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# Platypnea and orthodeoxia syndrome due to a right-to-left shunt via the foramen ovale in the absence of pulmonary hypertension after orthotopic liver transplantation: Sequelae leading to brain abscess: A case report

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All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author. (Suneerat Kongsayreepong, email address: suneerat-kong@gmail.com)

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## ABSTRACT:

**Introduction:** Platypnea and orthodeoxia syndrome (POS) refers to the worsening of dyspnea and desaturation in the upright position. The most common cause of POS is a right-to-left intra-cardiac shunt. Patent foramen ovale (PFO) is a remnant of normal fetal anatomy that can continue into adulthood. Most are asymptomatic as the pressure in the left atrium is higher than in the right atrium, leading to the functional closure of the foramen ovale.

**Case presentation:** We report an autosomal dominant polycystic kidney and liver disease (ADPKD) patient with PFO Grade II–III, atrial septal aneurysm (ASA), and dilatation of the aortic root complicated with multiple dental caries and chronic gingivitis. He developed POS and brain abscess after liver and kidney transplantation. Right-to-left shunt was proved by the air contrast transesophageal echocardiography (TEE) review in the normal right atrium and pulmonary artery pressure. Concomitant cardiac pathology of ASA, dilatation of the aortic root, and elevation of the right hemidiaphragm after surgery might reposition the atrium septum and redirect inferior vena cava blood flow through PFO to the left atrium, causing reopening of PFO and right-to-left shunt. Multiple dental caries and chronic gingivitis might be the cause of brain abscess from paradoxical septic embolism. With the condition of complex and high-grade PFO and high Risk of Paradoxical Embolism (ROPE) score with POS, questions were raised concerning the closure of PFO either in the preoperative or especially postoperative period after POS was detected after liver transplantation to prevent paradoxical embolism. With the potential risk of complications with the closing of PFO, this issue should be addressed in a multidisciplinary approach, with the patient and family. However, aggressive treatment of intraoral infection is an important issue.

**Conclusions:** POS could happen in patient with underlying PFO associated with ASA undergoing orthotopic liver transplantation with elevation of right hemidiaphragm. Multidisciplinary care team approach should be arranged for the decision of closure of this PFO to prevent intraoperative and serious postoperative complications.

**Keywords:** Platypnea and orthodeoxia syndrome; Reopen PFO without pulmonary hypertension; Brain abscess; Liver transplantation

## INTRODUCTION

Platypnea-orthodeoxia syndrome (POS) is characterized by dyspnea and oxygen desaturation that occur in the upright position and improve when lying down. Intracardiac right-to-left shunts are the most common etiology [1]. Patent foramen ovale (PFO) is a remnant of normal fetal anatomy that arises from incomplete fusion of the septum primum and secundum. Because left atrial pressure typically exceeds right atrial pressure, most adults remain asymptomatic due to functional closure of the foramen ovale [2]. Reopening of the foramen ovale can result in a right-to-left shunt and lead to paradoxical embolism.

## CASE PRESENTATION

A 52-year-old male with autosomal dominant polycystic kidney and liver disease (ADPKD) underwent a right-sided nephrectomy along with liver and kidney transplantation. His medical issues included severe hypertension, asymptomatic PFO, and a low-risk Model for End-Stage Liver Disease (MELD) score. He also had multiple dental caries and chronic gingivitis–periodontal disease, which received partial treatment before surgery. He had no clubbing, cyanosis, or evidence of chronic hepatic or pulmonary disease. Heart sounds were normal, and room air SpO<sub>2</sub> was 96% without respiratory distress. He had no history of stroke or palpitation. Preoperative transthoracic echocardiogram (TTE) revealed a PFO with no right-to-left shunt and no pulmonary hypertension. Abdominal ultrasound (Figure 1) showed numerous cystic components with no signs of portal hypertension or splenomegaly.

His surgery was uneventful, and he was extubated the next day. A few hours later, while seated upright, he developed respiratory distress with room air SpO<sub>2</sub> of 80–86% that did not respond to high-flow nasal cannula support. No new murmur, pulmonary rale, or peripheral edema was detected. His abdomen was distended, and bowel sounds were absent, with an intra-abdominal pressure of 12 mmHg. Fluid balance was positive at 1300 ml in the first 24 hours. A chest x-ray revealed no pulmonary infiltration or edema with elevated right hemidiaphragm and dilated bowel (Figure 2).

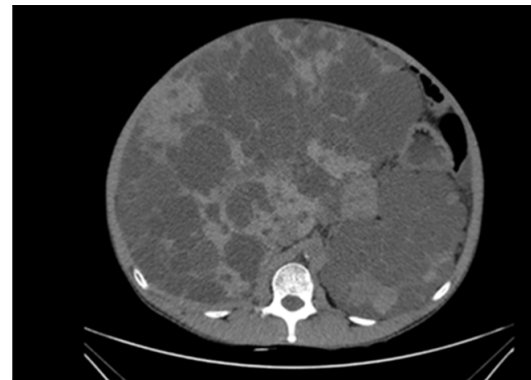
After reintubation, he experienced concurrent desaturation and respiratory distress in a postural-dependent manner, with no signs of hemodynamic impairment. Peripheral oxygen saturation decreased in the upright sitting position but improved when the patient was lying down. Arterial blood samples confirmed orthodeoxia, as shown in Table 1, consistent with POS.

The patient's condition raised suspicion of shunt pathology, possibly intrapulmonary or extrapulmonary, or an intracardiac right-to-left shunt. Point-of-care TTE was conducted to assess for intra-cardiac shunt. Initial results showed normal left (LV) and right (RV) ventricular systolic function, with a mean pulmonary artery pressure (mPAP) of 17.13 mmHg calculated using the method of Abbas et al. [3]. No intracardiac shunt was clearly seen at the flap PFO in either the supine or upright position.

A review of the pre-operative chest CT scan showed no evidence of pulmonary arteriovenous malformations

## KEY MESSAGES:

- Platypnea and orthodeoxia syndrome (POS) can occur in a patent foramen ovale (PFO) without elevated right atrial or pulmonary pressure, especially when concomitant with an atrial septal aneurysm, aortic root dilation, and right hemidiaphragm elevation.
- Repositioning of the atrial septum and redirection of caval blood flow through the septal defect may underlie the right-to-left shunt in the upright position and paradoxical embolism.
- In high-risk patients with complex PFOs, POS, and high risk of paradoxical embolism scores, prophylactic PFO closure—preoperatively or especially postoperatively—should be evaluated via a multidisciplinary approach, with thorough risk-benefit discussions involving the patient and family.



**Figure 1.** Abdominal CT scan shows large multiple liver and kidney cysts.



**Figure 2.** Chest X-ray after extubation showed dilated bowel with elevation of the right hemidiaphragm.

**Table 1.** Desaturation parameters.

Parameter	Supine	Upright 1 min	Upright 3 min	Upright 5 min
FiO <sub>2</sub>	0.3	0.3	0.3	1.0
PaO <sub>2</sub> (mmHg)	104	72	65.9	47.90
SpO <sub>2</sub>	99	95.5	93.6	85.3
Heart rate (bpm)	82	133	126	101
Blood pressure (mmHg)	101/65	124/119	120/108	112/105

**Abbreviations:** bpm: beats per minute; FiO<sub>2</sub>: fractional inspired oxygen; PaO<sub>2</sub>: partial pressure of oxygen; SpO<sub>2</sub>: oxygen saturation

(PAVMs) in either lower lung region. A technetium-99m macro aggregated albumin (Tc-99m MAA) lung scan revealed multiple small areas of radioactivity in the brain, lungs, and transplanted kidney, indicating a right-to-left shunt in multiple locations (Figure 3).

Because the TTE could not clearly demonstrate an intracardiac shunt, so transesophageal echocardiography (TEE) was performed. It revealed an atrial septal aneurysm (ASA) and a flapped PFO measuring 11 mm, with normal tricuspid and mitral valves, a small eustachian valve, and a normal inferior vena cava diameter. The central venous pressure (CVP) was 4 mmHg before repositioning the patient to a 30-degree upright position. Air mixed with 10 ml of 5% iso-oncotic albumin was then injected through a cephalic vein. With the Valsalva maneuver, TEE showed that most microbubbles passed from the right atrium, through the open PFO flap, into the left atrium within the first 3 cardiac cycles. This finding was consistent with a grade II–II PFO [2] and confirmed a right-to-left shunt at the atrial level (Figure 4).

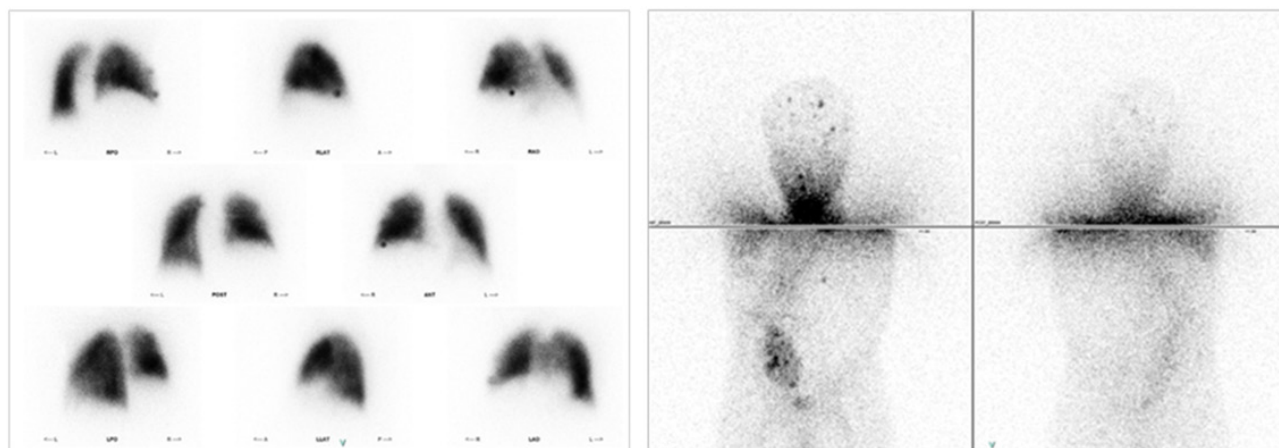
This clinical diagnosis indicated an open flap foramen ovale with a right-to-left shunt, resulting in POS. After extubation, the patient was advised to avoid sitting and a cardiologist consultation for possible PFO closure. Several days later, he felt drowsy and experienced new jerking movements on his left side for 3 minutes. He regained consciousness but remained confused for 15 minutes, with muscle strength at 4/5 in his left arm and leg. An emergency contrast-enhanced CT scan of the head showed a well-defined hypodense lesion in the right basal ganglia, right insular lobe, and periventricular region, identified as a brain abscess (Figure 5).

The patient's spouse declined the stereotactic procedure to drain the abscess and obtain a pus culture. A repeat TTE by the cardiologist identified the PFO and ASA, along with the dilation of the aortic root and ascending aorta. The agitated saline test confirmed a right-to-left shunt through the foramen ovale without elevated right atrial or pulmonary pressures. Transcatheter PFO closure was considered inappropriate at this time. His treatments were meropenem combined with sulfamethoxazole-trimethoprim for 2 weeks. A 2-week follow-up brain CT showed a gradual decrease in lesion size.

## DISCUSSION

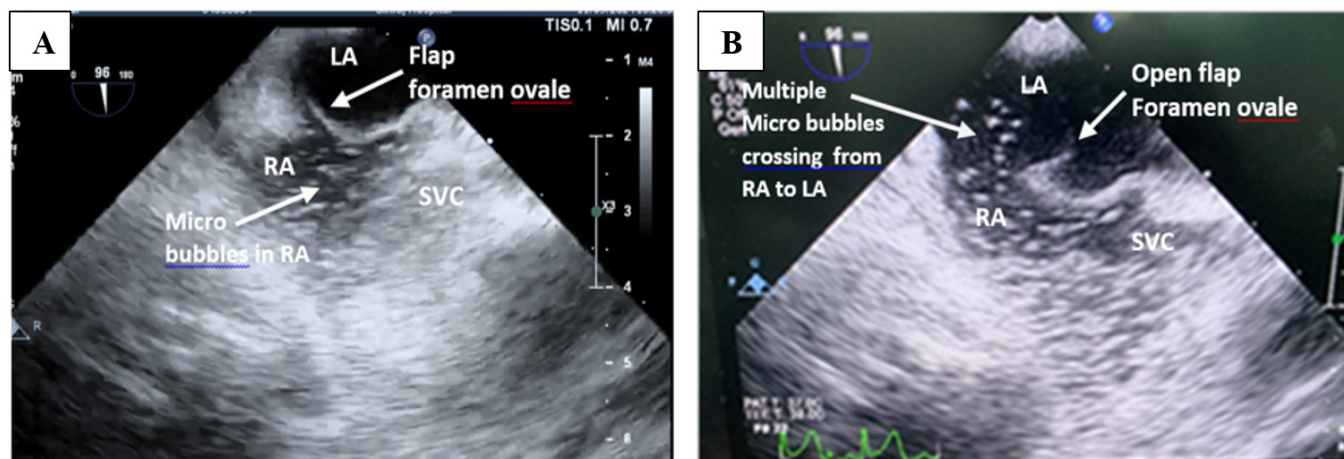
Platypnea refers to dyspnea in an upright position, and orthodeoxia indicates documented hypoxia in the same posture. Both conditions improve upon lying down. The diagnosis of POS is characterized by a decrease in SpO<sub>2</sub> of more than 5% and PaO<sub>2</sub> of more than 4 mmHg when moving upright, which resolves upon lying down [1,2]. The primary mechanism of POS often involves a right-to-left shunt, either intracardiac or extrapulmonary, and usually indicates an underlying disease. The severity of hypoxemia in POS correlates with the volume of shunted blood. A PaO<sub>2</sub> < 70 mmHg suggests a shunt fraction of about 20% to 25% [2].

Hepatopulmonary syndrome (HPS), PAVMs, and acute respiratory distress syndrome are common extracardiac causes of POS [2]. Given the patient's history of large liver cysts, HPS was initially suspected of causing hypoxemia. The MELD score is used to predict short-term survival in



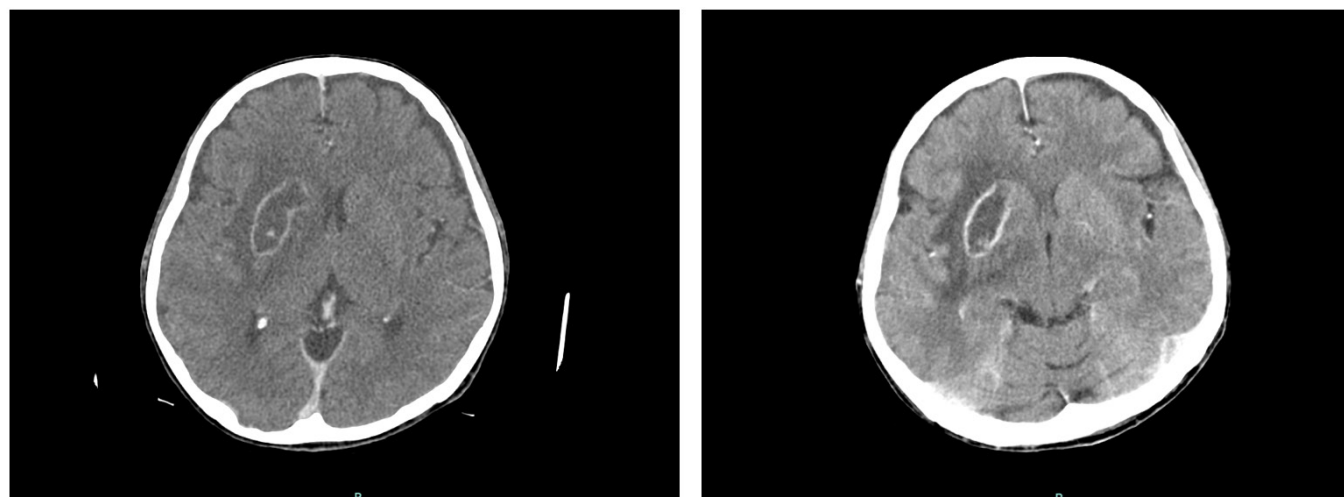
**Figure 3.** Radionuclide perfusion lung scan using technetium-99m macro aggregated albumin (Tc-99m MAA) revealed multiple focal areas of radioactivity in the brain, lungs, and transplanted kidney, suggestive of a right-to-left shunt.





**Figure 4.** Transesophageal echocardiogram air contrast study. The bicaval view, following the injection of agitated 5% iso-oncotic albumin 10 ml. into the cephalic vein, demonstrated majority of micro bubbles passed from the right atrium to the left atrium across the open flap PFO within the first 3 seconds in the 30-degree upright position. (A) Supine position (B) 30-degree sitting upright.

**Abbreviations:** LA: left atrium; RA: right atrium; SVC: superior vena cava



**Figure 5.** Contrast-enhanced CT of the head showed a well-defined hypodense lesion in the right basal ganglia, right insular lobe, and periventricular region.

patients with advanced liver disease, with higher scores correlating with HPS [4]. In this patient, who had no sign of chronic liver disease, the pre-transplant MELD score was not elevated, and the preoperative abdominal ultrasound did not show portal-related hypertension. So, it is unlikely that HPS was the cause of POS.

PAVMs are abnormal connections between pulmonary arteries and veins that directly bypass the capillary bed. Orthodeoxia in PAVMs is associated with large or multiple malformations in the basal lung regions, usually with a shunt fraction over 20% of cardiac output. Contrast-enhanced CT scanning is the preferred imaging study [5]. However, no such malformations were visible in this patient's chest imaging.

Radionuclide perfusion lung scanning with Tc-99m MAA is an effective technique for confirming the presence of a shunt [6]. In this patient, the perfusion lung scan revealed multiple focal areas of right-to-left shunt in the brain, lungs, and transplanted kidney. However, this finding does not clarify whether a significant right-to-left shunt is present in this patient.

Over 80% of POS cases arise from intracardiac abnormalities such as a PFO, an ASA, or an atrial septal defect (ASD). PFO, the most reported intracardiac shunt [7], is a remnant of normal fetal anatomy that persists into adulthood in approximately 25% of cases. Most are asymptomatic because left atrial pressure typically exceeds right atrial pressure, causing the foramen to close functionally. However, blood can shunt across this interatrial communication when right atrial pressure is normal or elevated [8].

In the setting of normal right atrial pressure, deoxygenated blood can pass from the right atrium to the left atrium through a PFO or an ASD if a co-existing secondary cardiac abnormality is present. Examples include aortic root dilatation [9] or a prominent Eustachian valve [10]. Similarly, extracardiac intrathoracic pathology, such as hemidiaphragm paralysis [11], may enable such shunting. In this scenario, changes in atrial septal positioning during upright sitting can redirect blood flow from the inferior vena cava into the left atrium through the interatrial defect [2].

**Table 2.** Risk of Paradoxical Embolism (ROPE) Score calculator [21].

Characteristic	Points
No history of hypertension	1
No history of diabetes	1
No history of CVA or TIA	1
Nonsmoker	1
Cortical infarct on imaging	1
Age (years)	
18-29	5
30-39	4
40-49	3
50-59	2
60-69	1
≥70	0
Total score (sum of individual points)	
Maximal score possible	10
Minimal score possible	0

**Abbreviations:** CVA: cerebrovascular accident; TIA: transient ischemic attack

**Table 3.** RoPE score and corresponding percentage of patients with a cCVA and PFO to which the PFO is attributable to the CVA [21].

RoPE score	cCVA with PFO % (95% CI)	Two-year risk of recurrent CVA/TIA % (95% CI)
0-3	0 (0-4)	20 (12-28)
4	38 (25-48)	12 (6-18)
5	34 (21-45)	7 (3-11)
6	62 (54-68)	8 (4-12)
7	72 (66-76)	6 (2-10)
8	84 (79-87)	6 (2-10)
9-10	88 (83-91)	2 (0-4)

**Abbreviations:** cCVA: cryptogenic cerebrovascular accident; PFO: patent foramen ovale; RoPE score: Risk of Paradoxical Embolism score

In this patient, a right-to-left shunt via the PFO was confirmed by air contrast study. The study showed most microbubbles crossing the open PFO (grade II-III) from the right atrium to the left atrium in the sitting position [12]. Because right atrial pressure was normal, the most likely mechanism of POS in this patient who had a PFO, an atrial septal aneurysm, an enlarged ascending aorta, and an elevated right hemidiaphragm was atrial septal repositioning. This shift might divert venous blood from inferior vena cava into the left atrium through the open PFO when upright [2]. While awaiting the cardiologist's opinion on possible PFO closure, the patient developed brain abscesses. These lesions may have arisen from paradoxical bacterial emboli, given his history of multiple dental caries and chronic gingivitis [13].

Should this PFO be closed? If closure is indicated, should it occur before liver transplantation or immediately after POS is diagnosed postoperatively? Reports of a reopening PFO leading to POS after orthotopic liver transplantation are scarce, although reopening of a PFO

during liver transplantation has been linked to higher cardiopulmonary complication rates [14]. The benefit of prophylactic PFO closure in patients undergoing liver transplantation remains unclear. Recent studies found no association between a PFO and elevated risk of postoperative cerebrovascular accidents in liver transplantation. [15]. However, a persistent right-to-left shunt through a PFO has been implicated in cryptogenic ischemic stroke and brain abscess [16]. Patients with a PFO are 2.9 times more likely to develop pyogenic brain abscesses that often appear as a single large lesion, such as in the basal ganglia. Streptococcus species and anaerobes are the most common pathogens [17].

PFO closure [18], including percutaneous transcatheter closure, can effectively resolve orthodeoxia and paradoxical embolism associated with an intra-cardiac right-to-left shunt. However, this intervention carries certain risks: the periprocedural complication rate is approximately 3.9%, and the incidence of atrial fibrillation is about 0.33% per year [19], with limited long-term data.

Therefore, PFO closure should be considered selectively in patients at high risk of stroke or paradoxical embolism, such as those with a complex PFO. Such complexity may include an ASA, a tunnel length exceeding 8 mm, or altered anatomy from aortic root dilatation [20]. Alternatively, the “Risk of Paradoxical Embolism (ROPE) Score Calculator” [21], as illustrated in Table 2, can be used to estimate the likelihood that a PFO contributes to cryptogenic cerebrovascular accident. Additional guidance is provided in Table 3.

This patient had a PFO with an 11 mm tunnel length and a coexisting ASA, as well as dilatation of the aortic root and ascending aorta. These features met criteria for a complex PFO [20]. Based on his RoPE score of 7, the estimated probability that his PFO caused his cerebrovascular accident was 72% (CI 66%-76%). The likelihood of recurrence was 6% (CI 2%-10%). He was therefore at high risk of paradoxical embolism and brain abscess.

The decision to close this PFO, either before transplantation or after postoperative detection of POS, should be discussed with the multidisciplinary team and the patient. This approach helps prevent paradoxical embolic complications, especially brain abscess. Optimal dental care, including thorough oral hygiene and treatment of oral infections, was also essential.

## CONCLUSION

We report a case of autosomal dominant polycystic kidney disease, a complex PFO, multiple dental carries, and chronic gingivitis. This patient developed POS and a brain abscess after liver and kidney transplantation. An atrial septal aneurysm, a dilated aortic root, and an elevated right hemidiaphragm might have repositioned the atrial septum in the sitting position. This shift diverted vena caval blood through the PFO and led to a right-to-left shunt, paradoxical embolism, and abscess formation, despite normal right-sided pressures. With his elevated risk of paradoxical embolism from a complex PFO and a high RoPE score, clinicians debated whether to close the PFO preoperatively or after POS emerged. Such decisions require careful evaluation of risks and benefits, with active participation from the patient and family. Rigorous dental hygiene and treatment of oral infections remain essential to avoid brain abscess.

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