Constrictive pericarditis as a rare cause of chylothorax: a case report

Camilla Simonsen Lyng1*, Johnny Vegsundvåg2, Alexander Wahba3,4, and Bjørnar Grenne1,4

1Clinic of Cardiology, St. Olavs Hospital, Postbox 3250 Sluppen, Trondheim NO-7006, Norway; 2Department of Cardiology, Ålesund Hospital, PO Box 1600, 6026 Ålesund, Norway; 3Clinic of Thoracic Surgery, St. Olavs Hospital, Trondheim, Norway; and 4Department of Circulation and Medical Imaging, Faculty of Medicine and Health Sciences, Norwegian University of Science and Technology, 7491 Trondheim, Norway

Received 23 May 2018; accepted 18 September 2018; online publish-ahead-of-print 22 October 2018

Background
Chylothorax is a rare clinical condition that results from thoracic duct damage with leakage of chyle from the lymphatic system to the pleural space. Rarely, constrictive pericarditis has been associated with chylothorax, but to our knowledge only in relation to secondary causes such as tuberculosis, HIV, or malignancy.

Case summary
A previously healthy 63-year-old man presented with effusive-constrictive pericarditis, recurrent right-sided pleural effusion, and chylothorax. There was no history of co-morbidities, surgical illness, or cardiac procedures. No single aetiologic factor was identified despite comprehensive assessment. Substantial immunosuppressive therapy was given without a sufficient clinical response. Pericardiectomy resulted in resolution of the constrictive haemodynamics and terminated chylous effusion.

Discussion
The hypothesized mechanisms for development of chylothorax in association with constrictive pericarditis are the increased effective capillary infiltration secondary to central venous hypertension and reduced lymphatic drainage due to high pressure in the left subclavian vein. Increased capillary filtration may result in excessive lymph formation. However, the mechanism is not completely understood.

Keywords
Effusive-constrictive pericarditis • Pleural effusion • Chylothorax • Thoracic duct • Case report

Introduction
Acute pericarditis is a common finding in patients evaluated for chest pain. There are numerous possible causes, both infectious and non-infectious. An infrequent consequence is constrictive pericarditis. Similarly, pleural effusion is common in hospitalized patients, with numerous aetiologies. A rare cause of pleural effusion is chylothorax, attributed to a damaged thoracic duct and characterized by a milky white pleural effusion rich in triglycerides. The damage is most commonly due to trauma or malignancy, particularly lymphomas. However, it has been postulated that any cardiac cause of elevated right-sided venous pressure may potentially lead to chylothorax.

Learning points
• Constrictive pericarditis may occur with the healing of acute fibrinous, serofibrinous pericarditis or chronic pericardial effusion, which in turn results in obliteration of the pericardial cavity and formation of granulation tissue.
• Chylothorax is an uncommon clinical condition, usually associated with trauma or neoplasm.
• Chylothorax due to constrictive pericarditis is rare. It may result from increased effective capillary infiltration secondary to central venous hypertension and reduced lymphatic drainage due to high pressure in the left subclavian vein.
Timeline

Initial presentation
- Gradual onset of chest pain and dyspnoea with elevated C-reactive protein (CRP) and D-dimer. Chest X-ray revealed pleural effusion, and echocardiogram was consistent with effusive constrictive pericarditis. Administration of anti-inflammatory treatment (naproxen + colchicine) was started.

Next 8 months:
- Repeated echocardiography showed regress of pericardial fluid, but persistent constrictive haemodynamics. Right-sided pleural effusion recurred regularly with need of a total of 15 pleurocenteses. Comprehensive investigations did not reveal any underlying aetiology. Cardiac magnetic resonance imaging (MRI) showed persistent pericardial inflammation. Treatment with diuretics, steroids, and eventually the interleukin-1 antagonist anakinra was added. The extensive anti-inflammatory treatment had no effect on symptoms, constrictive haemodynamics, or the recurrence of pleural fluid. However, the systemic inflammatory response did diminish with normalized CRP and D-dimer.

Transfer to university hospital after 9 months:
- Echocardiography, cardiac MRI, and cardiac catheterization with simultaneous left- and right-sided pressure recordings confirmed constrictive pericarditis. No aetiology of the constrictive pericarditis was found.
- Right-sided pleurocentesis demonstrated chylothorax. Lymphoscintigraphy was normal with no signs of physical damage to the thoracic duct or its major branches. Computed tomography scans did not reveal any malignancy or lymphadenopathy.
- After total pericardiectomy there was rapid resolution of symptoms, pleural effusion, and chylothorax.

Post-operative controls 3 and 6 months later:
- Following pericardiectomy, clinical improvement was substantial and the patient resumed full-time physical work. Pleural effusion did not recur, and echocardiograms were normal without evidence of constrictive haemodynamics.

Operative findings demonstrated a calcified, thickened pericardium, with adhesion to the heart. The heart immediately expanded effusions and moderate pericardial effusion (Figure 2A). Transthoracic echocardiogram demonstrated pericardial thickening and effusion, normal ventricular dimensions with good contractility, bi-atrial enlargement, and a distended inferior vena cava without diameter changes on respiration. Doppler recordings demonstrated marked reciprocal respiratory variations in right ventricle (RV) and left ventricle (LV) diastolic inflow velocities, annulus paradoxus, and septal bounce, consistent with the diagnosis of effusive-constrictive pericarditis (Figure 1A–F). Comprehensive testing for infectious or immunological causes were negative (Table 1). Anti-inflammatory treatment [naproxen 500 mg twice a day (b.i.d) and colchicine 0.5 mg b.i.d] was initiated, with a follow-up plan at the outpatient clinic.

One month later, the patient’s symptoms returned, now also including bilateral leg oedema and distended neck veins. Chest X-ray revealed massive right-sided pleural effusion (Figure 2B), and drainage was performed. Analysis of the pleural fluid showed a transudate, with negative tests for malignant cells or microbiological aetiology (Table 1). Thoracic and abdominal CT scans showed no evidence of malignancy or lymphadenopathies. Repeat echocardiography revealed regression of pericardial effusion, and persistent constrictive haemodynamics.

Despite 3 months of anti-inflammatory treatment and diuretics the condition did not improve. Cardiac magnetic resonance imaging (MRI) showed pericardial thickening and late pericardial contrast enhancement after intravenous gadolinium, findings consistent with active pericardial inflammation (Figure 2C). Comprehensive testing for infectious or immunological causes were still negative, and a corticosteroid was added (prednisolone 40 mg q.d). Due to the suspicion of an ongoing inflammatory or immunological process, additional therapy with anakinra (sc 100 mg q.d) was initiated 2 months later, still without clinical response. During the following 6 months of treatment, the patient suffered from recurrent symptomatic right-sided pleural effusion, with the need of a total of 15 pleurocenteses. Approximately 60 L of pleural fluid was drained during this period.

The patient was referred to the University Hospital for further evaluation and treatment. Echocardiography, cardiac MRI, and simultaneous left and right catheterization confirmed the presence of constrictive pericarditis (Figure 3A). There was consistent pericardial thickening. At this point, pericardial effusion was minimal and laboratory findings were normalized with CRP levels <5 mg/L and D-dimer <0.5 mg/L. Drainage of recurrent right-sided pleural effusion now demonstrated a milky/yellowish fluid (Figure 3B). Analysis of the pleural fluid still revealed a transudate but with strikingly elevated triglyceride levels of 4.5 mmol/L (normal reference <1.24 mmol/L) and cholesterol level 1.6 mmol/L (normal reference <5.18 mmol/L), findings diagnostic for chylothorax. Lymphoscintigraphy was normal, with no signs of damage to the thoracic duct or its major branches. In view of chronic constrictive pericarditis with no response to medical therapy and probable secondary chylothorax, the patient was scheduled for surgical pericardiectomy. A complete pericardiectomy through a median sternotomy was performed. Resection of the pericardium extended beyond the left, right, and inferior cardiac border, to the great vessels superiorly and to the diaphragmatic surface and inferior vena cava inferiorly.

Operative findings demonstrated a calcified, thickened pericardium, with adhesion to the heart. The heart immediately expanded...
and the heart rate decreased. Histopathological findings showed pericardial fibrosis with calcifications, while there were no granulomas or carcinomatosis (Figure 3C). Tissue cultures for bacteria, fungi, and mycobacteria were negative. The patient was discharged, anti-inflammatory treatment stopped and corticosteroids gradually withdrawn. During outpatient follow-up 3 and 6 months post-operative, clinical improvement was substantial and the patient resumed full-time physical work. The pleural effusion did not recur (Figure 2D).

Echocardiograms were normal without evidence of constrictive haemodynamics and normal ventricular interdependence.

**Discussion**

Constrictive pericarditis is a chronic inflammatory process leading to pericardial fibrosis, encasing the heart in a fibrotic and usually...
Figure 2  (A) Chest computed tomography at first admission: bilateral pleural effusion; right side 5 cm and left side 3 cm. Pericardial effusion 9 mm. (B) Chest X-ray at second admission: massive right-sided pleural effusion. (C) Cardiac magnetic resonance imaging, with pericardial gadolinium contrast enhancement (arrow). (D) Chest X-ray at post-operative control.

Table 1  Analyses of serum and pleural fluid

- Serology: normal haemogram, CRP 40 mg/L, troponin T 14–<10 ng/L, pro-BNP 148 ng/L, and d-dimer >4 mg/L
- Microbiology: negative: HIV, HCV, HHV6, and Borrelia IgG/IgM
- PCR: negative for M. tuberculosis-complex, adenovirus, CMV, EBV, enterovirus, and coxiella
- Rheumatology: negative ANA/ANCA, RF, anti-GBM, normal IgE and IgG+ subclasses, and normal C3 and C4
- Pleural effusion at second admission: pale yellow, transudate. PH 7.51, glucose 6 mmol/L, albumin 18 g/L, protein 29 g/L, LD 158 UI/L, LD/protein ratio 0.5. The cytology for malignant cells: negative
- Negative for culture of pyogenic organisms as well as M. tuberculosis in serum and pleural effusion
- Microscopy by gram and ZN stain revealed negative results

ANA/ANCA, antinuclear antibody/antineutrophil cytoplasmic antibody; anti-GBM, anti-glomerular basement membrane antibody; CMV, cytomegalovirus; EBV, Epstein-Barr virus; HCV, hepatitis C; HHV-6, human herpesvirus 6; LD, lactic dehydrogenase; RF, rheumatoid factor; ZN, Ziehl-Neelsen.
thickened pericardium. This causes impaired diastolic cardiac function leading to heart failure. Pulmonary congestion is usually not a feature because of reduced right-sided output from compression.

The constraining pericardium results in fixed total cardiac volume and prevents normal transmission of thoracic pressures to the cardiac chambers. The stiff pericardium limits the expansion of the heart, causing elevation, and equalization of diastolic pressures in all cardiac chambers, including caval and pulmonary veins. Furthermore, the fixed cardiac volume necessitates enhanced ventricular interdependence to maintain cardiac output.

Chylothorax is a rare condition with accumulation of chyle in the pleural cavity. The condition is suggested by aspiration of milky white pleural fluid. Pleural effusion with triglyceride levels >1.24 mmol/L (110 mg/dL) and cholesterol levels <5.18 mmol/L (200 mg/dL) are diagnostic of chylothorax. As approximately 2.4 L of chyle is transported through the lymphatic system every day, damage or obstruction of the duct can give rise to a large and rapid accumulation of chyle in the pleural space. Traumatic cases constitute approximately 50% of cases of chylothorax and can be sub-classified as iatrogenic (80%, with cardiothoracic surgery as the leading cause) or non-iatrogenic (20%, with rupture after childbirth, vomiting, and gunshot as common causes). Non-traumatic aetiologies include malignancy (30%), most frequently lymphoma, representing the second most frequent cause of chylothoraces. Other causes include sarcoidosis, inferior vena cava thrombosis, liver cirrhosis, nephrotic syndrome, right heart failure, and diseases of the lymph vessels. Chylothoraces are typically exudative in 86% and transudative in 14% of cases. The transudative profile was found in patients with cirrhosis, nephrotic syndrome, and right heart failure.

Pleural effusions may be found with constrictive pericarditis. However, there are very few reports of chylothorax due to constrictive pericarditis. Explanatory hypotheses postulate that increased systemic venous pressure leads to increased effective capillary filtration and consequently increased lymph production. Furthermore, if pressure rises in the superior vena cava, a parallel increase of pressure can be observed in the thoracic duct. In constrictive pericarditis there is increased pressure in the cervical veins, causing a functional obstacle to the drainage of lymph flow from the thoracic duct. This impairment of thoracic duct outflow might contribute to leakage of chyle in the pleural cavity through hydrostatic forces.
Our patient with constrictive pericarditis presented eventually with chylothorax. The effusive-constrictive pericarditis might have been caused by an acute inflammatory process, and developed to a chronic constrictive pericarditis. Even though the constriction did not resolve on medical treatment, the systemic inflammatory response diminished. Nevertheless, despite comprehensive assessment, no single aetiological cause could be identified.

Conclusion

This case demonstrates a rare concomitance of constrictive pericarditis and chylothorax.

The rapid and lasting resolution of pleural effusion following pericardiectomy strongly suggests that our patient’s chylothorax was indeed secondary to constrictive pericarditis.

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Acknowledgements

The authors thank Rune Wiseth for critical review of the manuscript.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

References