

## **Pericardial Mesothelioma Presenting as Constrictive Pericarditis**

**Brief Title: A Rare Case of Constrictive Pericarditis: Pericardial Mesothelioma**

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**Total word count: 1286**

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**Funding:** None

**Disclosures:** A. Klein: research funding from Kiniksa Pharmaceuticals, Ltd; scientific advisory boards Kiniksa Pharmaceuticals, Ltd., Swedish Orphan Biovitrum AB, Cardiol Therapeutics and Pfizer, Inc

**Data Availability:** Data available upon reasonable request.

**Ethical Statement:** This material is our own work and is not being considered for publication anywhere else.

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## **ABSTRACT**

A 46-year-old woman underwent pericardiocentesis and pericardial window for recurrent pericardial effusion. She presented 17 months later with signs and symptoms consistent with constrictive pericarditis. Cardiac magnetic resonance imaging revealed an infiltrative mass surrounding the pericardium. A transcutaneous core needle biopsy of the pericardium confirmed the diagnosis of pericardial mesothelioma.

## **KEYWORDS:**

Constrictive pericarditis

Malignant pericardial effusion

Pericardial mesothelioma

Cardiac magnetic resonance imaging

## **ABBREVIATIONS**

CMR = Cardiac magnetic resonance

FDG = Fluorodeoxyglucose

PET = Positron emission tomography

## **INTRODUCTION:**

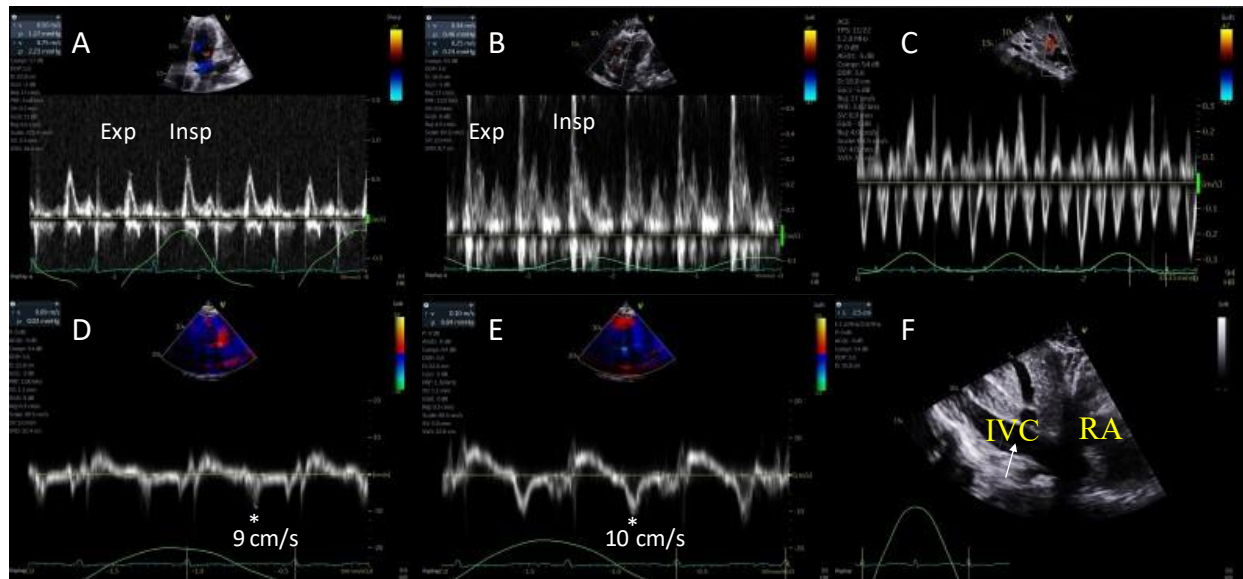
Pericardial mesothelioma is an exceedingly rare primary tumor of the pericardium that carries a guarded prognosis. It is the most common primary malignant pericardial tumor, however far less common than secondary tumors including breast cancer, lung cancer, and malignant melanoma.<sup>1,2</sup> Diagnosis and management can be difficult, as patients may present with non-specific symptoms. Here, we present a case of a middle-aged female who presented with constrictive pericarditis secondary to mesothelioma.

## **CASE PRESENTATION:**

A 46-year-old woman with no significant past medical history presented to an outside hospital in summer 2019 with complaints of shortness of breath and chest discomfort. Transthoracic echocardiogram (TTE) obtained at that time showed a large pericardial effusion with early tamponade physiology. She was admitted to the hospital and subsequently underwent a pericardiocentesis with drainage of 800 ml hemorrhagic fluid that was negative for neoplastic cells. She was discharged on 0.6 mg Colchicine daily, however returned to the hospital with recurrent pericardial effusion prompting a pericardial window procedure. A biopsy of the pericardium revealed mesothelial-lined fibrous tissue with chronic inflammation without evidence of neoplastic cells.

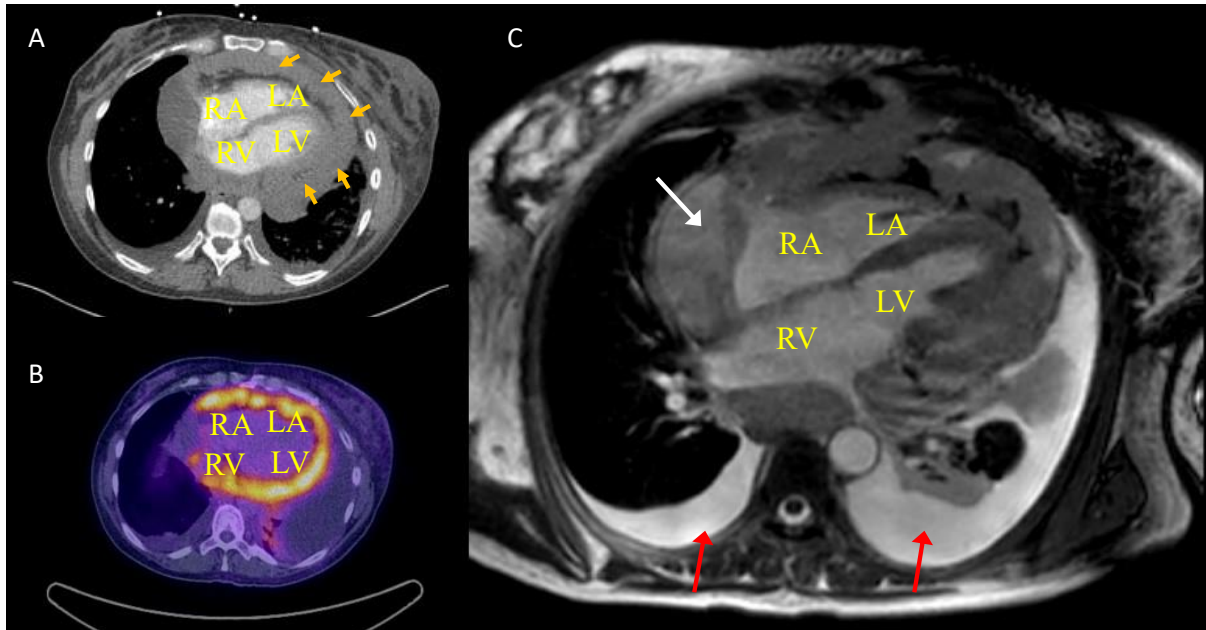
The patient was doing well following the procedure until winter 2020 when she developed progressive dyspnea on exertion, orthopnea, leg swelling, abdominal fullness, and weight gain. She was referred to our pericardial center for evaluation following a right heart catheterization that showed evidence of constrictive physiology. On presentation, physical exam findings were significant for elevated jugular venous pressure (15-20 cm H<sub>2</sub>O), kussmaul's sign, pericardial knock, ascites, and bilateral lower extremity pitting edema. She was admitted for

further management and evaluation. She underwent electrocardiography (EKG) which revealed low voltage and non-specific T-wave inversions. A chest X-ray showed a left-sided pleural effusion. TTE showed a large pericardial effusion adjacent to the right atrium with signs of constrictive physiology including diastolic septal bounce, respirophasic septal shift and variations in the mitral valve and tricuspid valve inflows with inspiration as well as a dilated and plethoric inferior vena cava (Figure 1).



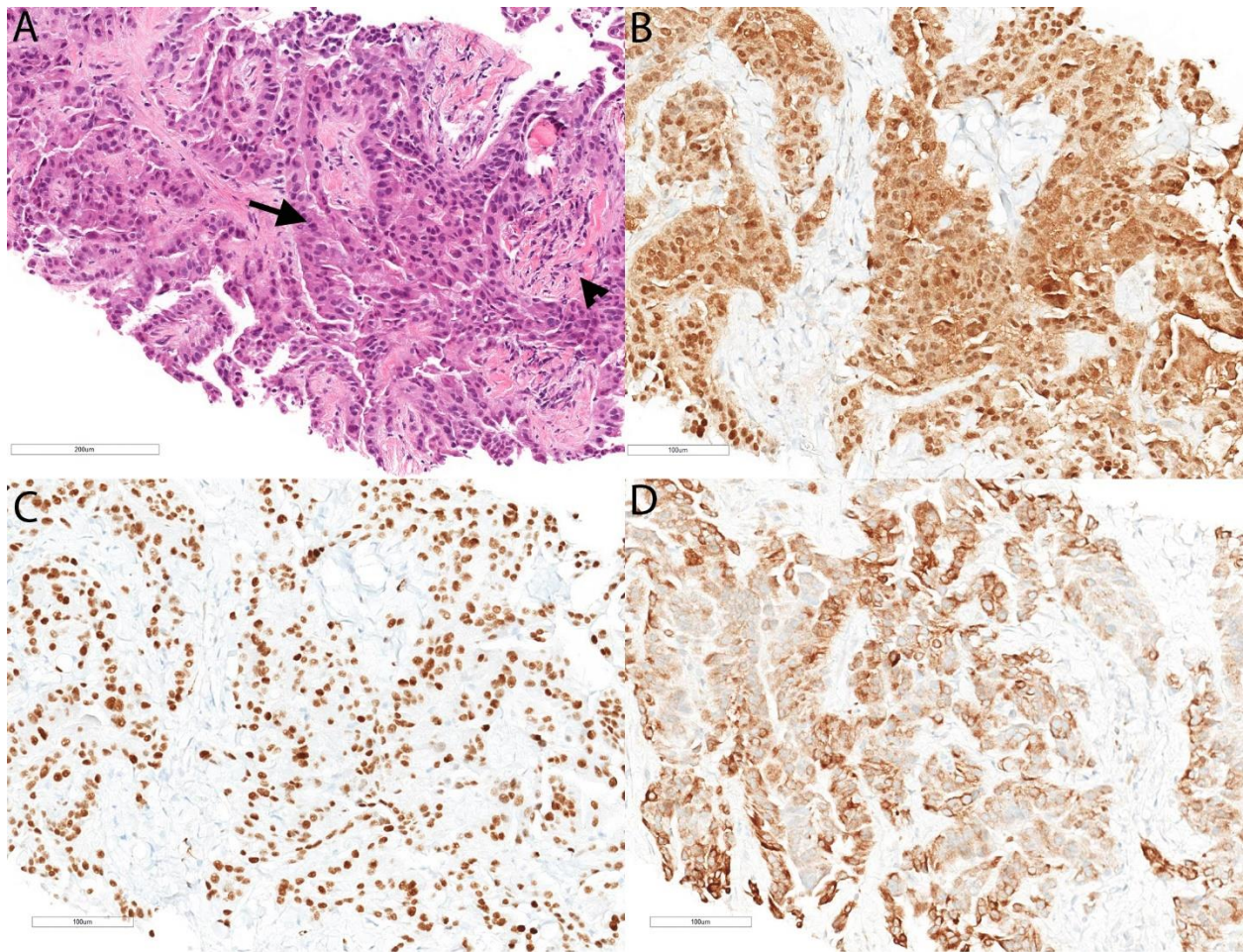
Additionally, an echo dense structure surrounding the heart was appreciated. Cardiac computed tomography and cardiac magnetic resonance imaging (CMR) confirmed the presence of constrictive physiology and a loculated pericardial effusion adjacent to the right atrium (Figure 2A,2B). Moreover, a large circumferential nodular mass surrounding the heart and extending superiorly to the great vessels causing luminal narrowing of the superior vena cava

and the pulmonary veins was described. Positron emission tomography (PET) showed an intense fluorodeoxyglucose (FDG) avid circumferential mass with extensive pericardial nodularity suggestive of neoplasm. No definitive extra-pericardial FDG uptake was found (Figure 2C).



Due to the preload dependence suggested by her imaging, a concern was raised that the patient would not be able to tolerate general anesthesia. A decision was made to proceed with a transcutaneous core needle biopsy of the pericardium. The pathological examination showed an infiltrative epithelioid malignant neoplasm with positive staining for calretinin, cytokeratin 5/6, and Wilms' tumor 1, consistent with pericardial mesothelioma (Figure 3).





The patient initially underwent chemotherapy in spring 2021 with pemetrexed/carboplatin followed by immunotherapy with nivolumab/ipilimumab from summer 2021. Palliative radiation was used adjuvant to immunotherapy. For the recurrent malignant pericardial effusions, she was managed with a pericardial window. The patient was re-admitted to the hospital in spring 2022 due to acute decompensated heart failure and a left pleural effusion. A therapeutic thoracentesis was done with analysis showing exudative effusion and atypical mesothelial cells. She had acute episodes of decompensation due to dyspnea, and atrial fibrillation which was attributed to the increasing size of the pericardial mesothelioma causing

constriction of her cardiac chambers with luminal narrowing of the left inferior pulmonary vein and effacement of the right ventricle outflow tract. Because of the progressive nature of pericardial mesothelioma, the patient decided to proceed with home hospice and unfortunately passed away.

## **DISCUSSION**

Our patient presented early with pericardial effusion, likely due to malignant involvement of the pericardium. Despite cytology examination of the pericardial fluid and a pericardial biopsy, no evidence of malignancy was found. The false-negative rates of pericardial fluid cytology and pericardial biopsy in the detection of malignant pericardial effusions have been reported as 7.9-14.7 % and 40-44.7%, respectively.<sup>3</sup> Thus, the possibility of a false-negative test should not be neglected, particularly in cases with low volume pericardiocentesis (<60 ml), which is associated with a significantly lower diagnostic yield.<sup>4</sup> Hemorrhagic pericardial effusion, such as that found in our patient, should increase the index of suspicion for malignant effusion. As demonstrated in this case, appropriate use of non-invasive multimodality imaging, including PET and CMR, can aid in the diagnosis of malignant involvement of the pericardium and its hemodynamic consequences.

While no standard treatment strategy has been established for pericardial mesothelioma, surgery, radiotherapy, and chemotherapy are commonly used.<sup>5</sup> Complete surgical resection is rarely achieved; however, surgery can be used palliatively for debulking or to relieve constriction. Based on its established safety and efficacy profile in treating mesotheliomas of pleural and peritoneal origin the chemotherapeutic agent pemetrexed is often used in combination with either carboplatin or cisplatin. Immunotherapy is a new addition to the treatment regimen, but no clear survival data exists.

## **CONCLUSIONS**

Pericardial mesothelioma is a rare cause of constrictive pericarditis. Appropriate use of non-invasive multimodality imaging can aid in the evaluation of malignant involvement of the pericardium and its hemodynamic consequences, particularly in cases for which the suspicion of malignant involvement is high.



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## FIGURES:

**Figure 1. Echocardiography features of constrictive pericarditis.** (A) Mitral and (B) tricuspid inflow pulsed wave Doppler showing respiratory (Insp=Inspiration, Exp=Expiration) variation in the inflow velocities, with an inspiratory change of 25.3% and -36% in the mitral and tricuspid inflow velocities respectively. (C) Expiratory diastolic flow reversal in the hepatic vein. Tissue Doppler of the lateral (D) and the medial (E) mitral valve annulus showing higher e' velocity (\*) in the medial annulus compared to the lateral annulus consistent with annulus reversus. (F) Dilated and plethoric inferior vena cava (white arrow) measuring 2.5 cm. *IVC: Inferior Vena Cava, RA: Right Atrium.*

**Figure 2. Multimodality imaging of pericardial mesothelioma.** (A) Axial computed tomography showing a pericardial mass (yellow arrows) surrounding the heart. (B) Cardiac magnetic resonance imaging in the four-chamber view revealing a pericardial mass encasing the heart, a loculated pericardial effusion adjacent to the right atrium (white arrow), and bilateral pleural effusions (red arrows). (C) Positron emission tomography showing a fluorodeoxyglucose avid mass with nodularity involving the pericardium. *LA: Left Atrium, LV: Left Ventricle, RA: Right Atrium, RV: Right Ventricle*

**Figure 3. Pathologic findings in core needle biopsy of pericardial/anterior mediastinal mass.** (A) A malignant epithelioid neoplasm (arrow) infiltrates a fibrous stroma (arrowhead). Hematoxylin-eosin (H&E), original magnification x20. The neoplastic cells were positive for immunohistochemical markers that support mesothelial differentiation, including calretinin (B), WT-1 (C) and CK5/6 (D). All immunohistochemical stains (B-D) are shown at original magnification x20.