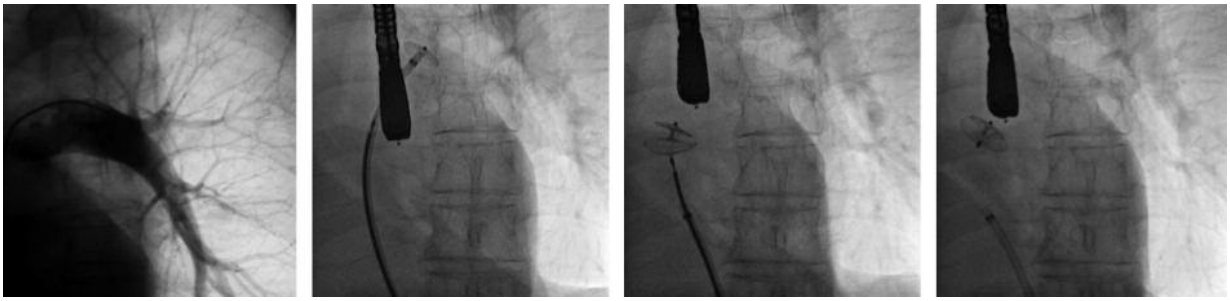

Figure 4. Interventional closure of patent interatrial septal cummunication by PFO-occluder.

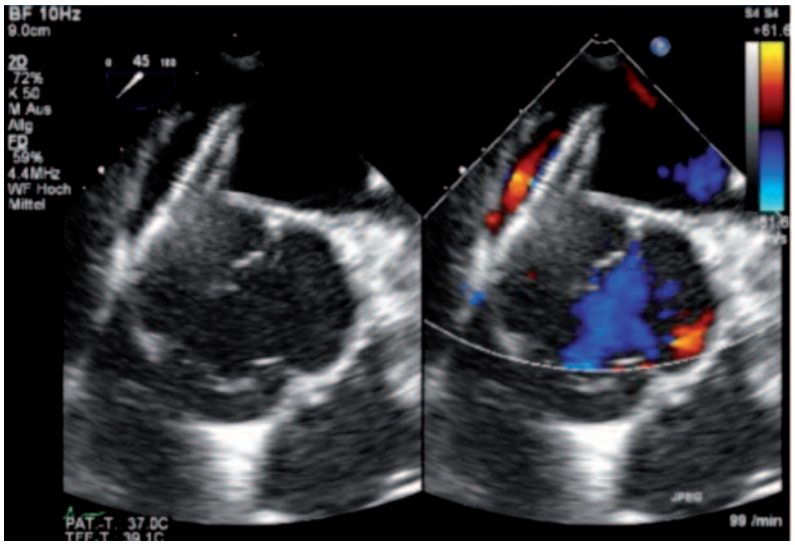

Figure 5. Transesophageal echocardiography in a patient with PFO-occluder implantation.

and liver transplantation is the only causal therapy. No other treatment like almitrine bismesylate, somatostatin analog, indomethacin or plasmapheresis had been effective. First management can be oxygen therapy, bed rest, salt restriction and diuretics. After transplantantion in 80% of patients oxygenation improves, but severe hypoxemia is a leading cause of perioperative mortality[4,8].

Underlying pulmonary diseases must be treated to improve ventilation-perfusion matching.

Conclusions

POS is still a relative rare condition, that often develops acute and shortly, but incidence is possibly underestimated. Shunting blood from the right to the left heart is the most common cause of the disease. Most patients suffer from PFO and the causative therapy is obvious, namely closing of PFO. Other defects of the interatrial septum also need percutaneous or surgical treatment. Probably, there are additional anatomic changes that finally lead to POS. These changes can follow lung surgery and malformations like kyphoscoliosis or they develop age-related. The concrete triggers of POS and the role of anatomic changes remain unclear and are possibly more individual. Nevertheless, increasing reports and case reports of POS call for attention and physicians should be attentive of patients with unexplained or paroxysmal hypoxia. Diagnosis is easy, if the track is followed in the right direction.

Conflict of interest

The Authors declare that they have no conflict of interests.

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