

Case report

When sitting suffocates: a rare cause of platypnoea- orthodeoxia syndrome

A 26-year-old female of Indian origin, a known case of chronic kidney disease and hypertension, presented to us with a 1-month history of on/off fever (undocumented) and worsening of shortness of breath for 1 week. Initially, she had shortness of breath only on exertion, which progressed to rest over the past 7 days. She reported a loss of appetite and a 10 kg weight loss in 1 month. There was no history of cough, haemoptysis, palpitations, cyanosis, oedema, syncope, orthopnoea and paroxysmal nocturnal dyspnoea associated with breathlessness.

On presentation in the emergency department the patient was conscious, oriented (E4V5M6), afebrile, tachypnoeic (respiratory rate 40 breathes·min⁻¹), tachycardiac (heart rate 130 beats·min⁻¹), with high blood pressure

(178/102 mmHg) and oxygen saturation of 80% on room air. Respiratory system examination revealed normal chest movements with bilateral diffuse crepitations. We performed a bedside point-of-care ultrasound, which revealed bilateral B-profiles with shred sign in bilateral lower zones with mild bilateral pleural effusion. Cardiac function was normal (ejection fraction ~60%) with mild pericardial effusion. An abdominal scan revealed mild ascites with bilateral shrunken kidneys.

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Task 1

What are the possible differential diagnoses according to given history and examination findings? (more than one answer possible)

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Platypnoea-orthodeoxia syndrome refers to shortness of breath and oxygen desaturation in an upright position. Ventilation/perfusion mismatch is a rare cause of the same. Herein, we report a case of bilateral lower lobe tuberculosis, causing platypnoea and orthodeoxia. <https://bit.ly/3jhEQ1>



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Answer 1

a) Hypertensive emergency; b) community-acquired pneumonia; c) tuberculosis; and d) sepsis with acute kidney injury and fluid overload

In the background of chronic kidney disease and hypertension, the patient presented with a recent worsening of breathlessness, a raised blood pressure of 178/102 mmHg, tachycardia, and tachypnoea with bilateral crepitations; hypertensive emergency is one of the likely differential diagnosis. The patient also reported on/off fever and significant

weight loss over 1 month (10 kg in 1 month) with a loss of appetite; therefore, tuberculosis became another possibility, especially in a region with a high prevalence of tuberculosis. Furthermore, in chronic kidney disease patients, a concomitant infection can precipitate an acute decline of renal function leading to fluid overload. We did further evaluation of the patient keeping these differentials in mind.

We started the patient on high flow oxygen and parenteral diuretics. Simultaneously lung ultrasound and chest radiograph were performed. We also subsequently performed a non-contrast high-resolution computed tomography (CT) scan of the chest.



Figure 1 Anteroposterior chest radiograph of the patient at presentation in the emergency department.

Task 2

What is the most likely diagnosis based on chest radiograph (figure 1) and CT chest (figure 2) provided?

- a) Acute respiratory distress syndrome (ARDS)
- b) Cardiogenic pulmonary oedema
- c) Pulmonary thromboembolism
- d) Atypical pneumonia

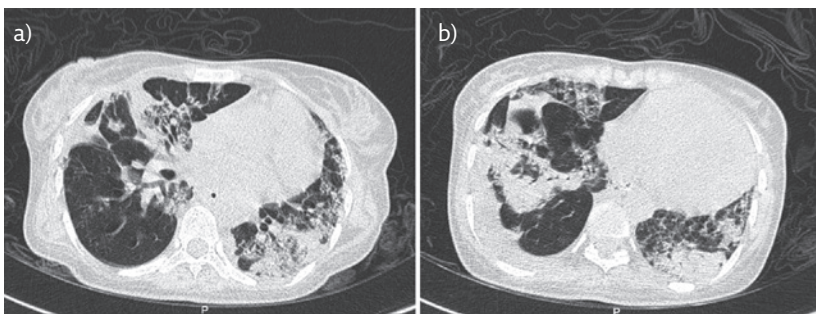


Figure 2 High-resolution CT chest sections of the patient at presentation in the emergency department. a) Bilateral lung fields show multiple areas of patchy consolidation and ground-glass opacities (left > right) with volume loss on left side. Few areas of fibroatelectatic and fibrobronchiectatic changes also seen in right middle and lower lobes. b) A section at a lower level than in (a) showing similar changes as described earlier in both lung fields.

Answer 2

a)

Chest radiography shows bilateral opacities (left>right) involving the middle and lower zones (more in the lower zones) of the lungs, which are silhouetting bilateral diaphragm and cardiac borders. A pulmonary oedema radiograph is likely to show bilaterally symmetrical distribution, an air space distribution in a batwing appearance, air bronchograms in cases with pulmonary alveolar oedema with fluid in interlobular fissures, upper lobe venous diversion (stag antler's sign), cardiomegaly, peribronchial cuffing, and perihilar haze [1]. We did not find any of these findings in our case, and there was no history of associated orthopnoea or paroxysmal nocturnal dyspnoea. It is challenging to differentiate ARDS from cardiogenic pulmonary oedema just based on a chest radiograph. However, cardiogenic pulmonary oedema seems unlikely, considering the above findings. In rare cases, pulmonary oedema can be unilateral without associated typical findings and clinical features. Bacterial pneumonia would usually be unilateral with a predominant lobar distribution. Atypical pneumonia is associated with patchy inflammatory changes usually confined to the interstitium of the lung. It is also associated with more pronounced constitutional symptoms like headache and myalgia [2]. Nevertheless, since infective pneumonia can progress to ARDS, it cannot be excluded entirely based on chest radiographs. In ARDS, a chest radiograph usually has diffuse coalescent opacities. A chest CT scan helps define a pattern suggesting the aetiology of ARDS. ARDS due to extrapulmonary diseases usually leads to symmetric ground glassing with consolidation with an anteroposterior gradient (more aerated lung posteriorly). In ARDS due to pulmonary causes, the abnormalities are usually asymmetrical with a mixed picture of non-dependent consolidation and ground glassing. In our case, the high-resolution CT scan showed bilateral lung field involvement with multiple areas of patchy consolidation, ground-glass opacifications (left>right), with right-sided

pleural effusion. Therefore, ARDS (with associated pneumonia, typical/ tubercular) is likely in this case based on the clinico-radiologic picture [3, 4].

We started the patient on broad-spectrum antibiotics, antihypertensives and diuretics. However, her condition deteriorated in the form of worsening arterial blood gas (ABG) parameters and metabolic acidosis. We intubated and mechanically ventilated her because of worsening type 1 respiratory failure and severe metabolic acidosis. Investigations revealed normal leukocyte count, blood and endotracheal aspirate did not grow any bacterial or fungal pathogen. We moved the patient to the intensive care unit and dialysed the patient for severe metabolic acidosis due to acute-on-chronic kidney disease. Subsequently, her condition improved and she was extubated on day five post-intubation and was moved to the general ward.

After extubation, the patient complained of breathlessness, more in the sitting position than the recumbent position. The patient maintained a 96% saturation with 4 L of oxygen in the recumbent position, and her saturation dropped to 80–82% in the sitting position, which further dropped in the standing position. She also developed tachycardia and tachypnoea in sitting position. Serial ABGs showed a 7% difference in saturation and a 16 mmHg difference in arterial oxygen tension (P_{aO_2}) in a recumbent and sitting position (table 1). We observed an increase in the alveolar-arterial gradient in the sitting position. After observing platypnoea-orthodeoxia, we performed a lung ultrasound in the sitting and recumbent positions. We have demonstrated the ABG correlation with the ultrasound images in a later section.

Task 3

What is the reason for this condition?

- Pulmonary embolism
- Bernheim effect
- Reverse-Bernheim effect
- Orthopnoea
- Platypnoea-orthodeoxia

Table 1 ABG parameters of the patient in the sitting and recumbent position

Parameters	Sitting position, room air [‡]	Recumbent position, room air [¶]
pH	7.477	7.402
P_{aCO_2}	23.2 mmHg	23.7 mmHg
P_{aO_2}	50.5 mmHg	60.6 mmHg
S_{aO_2}	83.3%	90.2%
HCO_3^-	17.3 mmol·L ⁻¹	17.1 mmol·L ⁻¹
Alveolar-arterial gradient	70.2 mmHg	59.5 mmHg

P_{aCO_2} : arterial carbon dioxide tension; S_{aO_2} : arterial oxygen saturation; HCO_3^- : bicarbonate ion concentration; S_{pO_2} : oxygen saturation measured by pulse oximeter; F_{IO_2} : inspiratory oxygen fraction.

[‡]: S_{pO_2} 84%, heart rate 113 beats per min, P_{aO_2}/F_{IO_2} 240; [¶]: S_{pO_2} 93%, heart rate 79 beats per min, P_{aO_2}/F_{IO_2} 314.

Answer 3

e)

This condition is called platypnoea-orthodeoxia syndrome (POS). Exacerbated shortness of breath when sitting up is known as platypnoea. It was first described in 1949 by BURCHELL *et al.* [5]. It is usually associated with oxygen desaturation in the upright position, a condition known as orthodeoxia, the combined syndrome being called POS. Quantitatively, orthodeoxia is defined as a drop in arterial oxygen saturation of 5% and P_{aO_2} of 4 mmHg in the upright position [6]. Furthermore, in the disease course, we ruled out Bernheim and reverse-Bernheim effect by echocardiography, which showed the absence of an extreme shift of the interventricular septum and normal systolic and diastolic function [7].

Task 4

Among the following, which is the most frequent cause for orthodeoxia?

- a) Hepatopulmonary syndrome
- b) Diaphragmatic paralysis
- c) Patent foramen ovale
- d) Upper lobe pneumonia

Answer 4

Among the causes described until now, the most frequent causes are intra-cardiac shunts, with patent foramen ovale being the most common cause.

Among the extra-cardiac causes, a pulmonary arteriovenous malformation is the most common cause. Lower lobe parenchymal involvement rarely causes platypnoea-orthodeoxia because of the ventilation/perfusion mismatch [8]. The other reported causes of orthodeoxia are as follows.

Intracardiac causes: patent foramen ovale; atrial septal defect; transposition of great vessels; partial anomalous pulmonary venous connection; atrial septal aneurysm; ascending aortic aneurysms; tricuspid regurgitation/stenosis; aortic valve replacement; fontan procedure; COPD; pulmonary hypertension; pericardial effusion; constrictive pericarditis; and pulmonary embolism.

Extra-cardiac causes: 1) intrapulmonary shunt - ARDS, hepato-pulmonary syndrome, massive pleural effusion; and pulmonary arterial-venous malformation; 2) ventilation/perfusion mismatch - interstitial lung disease, COPD, cryptogenic organising fibrosis and pneumonectomy.

Other causes: diabetic autonomic neuropathy; radiation-induced bronchial stenosis; bronchogenic carcinoma causing left main stem obstruction; organophosphorus poisoning; Parkinson's disease; amiodarone toxicity; fat embolism; severe kyphosis; large hepatic hydatid cyst; and hemi-diaphragmatic paralysis [9].

Task 5

What is the mechanism of orthodeoxia? (more than one answer possible)

- a) Ventilation/perfusion mismatch
- b) Increased lung hydrostatic pressure
- c) Increased bronchial artery pressure causing interstitial oedema
- d) Mixing of deoxygenated and oxygenated blood through a shunt

Answer 5

a) and d)

Mixing of deoxygenated venous blood with oxygenated arterial blood through an intra-cardiac or an extra-cardiac shunt is the most common cause for orthodeoxia. In rare occasions when it is due to pulmonary parenchymal disease, particularly involving the lower lobes, orthodeoxia occurs due to zone one phenomenon [9, 10].

Task 6

What is correct about West's lung zones regarding arterial (P_a), alveolar (P_A) and venous (P_v) pressures?

- a) West zone 1 has $P_A > P_a > P_v$
- b) West zone 2 has $P_a > P_v > P_A$
- c) West zone 3 has $P_A > P_a > P_v$
- d) West zone 2 has continuous blood flow through both systole and diastole

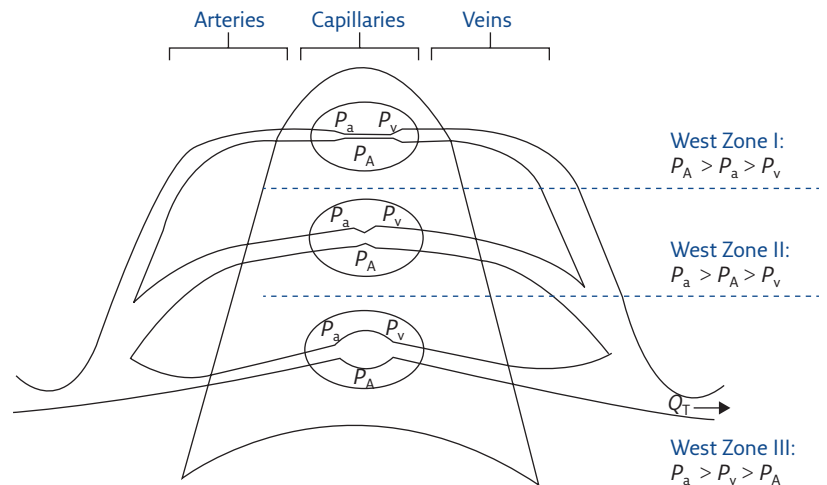


Figure 3 West lung zones showing the gravity-dependent blood flow through the lungs.

Answer 6

a)

We can divide the lung into four discrete regions called West's zones (figure 3) on the interplay among P_a , P_A and P_v :

- Zone 1: P_A higher than P_a and P_v
- Zone 2: P_A lower than P_a but higher than P_v
- Zone 3: Both P_a and P_v higher than P_A
- Zone 4: Interstitial pressure higher than P_A or P_v [11]

The regional distribution of ventilation and blood flow is not only affected by gravity but also due to the typical pattern of asymmetric branching of the airways and blood vessels. Any kind of disturbance affecting this pattern will cause impaired gas exchange. Thus, if this impairment occurs in the lower zones, this will lead to maximum oxygenation impairment leading to more symptoms.

We did a bubble contrast echocardiography by intravenous administration of agitated normal saline for further evaluation of the cause for platypnoea-orthodeoxia.

POS can also be due to hepato-pulmonary syndrome, a triad of liver disease, inadequate oxygenation and pulmonary vasodilation. This increased pulmonary vasodilation causes disproportionately greater perfusion without much change in ventilation, which is more evident in the lower lobes of the lungs when in the standing position. The prevalence of this syndrome in cirrhotic patients is ~4–32%. Vasodilation occurs due to increased endothelial and inducible nitric oxide synthase, and upregulation of pulmonary vascular nitric oxide receptors [12].

We performed an ultrasound and a splenoportal axis doppler to rule out chronic liver disease associated with hepato-pulmonary syndrome as a cause of platypnoea-orthodeoxia.

Task 7

In our case, even after three cycles, no bubbles were seen in the left heart. What does this signify?

- a) Atrial septal defect with pulmonary arterial hypertension (PAH)
- b) Ventricular septal defect with PAH
- c) Patent ductus arteriosus with PAH
- d) Absence of intra-cardiac and extra-cardiac shunts

Answer 7

Bubbles confined only to right-sided cardiac chambers imply a negative contrast study.

In contrast, after injection through a large bore cannula in the arm, the bubbles, if found in the left-side chambers after being visualised in the right atria, are considered a positive study.

- 1) Bubbles in the left ventricle: ventricular septal defect with PAH
- 2) Bubbles in the aorta: patent ductus arteriosus with PAH
- 3) Bubbles in the left atrium: immediately is atrial septal defect with PAH, after three beats is pulmonary arteriovenous malformation
- 4) Bubbles initially in the left atrium rather than right: when injected into the left arm left-sided superior vena cava might be present; when injected into the right arm superior vena cava draining into left atria might be present; and when injected into either arm a possibility of total anomalous systemic venous drainage is present [13, 14].

We could not detect any opacification of the left atrium with microbubbles, even after three cycles, thus excluding the presence of intra-cardiac and

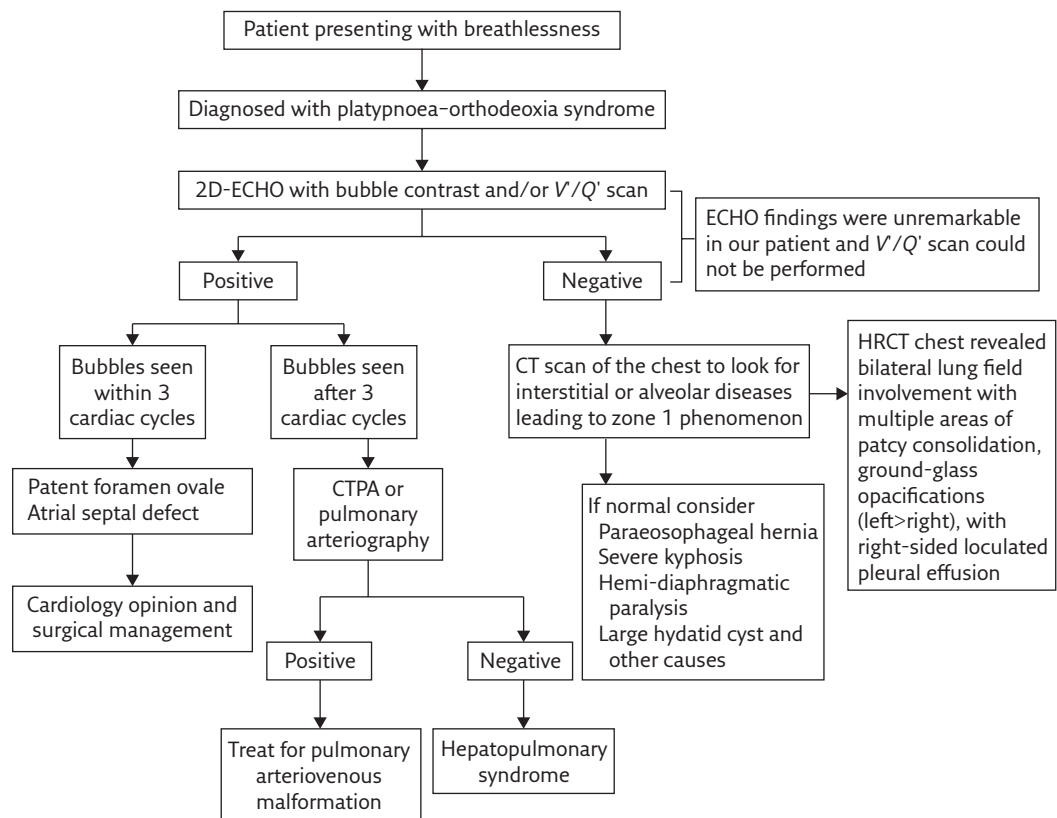


Figure 4 Flowchart on the workup of platypnoea and orthodeoxia in our patient. V/Q: ventilation/perfusion mismatch; 2D ECHO: two-dimensional echocardiography; CTPA: computerised tomography pulmonary angiogram; HRCT: high-resolution CT scan.

extra-cardiac shunts. All valves appeared normal, and the ejection fraction was 60%. There was no evidence of pulmonary hypertension, left ventricular hypertrophy, or findings suggestive of cor pulmonale.

A non-contrast chest CT scan was performed (deranged renal function tests precluded a contrast-enhanced CT scan) for further evaluation and to rule out pulmonary arteriovenous malformations. It showed multiple ill-defined areas of consolidation in the left upper and lower lobe, right middle lobe, right lower lobe, and mediastinal adenopathy with bilateral pleural effusion (figure 4).

Meanwhile, *Mycobacterium tuberculosis* was positive on endotracheal tube aspirate Gene-Xpert and was rifampicin sensitive. Based on this, we made a diagnosis of pulmonary tuberculosis, and we started her on treatment for the same with anti-tubercular therapy.

The patient improved with treatment and chest physiotherapy. We performed a repeat chest radiograph (figure 5) to look at the change in underlying lung condition before her discharge after a hospital stay of approximately 1 month. It showed significant improvement compared to the presenting radiograph.

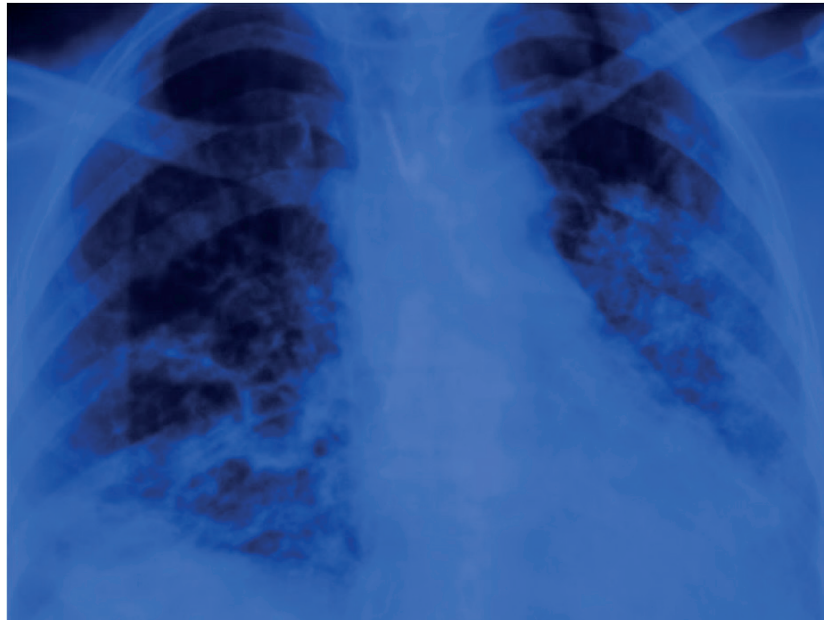


Figure 5 Chest radiograph posteroanterior view of the patient before discharge.

Task 8

What are the lung ultrasound findings (figure 6) expected in this case with a position change?

- a) Decrease in B-lines while sitting
- b) The disappearance of B-lines in the recumbent position
- c) No change with position
- d) Increase in B-lines while sitting

Answer 8

d)

Lung ultrasound shows a bilateral increase in B-lines when changing from the recumbent to sitting/standing position, indicating POS.

Discussion

POS is a rare phenomenon in which the room oxygen saturation falls by 5% or the P_{aO_2} falls by >4 mmHg in the sitting position compared to the recumbent position [9]. A review article on POS analysed the epidemiology among all cases reported up to November 2016 and reported 239 patients [9]. We further searched PubMed using the keywords “orthodeoxia” or “platypnea” and found two more case reports between 2017–2020, both attributed to patent foramen ovale. Out of the 241 cases reported (in PubMed), 210 (87.1%) had intra-cardiac shunts, the most common being patent foramen ovale, 22 (9.2%) patients had pulmonary

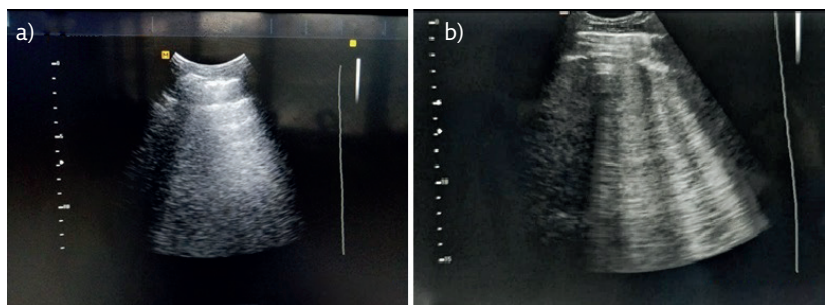


Figure 6 Lung ultrasound images of the patient in the a) recumbent and b) sitting position showing an increase in B-profile when sitting.

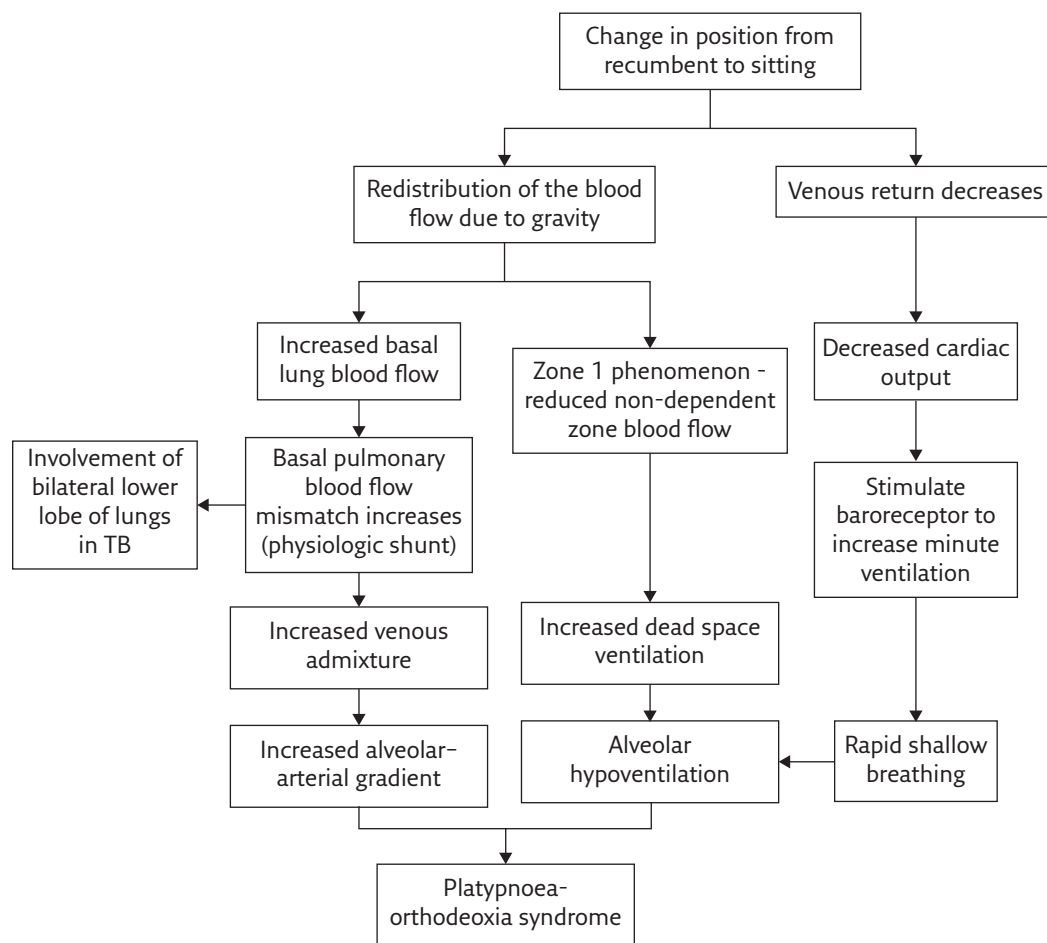


Figure 7 A flowchart explaining the mechanism of platypnoea-orthodeoxia in our patient. TB: tuberculosis.

arteriovenous shunts, and nine (3.7%) patients had pulmonary parenchymal disease [9, 15, 16]. Lower lobe pulmonary parenchymal involvement explains orthodeoxia in our patient. The gravity-dependent blood flow of lung parenchyma is accentuated when the person is upright. The density of alveoli is more in the lower lobes than the other lobes, and maximum contribution to gas exchange occurs by the lower lobes when a person is in an upright position. This contribution decreases when the patient assumes a recumbent position due to the diaphragm's upward movement and redistribution of blood flow. There may be a ventilation/perfusion mismatch in the upright position when there is predominantly lower lobe lung involvement. In lower lobe parenchymal involvement cases, the alveolar pressures become elevated because of the disease process. An upright posture lowers the pulmonary arterial pressure in the upper lobes (gravitational effect). Thus, a diffusely scattered zone 1 is produced in these cases, accentuated when the person assumes an upright posture, owing to the gravity-dependent lowering of pulmonary arterial pressures [17, 18]. Also, in our case we attributed orthodeoxia to this diffuse zone 1 phenomenon of the lungs (figure 7).

Pulmonary tuberculosis is quite a common condition in the Indian subcontinent, with a prevalence of 295.9 per 100000 population. It usually involves the lung's upper lobes, and hence orthodeoxia is not expected. The upper lobe involvement presumably occurs because of the high oxygen tension in lung apices, which is favourable for mycobacteria growth and relatively spared antigenic clearance from the lung apices [19, 20]. To the best of our knowledge, there has not been any prior report of pulmonary tuberculosis causing POS. Only 10.5% of patients had lower lobe involvement in pulmonary tuberculosis in a study conducted by AHMAD and ZAHEER [21]. A higher prevalence of lower lobe involvement was seen in HIV-infected and diabetic patients, 46.15% and 18.59%, respectively. Another study published from a teaching hospital in Madhya Pradesh, India, reviewed 2136 cases of pulmonary tuberculosis, out of which 215 (~10%) had lower lobe tuberculosis. In their study, lower lobe tuberculosis was more common among females (62%) with a high relative risk among diabetics, end-stage renal disease, HIV positive patients, or patients on corticosteroid therapy [22]. People with chronic liver diseases have a higher prevalence of lower lobe tuberculosis [23].

Our patient was a female patient with chronic kidney disease with predominant lower lobe involvement by the tubercular process. In our patient, we noticed that the patient had a confluent B-profile while sitting up with a decreased number of B-lines while recumbent, likely due to worsening ventilation/perfusion mismatch in the upright position; providing direct evidence of the mechanism of POS in this case. Platypnoea-orthodeoxia improved over 1 month of treatment.

Interpretation

After a thorough evaluation in our case, the underlying parenchymal disease, *i.e.* pulmonary tuberculosis, caused the POS. The diffuse zone 1 phenomenon, as discussed, was hypothesised as the reason in our case for the orthodeoxia. Pulmonary tuberculosis may rarely lead to the uncommon manifestation of platypnoea-orthodeoxia, as seen in the present case.

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Conflict of interest

None declared.

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