CASE REPORT

Diverse echocardiographic changes in the course of hypoxia due to acute exacerbation of idiopathic pulmonary fibrosis

İdiyopatik pulmoner fibrozun akut alevlenmesine bağlı olarak hipoksinin seyrindeki çeşitli ekokardiyografik değişiklikler

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Summary– Idiopathic pulmonary fibrosis (IPF) is a progressive parenchymal disease. Pulmonary hypertension (PH) is a potentially lethal complication in the course of IPF. In almost all cases of IPF-PH there is gradual deterioration, but patients can also decline suddenly due to hypoxia. This case report describes the different echocardiographic changes observed in 2 episodes of hypoxic attack in a 73-year-old man. On admission, the tricuspid regurgitation peak gradient (TRPG) was 21 mmHg and the oxygen saturation rate was 94% (O_2: 4 L/min). Five days after admission, the TRPG and oxygen saturation rate deteriorated [TRPG: 85 mmHg, oxygen saturation: 72% (O_2; 4 L/min)]. He was diagnosed with IPF-PH due to hypoxic pulmonary vasoconstriction. Oxygen therapy and methylprednisolone pulse therapy (MPT) were administered. Five days after the MPT treatment, the hypoxia and PH improved [TRPG: 21 mmHg, oxygen saturation: 95% (O_2: 4 L/min)]. Acute exacerbation of IPF (IPF-AE) occurred 20 days after the MPT, and a second dose of MPT was administered. The TRPG and oxygen saturation rate did not decline [TRPG: 27 mmHg, oxygen saturation: 94% (O_2: 4 L/min)]. The patient died 10 days after the second dose of MPT. Divergent echocardiographic findings were observed during the deterioration of IPF-AE in the presence of IPF-PH.

Özet– İdiyopatik pulmoner fibroz (İPF) ilerleyici bir parankimal hastalıktır. Pulmoner hipertansiyon (PH), İPF seyrinde ortaya çıkabilen potansiyel olarak ölümcül bir komplikasyondur. İPF-PH olgularının sağlık durumu genellikle tedrici olarak kötüleşirken bazen hastaların sağlık durumu hipoksi nedeniyle aniden bozulabilir. Bu olgu raporu, 73 yaşında bir erkekte 2 hipoksik atak epizodunda gözlenen farklı ekokardiyografik değişiklikleri göstermektedir. Başvuru anında, triküspit yetersizliği pik gradyanı (TRPG) 21 mmHg ve oksijen satürasyon oranı %94 (O_2: 4 L / dak) idi. Hastaneye kabulden beş gün sonra, TRPG ve oksijen satürasyonu kötüleşti [TRPG: 85 mmHg, oksijen satürasyonu: %72 (O_2; 4 L / dak)]. Hipoksik pulmoner vazokonstriksiyon nedeniyle hastaya İPF-PH tanısı konuldu. Oksijen tedavisi ve metilprednizolon puls tedavisi (MPT) uygulandı. MPT tedavisinden beş gün sonra, hipoksi ve PH iyileşti [TRPG: 21 mmHg, oksijen satürasyonu: %95 (O_2: 4 L / dak)]. MPT'den 20 gün sonra oluşan İPF'nin akut eksaserbasyonu (İPF-AE) nedeniyle ikinci bir MPT dozu uygulandı. TRPG ve oksijen satürasyonu düşmedi [TRPG: 27 mmHg, oksijen satürasyonu: %94 (O_2: 4 L / dak)]. Hasta ikinci MPT dozundan 10 gün sonra hayatını kaybetti. İPF-PH varlığında İPF-AE'nin bozulmasıyla sıradışı ekokardiyografik bulgular gözlendi.

Idiopathic pulmonary fibrosis (IPF) is a progressive parenchymal disease. Pulmonary hypertension (PH) can emerge as a lethal complication of IPF.[1] IPF-PH is divided into 2 types: slow progression and acute onset. Almost all cases of IPF-PH are the slowly progressive type. In cases of acute onset, it may be attrib-

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utable to hypoxic PH caused by hypoxic pulmonary vasoconstriction (HPV), but hypoxia does not always result in HPV and hypoxic PH. This is a report of diverse echocardiographic findings observed in the course of hypoxia due to acute exacerbation of IPF (IPF-AE).

CASE REPORT

A 73-year-old man was admitted to the hospital due to worsening dyspnea. He had previously been diagnosed with IPF, but had been clinically stable with prednisolone 15 mg/day and home oxygen therapy. On admission, his oxygen saturation rate was 94% while breathing 4 L/min oxygen. Transthoracic echocardiography (TTE) revealed no evidence of flattening of the interventricular septum [left ventricular (LV) eccentricity index 1.02 >in systole] (Fig. 1a, b), a tricuspid regurgitation peak gradient (TRPG) of 21 mmHg (Fig. 1c), and no evidence of right ventricle (RV) dilatation (RV basal diameter: 44.2 mm; RV mid-cavity diameter: 33.9 mm; RV longitudinal diameter: 78.9 mm; RV/LV basal diameter ratio: 0.92), suggesting no evidence of RV overload. Five days after his admission, his oxygen saturation rate fell to 72% and atrial blood gas analysis results indicated the presence of acidemia (pH: 7.34), hypoxia (PO_2: 57 mmHg), and hypercapnia (PCO_2: 68 mmHg) while breathing 4 L/min oxygen. TTE revealed flattening of the interventricular septum dominant in end-systole (LV eccentricity index 1.71 >in systole) (Fig. 1d, e), a TRPG of 85 mmHg (Fig. 1f), and RV dilatation (RV basal diameter: 52.5 mm; RV mid-cavity diameter: 44.9 mm; RV longitudinal diameter: 78.9 mm; RV/LV basal diameter ratio: 1.54). Acute pulmonary embolism was suspected and enhanced computed tomography (CT) imaging was performed. High resolution CT images revealed a honeycomb appearance in the subpleural area of the bilateral lower lobes (Fig. 2a) and partial ground-glass opacities in the upper areas of the left lung (Fig. 2b). However, there was no evidence of deep vein thrombosis or massive pulmonary embolism in main pulmonary artery (Fig. 2c). These findings suggested

Abbreviations:

CT	*Computed tomography*
HPV	*Hypoxic pulmonary vasoconstriction*
IPF	*Idiopathic pulmonary fibrosis*
IPF-AE	*Acute exacerbation of idiopathic pulmonary fibrosis*
LV	*Left ventricle*
MPT	*Methylprednisolone pulse therapy*
PH	*Pulmonary hypertension*
RV	*Right ventricle*
TRPG	*Tricuspid regurgitation peak gradient*
TTE	*Transthoracic echocardiography*

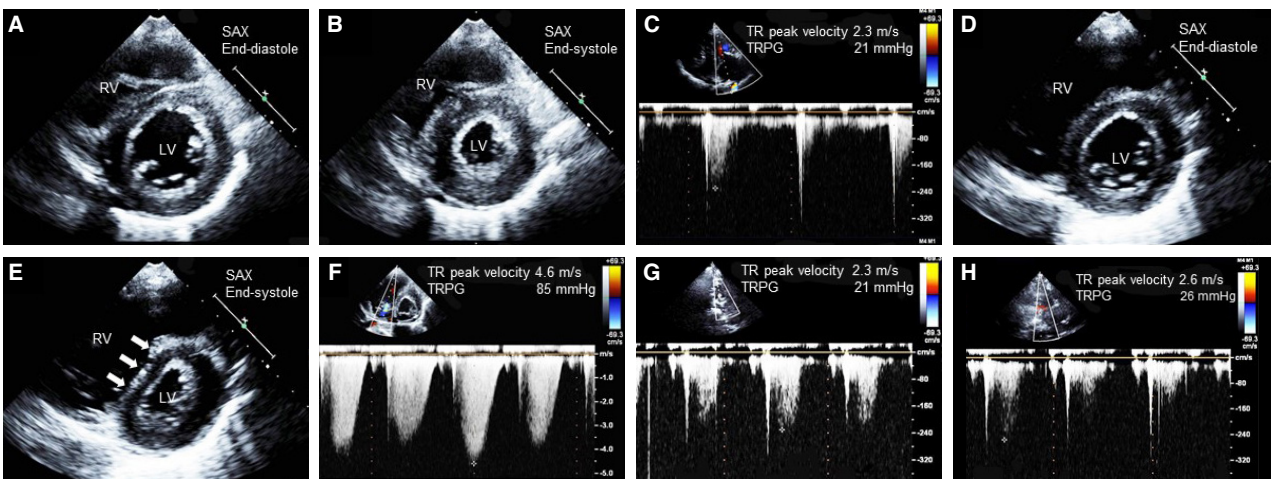

Figure 1. Transthoracic echocardiograms: **(A-C)** on admission, **(D-F)** 5 days after admission, **(G)** 10 days after admission, (H) 25 days after admission. **(A)** The tricuspid regurgitation (TR) peak velocity is 2.3 m/s and the tricuspid regurgitation peak gradient (TRPG) is 21 mmHg. The parasternal short axis (SAX) view at the level of the papillary muscle in the end-diastolic phase; **(B)** There is no evidence of flattening of the interventricular septum. The parasternal SAX view at the level of the papillary muscle in the end-systolic phase. **(C)** There is no evidence of flattening of the interventricular septum; the TR peak velocity is 4.6 m/s and the TRPG is 85 mmHg; **(D)** The parasternal SAX view at the level of the papillary muscle in the end-diastolic phase; **(E)** Right ventricle dilatation and a slightly flattened interventricular septum are visible; **(F)** The parasternal SAX view at the level of the papillary muscle in the end-systolic phase illustrating flattening of the interventricular septum (arrow); **(G)** The TR peak velocity is 2.3 m/s and the TRPG is 21 mmHg; **(H)** The TR peak velocity is 2.6 m/s and the TRPG is 26 mmHg. LV: Left ventricle; RV: Right ventricle; SAX: Short axis view; TR: Tricuspid regurgitation; TRPG: Tricuspid regurgitation peak gradient.

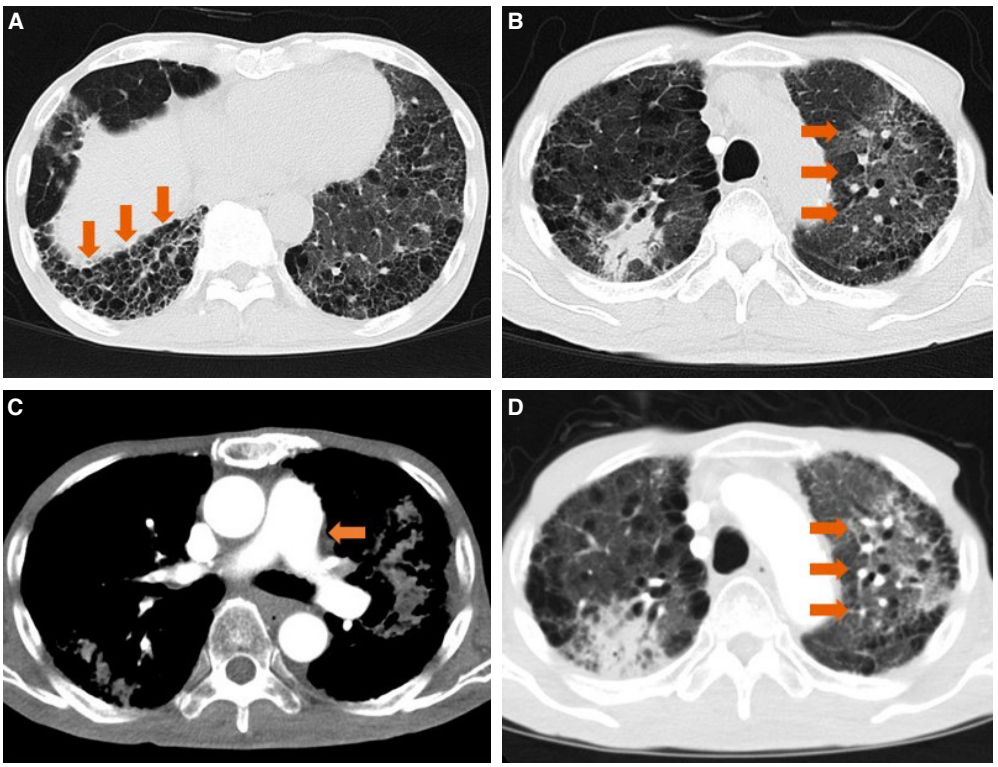

Figure 2. High resolution computed tomography images: **(A-C)** 5 days after admission and **(D)** 25 days after admission. **(A)** The honeycomb appearance (arrow) seen in the subpleural area of the bilateral lower lobes; **(B)** The partial ground-glass opacities (arrow) observed in the upper areas of the lungs; **(C)** There was no evidence of massive pulmonary embolism in the main pulmonary artery (arrow); **(D)** The partial ground-glass opacities (arrow) seen in the upper areas of the lungs.

severe PH and the possible involvement of extreme hypoxia consistent with IPF-AE. Since this episode occurred suddenly during a CT examination, his initial treatment was delayed. Methylprednisolone pulse therapy (MPT) was administered. The IPF-AE ameliorated immediately and the oxygen saturation rate improved to 95% while breathing 4 L/min oxygen. The echocardiographic parameters also improved [TRPG: 21 mmHg (Fig. 1g), and there was no evidence of RV dilatation (RV basal diameter: 42.5 mm; RV mid-cavity diameter: 39.1 mm; RV longitudinal diameter: 78.7 mm), and RV/LV basal diameter ratio: 0.99)]. There was a relapse of IPF-AE 25 days after admission. CT showed an area of partial ground-glass opacities in the upper areas of the left lung that was worse than the previous episode of IPE-AE (Fig. 2d), and his oxygen saturation rate declined to 74% while breathing 4 L/min oxygen. Atrial blood gas analysis could not be performed because the patient did not agree to undergo an invasive examination. The TRPG did not become elevated, however, with a value of 26 mmHg (Fig. 1h). MPT was re-administered, but the patient died 35 days after admission.

DISCUSSION

PH is recognized as a potentially lethal complication of IPF[1] and is classified into 2 types: slow progression and acute onset. Almost all cases of IPF-PH are the slowly progressive type, in which vascular remodeling or thrombosis causes the loss of pulmonary arterial lumen leading to the elevation of pulmonary arterial pressure. Slowly progressive IPF-PH occurs in 60% of end-stage IPF cases.[2] The acute-onset type is relatively rare and clinically it often mimics an acute pulmonary embolism, which was excluded in our case with enhanced CT imaging. Acute onset cases may be attributable to hypoxic PH caused by HPV. However, not all hypoxic cases result in HPV, which depends on various factors, such as extracellular-pH, PCO_2, temperature, age, and, iron status. HPV has 2 phases. First, an acute phase develops in 0 to 30 minutes. Next, HPV transitions to a sustained phase

in which the hypoxia is prolonged for more than 30 minutes.[3,4] In our case, echocardiographic changes compatible with acute onset IPF-PH were observed in the first hypoxic episode, but did not appear in the second episode. The exact mechanism of the divergent response of HPV remains to be explained, but hypercapnia due to delayed initial treatment may have the potential to evoke HPV. Moreover, acidemia due to the use of prednisolone may account in part for the event. The development of HPV can cause hypoxic PH and right heart failure, and has a poor prognosis.[5] Zhao et al.[6] reported that sildenafil inhibited hypoxic PH in the acute-onset type of IPF in experimental animals. However, the evidence related to the treatment of acute onset IPF in a clinical setting is limited and there is currently no recommendation in the European Society of Cardiology/European Respiratory Society guidelines.[7] Therefore, to determine the evidence for the treatment of acute onset IPF it is important to detect the presence of IPF-PH using echocardiography. To the best of our knowledge, this is the first report of different echocardiographic changes with or without hypoxic PH due to IPF-AE.

This was a case of a different course of hypoxia with IPF. Hypoxia does not necessarily cause hypoxic PH, but it can become worse in the event of delayed diagnosis and treatment. Echocardiography is a useful examination to evaluate an early diagnosis of PH.

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