

Platypnoea–orthodeoxia syndrome in COVID-19

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SUMMARY

Platypnoea–orthodeoxia syndrome (POS) is a rare entity characterised by respiratory distress and/or hypoxia developing in the sitting/upright posture, which is relieved in the supine posture. It is caused by cardiac, pulmonary and non-cardiopulmonary diseases. COVID-19 can have varying respiratory manifestations including acute respiratory distress syndrome (ARDS) and sequelae-like pulmonary fibrosis. POS has been rarely reported in patients with COVID-19. Here we report a case of POS in a patient recovering from severe COVID-19 ARDS. As he was gradually mobilised after his improvement, he had worsening dyspnoea in the sitting position with significant relief on assuming a supine posture. He was diagnosed with POS after ruling out other causes of POS. He was treated with oxygen support in upright posture and chest physiotherapy was continued, to which he showed improvement. POS is a rare manifestation of COVID-19 which needs awareness as it can be diagnosed easily and can respond to continued supportive care.

BACKGROUND

COVID-19 is caused by the SARS-CoV-2 virus, and respiratory system is the most commonly involved organ system in COVID-19.¹ The respiratory manifestations of COVID-19 range from mild upper respiratory symptoms to life-threatening severe acute respiratory distress syndrome (ARDS) requiring invasive mechanical ventilatory support. CT of the chest shows typically bilateral ground-glass opacities predominantly in the lower lobes,

mainly in a peripheral and subpleural location. Patients with COVID-19 can have postural variation of respiratory distress, and this fact is used in the strategy of awake proning in the management of COVID-19 ARDS.² However, platypnoea–orthodeoxia syndrome (POS) is a rare manifestation in COVID-19 and has been sparsely reported. Here we report an interesting case of COVID-19 who showed characteristic features of POS during the recovery phase.

CASE PRESENTATION

A 46-year-old man from Delhi presented with fever of 7 days and breathlessness of 3 days' duration. At the time of presentation, the patient had modified Medical Research Council (mMRC) grade 4 dyspnoea and complained of severe breathlessness both in lying down as well as upright postures. There was no history of cough, expectoration, haemoptysis or chest pain. He had a history of diffuse large B-cell lymphoma for which he underwent chemotherapy and autologous stem cell transplantation 5 years ago. On examination, he was conscious, oriented, with mild pallor, tachycardia and tachypnoea. His blood pressure was 110/70 mm Hg, but oxygen saturation of haemoglobin in room air was 90% and 94% with oxygen via non-rebreathing mask at 10L/min. Respiratory system examination showed normal vesicular breath sounds with bilateral coarse diffuse crepitations without any wheeze or stridor. Examination of other systems including the cardiovascular system was also within normal limits.

His COVID-19 reverse transcription-PCR (RT-PCR) of throat and nasopharyngeal swab came out positive and he was transferred to a COVID-19 facility.

Hence, a diagnosis of severe COVID-19 ARDS was made, and he was initiated on treatment with dexamethasone and remdesivir as per institutional guidelines.³ Arterial blood gas (ABG) estimation was suggestive of type I respiratory failure (pH 7.41, PO₂ 54 mm Hg, PCO₂ 29 mm Hg). His complete blood count showed pancytopenia. Serum creatinine, transaminases, blood sugar and electrolytes were normal. Oxygen support was initiated with high-flow nasal cannula at 60L/min and 60% FiO₂. He was also encouraged to assume prone positioning, which he tolerated well. He was given broad-spectrum antibiotics in view of neutropenia and packed red blood cells and platelet transfusion for anaemia and thrombocytopenia, respectively. Heparin was withheld in view of thrombocytopenia. His oxygen requirement gradually decreased, and on day 3, he was maintaining saturation 94% with oxygen of 4L/min via nasal prongs.

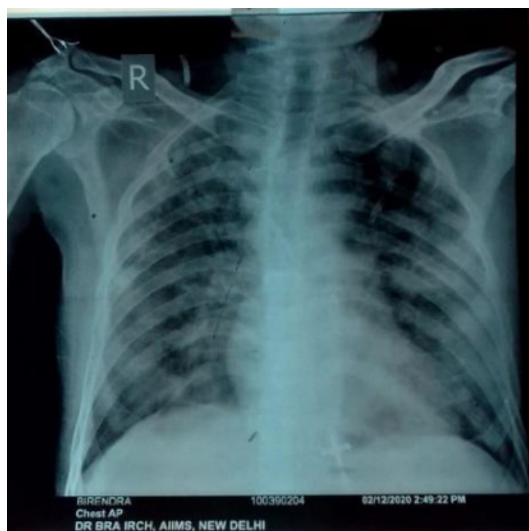


Figure 1 Chest radiograph showing bilateral peripheral ground-glass opacities in mid and lower zones of the lungs. R, right.



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Table 1 Investigations

Haemoglobin: 68 g/L	Calcium/phosphorus: 8.2/3.9 mEq/L	ALP: 92 IU/L
Total count: 1980 cells/mm ³	PT INR: 1.38	Total protein/albumin: 6.5/3.2 g%
Platelet: 24 000/dL	aPTT: 29/30 s	Urine routine: normal
Urea/creatinine: 37.0/0.4 mg%	Bilirubin total/direct: 0.8/0.3 mg%	D dimer: 843 ng/mL
Sodium/potassium: 137.0/4.2 mEq/L	AST/ALT: 46/42 IU/L	

ALP, Alkaline Phosphatase; ALT, Alanine aminotransferase; aPTT, activated Partial Thromboplastin Time; AST, Aspartate aminotransferase; PT INR, Prothrombin Time International Normalization Ratio.

However, on day 4 of admission, he complained of increasing dyspnoea specifically in the sitting position, which reversed on assuming the supine position. His SpO₂ as measured by pulse oximeter (DrTrust) decreased from 94% in the supine position to 88% in the recumbent position. The finding was confirmed with the help of another pulse oximeter (AccuSure). An ABG analysis was done in the sitting position and repeated in the supine posture, which showed a decrease in SaO₂ by 7% and PaO₂ by 13 mm Hg in the upright posture. Hence, a diagnosis of POS was made. By day 5, he was on 2L oxygen via nasal cannula; however, his positional variation of saturation persisted and he was further evaluated for the likely cause.

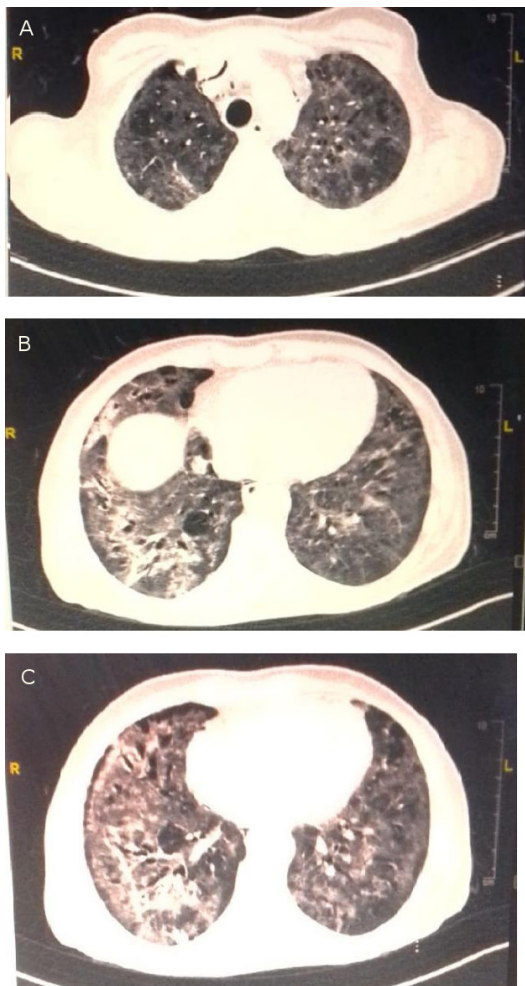


Figure 2 (A–C) High-resolution CT of the thorax showing bilateral ground-glass opacities, consolidation and crazy pavement appearance of the lungs. L, left; R, right.

Table 2 Mechanisms of POS in COVID-19

Serial number	Pathology	Mechanism
1	Preferential involvement of lung parenchyma in lower and posterior segments	Gravitational shunting of blood to poorly ventilated lower zones in upright posture causing V/Q mismatch
2	Coagulopathy causing pulmonary microthrombosis and vasculopathy	Increase in pulmonary dead space and V/Q mismatch, further contributing to wasted ventilation. This is exaggerated in upright position due to gravitational redistribution leading to POS
3	Myocardial dysfunction	(1) Reduced cardiac output decreases blood flow to non-dependent lung zone exaggerating wasted ventilation; (2) low cardiac output stimulates baroreceptors causing an increase in minute ventilation, rapid shallow breathing and increase in dead space ventilation. Decrease in venous return in upright position contributes to reduced cardiac output.

POS, platypnoea–orthodeoxia syndrome; V/Q, ventilation–perfusion.

INVESTIGATIONS

The results of routine blood and urine investigations are enumerated as follows (table 1).

His inflammatory markers including ferritin, lactate dehydrogenase, C reactive protein and interleukin-6 were elevated.

His chest radiograph showed non-uniform diffuse bilateral predominantly peripheral ground-glass opacities in mid and lower zones of the lungs (figure 1).

A high-resolution CT of the thorax was done, which showed bilateral ground-glass opacities throughout the lung fields. However, consolidation and crazy pavement appearance were noted involving predominantly lower zones (figure 2A–C).

ECG showed normal sinus rhythm. A 2D echocardiography was done, which showed good left and right ventricular functions without any pericardial effusion and no evidence of pulmonary embolism. A bubble contrast echocardiography could not be done owing to technical difficulty in the midst of the COVID-19 pandemic.

An ultrasound abdomen revealed normal echotexture and size of the liver.

TREATMENT

Chest physiotherapy was continued, along with other supportive treatment and oxygen. His steroids were discontinued after 10 days (from initiation) as per protocol.

OUTCOME AND FOLLOW-UP

His POS improved and his oxygen support was withdrawn by day 8 of hospitalisation. He was subsequently discharged 3 days after discontinuation of oxygen therapy. When he had his first follow-up after 1 month of discharge, he was relieved of his symptoms.

DISCUSSION

POS is a rare entity characterised by dyspnoea in upright posture which is relieved on supine posture (platypnoea) and concomitant arterial oxygen desaturation in upright posture (orthodeoxia). A fall in SaO₂ of >5% or PaO₂ of >4 mm Hg from supine to upright/sitting position is essential for diagnosis.⁴ Burchell and Wood reported the first case of POS in 1949 in a patient with post-traumatic intrathoracic arteriovenous shunts.⁵ The terms platypnoea and orthodeoxia were coined by Altman and Robin, respectively.⁶

Table 3 POS in COVID-19: literature review

Serial number	Article	Journal	Authors	Patients (n)	COVID-19 severity	Follow-up
1	Reversible POS in COVID-19 acute respiratory distress syndrome survivors	<i>Elsevier Respiratory Physiology and Neurobiology</i> , August 2020	Geak Poh Tan, Sharlene Ho and Bingwen Eugene Fan	5 patients	1 asymptomatic 1 mild 2 moderate 1 severe	All recovered
2	POS in a patient with severe COVID-19 pneumonia	<i>Monaldi Archives for Chest Disease</i> 2020, volume 90:1609	Komal Singh, Harshit Kadnur and Animesh Ray	1 patient	Severe	Recovered

POS, platypnoea–orthodeoxia syndrome.

The basic pathophysiology of arterial desaturation is mixing of deoxygenated venous blood with oxygenated arterial blood through a shunt. Both anatomical and functional aberrations are usually needed for this shunting to occur, and the shunting is exaggerated in the upright posture, resulting in the characteristic feature of POS. This pathophysiology is responsible for most of the cardiac causes of POS like patent foramen ovale, atrial septal defect, atrial septal aneurysm, etc.⁷ In POS due to lung-related causes, shunting occurs outside the heart, for example, pulmonary arteriovenous malformation (AVM). In upright posture, the gravity-dependent increased blood flow to the dependent portions of the lungs causes an increase in shunting through the pulmonary AVM causing POS.⁸ In the supine posture, there is less shunting resulting in improvement in oxygenation. This mechanism is also seen in advanced cirrhosis with hepatopulmonary syndrome.⁹

However, POS is also observed in parenchymal lung diseases like emphysema, interstitial lung diseases and consolidation involving preferentially the lung bases, which leads to severe ventilation–perfusion (V/Q) mismatch in the upright posture owing largely to the effect of gravity-driven preferential blood flow to the bases.¹⁰

In COVID-19, there may be preferential involvement of the lung parenchyma of posterior and lower zones.¹¹ So, the

gravitational shunting of blood to the poorly ventilated lower and posterior segments can cause significant V/Q mismatch. Wasted ventilation is also thought to be exaggerated in the presence of pulmonary microangiopathy and microthrombosis seen in severe COVID-19.¹² The proposed mechanisms of POS in COVID-19-related POS are enumerated as follows (table 2).¹³

As our patient was not given heparin due to thrombocytopenia, we hypothesise that this could have predisposed to microthrombosis in pulmonary vasculature and might have played a part in the pathogenesis of POS.

COVID-19-related POS may be reversible.¹⁴ Our patient also responded to chest physiotherapy and other supportive management.

This case report highlights a rare manifestation of COVID-19 pneumonia. Although peripheral and lower lobe lung involvement is commonly encountered in COVID-19, POS has been rarely reported with this novel disease. The possible reasons can be (1) postural variation of saturation is only rarely checked in most patients, especially intubated patients; by the time the patient is mobilised and made to sit up, the lung lesions would have started resolving, leading to resolution of hypoxaemia; (2) there is also a lack of awareness of this entity among physicians, which leads to under-reporting of cases. We also reviewed the existing literature to look for similar cases of POS reported in the backdrop of COVID-19 (table 3).

Patient's perspective

I was admitted with shortness of breath and was tested to be positive for COVID-19. I was treated with oxygen, tablets and injectable medicines. Slowly, my symptoms resolved, but as I started to sit up on my bed, I got more and more breathless. I was worried that my lungs had permanent damage and I could not understand why it was happening even though the fever had gone. My doctors confirmed that oxygen level in blood was falling when I was sitting up but not when I was lying on the bed. They also did a study of the heart and other tests, which were normal. They suggested that I continue to use oxygen while sitting up and also to undergo chest physiotherapy diligently. After a few days, I felt better, my oxygen level became normal and I got discharged. I am relieved that it all turned out well.

Learning points

- ▶ A high index of suspicion is needed to diagnose platypnoea–orthodeoxia syndrome (POS) because the symptoms are subtle, and postural variation may be missed if not specifically sought.
- ▶ POS can occur in the backdrop of COVID-19.
- ▶ One should actively consider/rule out its presence when the symptoms and/or signs are suggestive.

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