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Case report

# Here's the rub: A case of constrictive pericarditis in an adult with cystic fibrosis

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ABSTRACT

We present a rare coexistence of constrictive pericarditis in a patient with cystic fibrosis. Careful attention to cardiac friction rub auscultated on initial examination prompted echocardiography revealing constrictive pericarditis further confirmed by cardiac magnetic resonance imaging that allowed for dedicated treatment in addition to management of his concurrent respiratory infection.

## 1. History of presentation

A 31-year-old male with cystic fibrosis (CF) presented with 5 days of fever, chills, fatigue, shortness of breath, and cough. He also complained of increasing abdominal girth, new bilateral lower extremity swelling, and 20-pound weight gain. Physical examination revealed fever, scattered pulmonary rales, and an unexpected pericardial friction rub. Chest computed tomography showed ground glass consolidation in the right lung base and small bilateral pleural effusions. He was admitted for CF exacerbation secondary to bacterial pneumonia and later developed squeezing chest pain and worsening dyspnea. Re-examination revealed jugular venous distention, more pronounced pericardial friction rub, and pulsus paradoxus of 16 mmHg.

## 2. Past medical history

Complicating his deltaF508 homozygous CF, past history included exocrine pancreatic insufficiency, chronic pansinusitis, type 1 diabetes, and short gut syndrome from distant prior bowel resections. Recently, hospitalizations for CF-related respiratory infections occurred 6–8 times per year.

## 3. Differential diagnosis

Given the extent of his lung disease and clinical signs of volume overload, the differential included right heart failure due to pulmonary hypertension, pulmonic or tricuspid valve disease, and pericarditis with effusion due to adjacent lung inflammation or viral or tuberculous pericarditis.

## 4. Investigations

Electrocardiogram revealed sinus tachycardia with subtle electrical alternans. Urgent transthoracic echocardiogram revealed multiple features concerning for pericardial constriction including thickened pericardium, respiratory variation of the mitral and tricuspid Doppler inflow velocities, septal bounce, and increased diastolic flow reversal on hepatic vein Doppler during expiration (Fig. 1, 2A-B). A trivial, circumferential pericardial effusion without evidence of tamponade was also present. Constrictive findings were further confirmed with cardiac magnetic resonance imaging (cMRI) revealing thickened pericardium at 7 mm with ventricular interdependence despite no fibrosis (Fig. 2C–D). Diuresis was continued to euvolemia and colchicine used to treat the inflammatory state manifest by elevation of erythrocyte sedimentation rate and C-reactive protein.

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**Abbreviations list**

| | |
|---|---|
| ECG | Electrocardiogram |
| TTE | transthoracic echocardiogram |
| cMRI | cardiac magnetic resonance imaging |
| CP | constrictive pericarditis |
| CF | cystic fibrosis |
| PCWP | pulmonary capillary wedge pressure |
| E | early diastolic transmitral inflow velocity |
| e' | early diastolic velocity of the mitral annulus |

Additionally, pulsus paradoxus greater than 10 mmHg during inspiration is reported in less than one-third of patients with CP unless an effusion is present to further restrict expansion of the right ventricle. Perturbations of jugular venous pressure as described by Kussmaul and Friedreich are also characteristic of CP. With our patient's pulsus paradoxus of 16 mmHg in the presence of a circumferential effusion, friction rub, and elevated inflammatory markers, his presentation was likely a product of acute pericarditis that evolved into an effusive-CP.

While no specific electrocardiogram findings exist for CP, multiple echocardiographic anomalies are associated with the condition. Annulus paradoxus is a hallmark of CP that differentiates it from myocardial disease [6]. This phenomenon involves a reversal of the normal, positive relationship between left-sided filling pressures and ratio of early diastolic blood flow across the mitral valve. In most cases of elevated pulmonary capillary wedge pressure (PCWP), early diastolic transmitral inflow velocity (E) increases while mitral annular velocity (e') is reduced thus setting up a positive correlation between PCWP and E:e' ratio. However in CP, pericardial limitations to lateral expansion accentuate longitudinal movement of the mitral annulus which increases e' despite elevated PCWP and thereby creates the inverse relationship between PCWP and E:e'. Additionally, while the medial/septal portion of the mitral annulus moves freely, the lateral portion is often restricted by fibrotic pericardium causing a characteristic annulus reversus as e' medial overtakes e' lateral. Other echocardiographic characteristics include hepatic vein expiratory diastolic flow reversal, respiratory variation in transmitral and transtricuspid flow (>25%, >40% respectively), and ventricular septal shift with respiration [7]. cMRI in CP allows for assessment of pericardial thickening, ventricular interdependence, and potential reversibility with medical management.

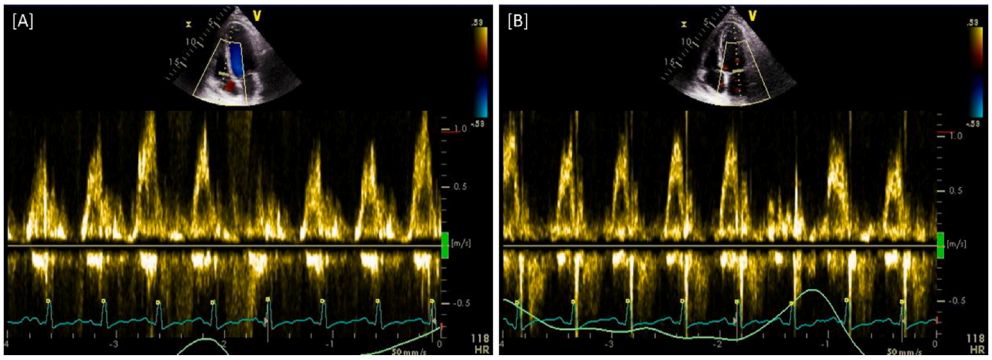


**Fig. 1.** *Respiratory Variation of Transvalvular Flow.* [A] Tricuspid Doppler inflow velocity increases through peak inspiratory efforts with a significant, sudden decrease upon expiration while [B] Mitral Doppler inflow velocity is suddenly reduced upon inspiratory efforts as seen by the lime green respiratory tracing along the bottom of each graphic. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

## 5. Management

Oral colchicine led to friction rub resolution by hospital day 4 and loop diuretics facilitated return to euvolemia. Usual therapies for CF exacerbation enabled pulmonary recovery and discharge home.

## 6. Discussion

Constrictive pericarditis (CP) is a disease of restrictive, inelastic pericardium that limits cardiac filling and manifests with signs and symptoms of right heart failure such as dyspnea on exertion, increased venous pressure, and peripheral edema [1]. Many signs and symptoms of severe CF are similar to those seen in CP. Dyspnea, fatigue, and cough are common with CF pulmonary disease while deficiencies in gastrointestinal absorption may lead to malnutrition, hypoalbuminemia, and edema [2]. As the median age of survival of patients with CF has risen, increased frequency of non-pulmonary complications – e.g. pulmonary hypertension, right heart dysfunction, cor pulmonale – have emerged [2]. CP itself is a rare disorder; most commonly idiopathic or viral in etiology. However, it can be associated with post-surgical or radiation changes as well as other systemic disorders and infections such as sarcoidosis, malignancy, and tuberculosis. Pericarditis has rarely been reported in patients with CF and the constrictive phenotype is extremely rare as most cases in this population involve transient inflammatory responses to pulmonary infections [1,3,4]. In our patient, who represents only the 3rd reported case of CP in a patient with CF, recurrent pneumonia associated with lung inflammation adjacent to the pericardium likely triggered acute pericarditis that conferred excessive tissue damage resulting in constriction [3,4].

The key finding that led to additional workup was the presence of a pericardial friction rub, which is more specific for acute pericarditis. In fact, the most common auscultatory finding in CP is a pericardial knock, reported in 47% of cases in one series, compared to rubs in only 16% [5].

Given his constellation of physical exam and imaging findings, our patient had early stage (subacute) disease and was appropriate for a guideline-based trial of medical management with non-steroidal anti-inflammatory drugs and colchicine for three months before reassessment. Diuretics were also administered as a supportive measure to achieve euvolemia. For patients whose symptoms or imaging findings persist at follow-up, a steroid course or immune modulating agent is warranted before considering cardiothoracic surgery evaluation. Pericardiectomy is the definitive management strategy of chronic CP. While surgical removal of fibrotic pericardium has been shown in one study to confer symptom resolution in up to 69% of patients at 4 years, the procedure carries significant mortality risk between 4 and 8%, and likely higher procedure-based risk in our patient with CF [5].

## 7. Follow-up

After discharge, this patient's condition persisted at 3-month follow-

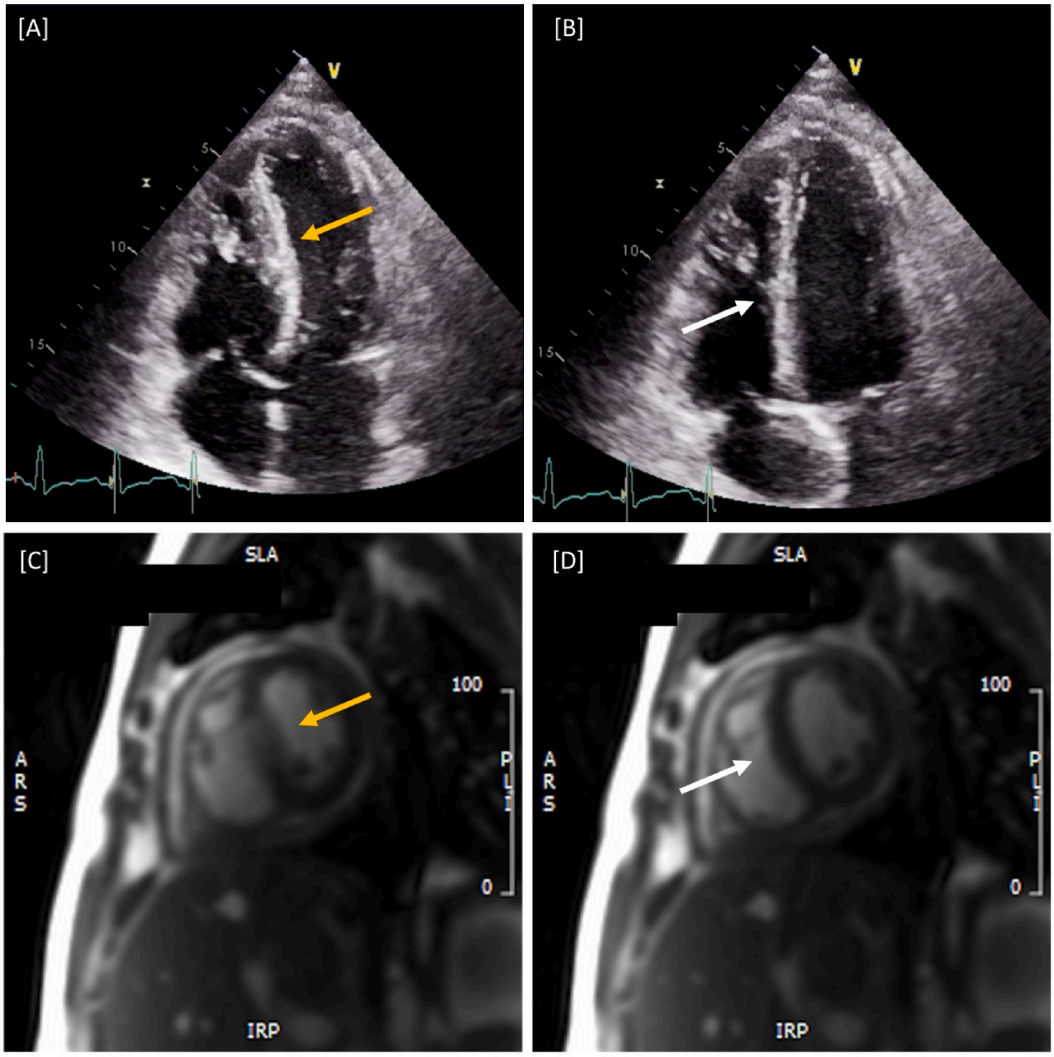


**Fig. 2.** *Paradoxical Septal Motion with Respiratory Variation.* [A-B] Apical Four Chamber Transthoracic Echocardiography and [C-D] Short Axis Cardiac Magnetic Resonance Imaging revealing accentuated septal movement towards the left ventricle (yellow arrows) during inspiration [A, C] with significant septal rebound back into the right ventricle (white arrows) during expiration [B,D] indicative of ventricular interdependence and consistent with constrictive pericarditis. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

up with echocardiogram and cMRI showing continued constriction despite effusion resolution. A course of oral prednisone was started at that time. Repeat echocardiogram at 6-months revealed persistent annulus paradoxus, respiratory variance in transmitral flow velocity of 28%, and a positive "sniff test" demonstrating continued ventricular interdependence. In addition, the echocardiogram now reported annulus reversus, concerning for binding of the lateral wall by newly formed fibrotic pericardium. Despite his now chronic CP, he has been managed with daily diuretics and corticosteroids, as his comorbid conditions make his surgical risk profile unacceptably high.

## 8. Conclusions

We describe the 3rd reported case of concomitant CP and CF. With the overlap in signs and symptoms of these two conditions, close attention to our patient's subtle changes in symptoms and physical examination findings prompted additional evaluation with echocardiogram and cMRI that revealed a subacute, effusive-CP likely triggered by acute pulmonary and pericardial inflammation which, despite optimal medical management, led to formation of fibrotic pericardium and chronic CP at 6 month follow-up.

## Learning objectives

1. To recognize the key clinical exam findings consistent with CP that help differentiate the condition from others
2. To identify hallmark echocardiographic and cMRI findings consistent with CP
3. To understand available medical and surgical treatments for management of CP

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## Declaration of competing interest

The authors have no conflicts of interest to disclose.

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