Case Report: An Unusual Cause for Recurrent Hemopericardium in a Patient With Dyspnea

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The case concerns a female presenting with dyspnoea resulting from recurrent hemopericardium. Pericardiocentesis, coronary angiography, and extensive laboratory and imaging studies did not reveal the underlying etiology of the hemopericardium. Only after repeat and exploratory surgery, diffuse venous pericardial hemorrhages with localized thrombi typical of angiosarcoma were discovered.

Keywords: hemopericardium, cardiac angiosarcoma, right heart sarcoma, dyspnea, pericardial effusion

INTRODUCTION

Dyspnea is a common symptom in pericardial effusive disease. The etiology of pericardial effusion varies widely but often remains unknown. Primary cardiac tumors are extremely rare (1, 2) and often go undetected until a late stage of the disease.

The present case highlights the importance of considering angiosarcoma of the heart as a potential diagnosis in patients presenting with recurrent pericardial effusion, even in the absence of malignant cells in the pericardial fluid and absence of macroscopic lesions on non-invasive imaging.

CASE DESCRIPTION AND DIAGNOSTIC ASSESSMENT

Part 1

A 52-year-old woman presented at the emergency room (ER) in a regional hospital with progressive dyspnea, a dry cough and fatigue during several weeks despite taking oral antibiotics because of a suspected pneumonia. Three days prior to presentation she had experienced a severe dull thoracic and epigastric pain accompanied by nausea and vomiting that had resolved spontaneously. Besides taking ferrofumarate and cholecalciferol for iron-deficiency anemia and vitamin D deficiency, she had no previous medical history.

On presentation, physical examination revealed a regular tachycardia of 116 beats per minute (bpm), a blood pressure of 120/75 mmHg, an oxygen saturation of 100% while breathing ambient air, and a core temperature of 38.0°C (100.4°F). Cardiac, pulmonary, and abdominal examinations were unremarkable. There were no signs of deep venous thrombosis and the Wells-score was 4.5 (3). The electrocardiogram (ECG) showed sinus tachycardia, normal electrical heart axis and normal PR- and QRS-intervals, but inverted T-waves in both antero- and inferolateral leads (Figure 1). A low hemoglobin level (5 mmol/L), elevated c-reactive protein (102 mg/ml), troponin-I (1036 ng/L, cut-off is <20) and NT-pro-BNP (366 ng/L, normally < 100) levels were the most prominent abnormal laboratory results.
Non-invasive diagnostic workup including ECG, echocardiography, DE-CMR, and CT.

FIGURE 1 | Non-invasive diagnostic workup including ECG, echocardiography, DE-CMR, and CT.

Computed tomography angiography of the thorax (CTA) ruled out pulmonary embolism, but demonstrated pericardial and pleural effusion. Subsequent transthoracic echocardiography (TTE) confirmed circumferential pericardial effusion of \(\sim 4.5 \text{ cm}\) with signs of haemodynamic compromise (dilated and poor collapsing inferior caval vein, early systolic right atrial (RA) collapse and \(>25\%\) respiratory variation in peak mitral E-wave). Urgent evacuation of \(\sim 1 \text{ L}\) of hemorrhagic fluid after pericardiocentesis immediately ameliorated symptoms. Investigation of this pericardial fluid did not reveal a tuberculous, bacterial, viral, or malignant etiology. A respiratory viral panel by polymerase chain reaction (influenzas A and B and respiratory syncytial virus) and a serum HIV antibody test were negative. After recurrent pericardial effusion was ruled out 1 week later, she was discharged home. While unconfirmed, a discharge diagnosis of post-infectious/post-viral pneumonia related pericardial and pleural effusion was made.

Already 5 days later, she presented again with progressive dyspnea, coughing, and nausea. A further decrease in hemoglobin (4.7 mmol/L) was noted and TTE showed recurrent circumferential pericardial effusion (\(\sim 3 \text{ cm}\)) but now a dense structure suggesting thrombus in the pericardial sac (Figure 1). Coronary angiography (CAG) was performed after which coronary artery disease including dissection could be ruled out.

Part 2
She was transferred to a tertiary university center and received a blood transfusion. Additional viral serology (adenovirus, coxsackievirus, echovirus, borrelia burgdorferi, cytomegalovirus, Epstein-Barr virus, and parvovirus), immunological testing (systemic lupus erythematosus, rheumatoid arthritis, vasculitis, complement screening, and M-protein), a tuberculosis test and blood culture analyses were normal. To re-assess the possibility of a malignant cause, a repeat CTA of the thorax and abdomen was performed. While macroscopic malignancies could be ruled out, the scan showed contrast extravasation into the pericardial space, suggesting active bleeding. After a multidisciplinary consultation between cardiologists and cardiothoracic surgeons, and given the
observation that the patient remained hemodynamically stable, it
was decided that urgent surgery was not yet indicated and that
there was still sufficient time for additional diagnostic workup.
On cine cardiac magnetic resonance imaging (CMR), left (LV)
and right ventricular (RV) systolic function were preserved and
pleural and pericardial effusion confirmed. During contraction,
the LV apex remained remarkably “fixed” to the pericardium
(Supplementary Video 1). On the delayed enhancement (DE)
images, the high intra-pericardial signal again suggested contrast-
e extravasation into the pericardial sac, whereas an extensive,
hypo-enhanced circumferential layer against the inner parietal
pericardium suggested thrombus (Figure 1). No intramyocardial
abnormalities were observed.

It was concluded that ongoing, albeit slow, intra-pericardial
bleeding was present. Since other diagnostic clues were missing at
this time, an initial post-viral and subsequent recurrent traumatic
or reactive pericardial effusion after pericardiocentesis were still
considered causative and urgent surgery was yet indicated.

Part 3
Since focal bleeding from a traumatic ventricular lesion after
initial pericardiocentesis could not be excluded, it was decided to
first perform a limited thoracotomy via a left-sided submammary
incision. After evacuating 2.5 L hemorrhagic pericardial fluid
with thrombi, careful inspection did not reveal a focal bleeding
site. Because of persistent bleeding, the incision was extended
further but again no focal bleeding source was discernable.
Instead, multiple active venous hemorrhages on the entire
epicardium were visible and hemostasis was attempted by placing
multiple fibrin sealant patches Tachosil (Baxter healthcare
cooperation, Illinois, USA). In addition, multiple biopsies of the
pericardium and pericardial fluid and thrombi were sent for
pathological examination.

The patient was subsequently transferred to the intensive
care unit (ICU), but went into cardiogenic shock the following
day. TTE showed recurrent pericardial effusion with a thrombus
compressing the RA. A conventional emergency sternotomy was
carried out. After thrombus removal, again diffuse hemorrhages
were observed and a single bleeding focus in the RA was sutured.

Unfortunately, within 3 days she had to be operated two
more times to relief recurrent cardiac tamponade and a
left-sided hemothorax. Repeatedly, extensive diffuse venous
epicardial hemorrhages were found that were difficult to
manage, causing her to remain hemodynamically unstable in the
ICU. After 9 days, pathology of the pericardium revealed an
epithelioid angiosarcoma with unfavorable prognosis. Refrain from more surgeries.

DISCUSSION AND PATIENT PERSPECTIVE

Dyspnea, fatigue, thoracic pain, nausea, anorexia, and
vomiting are common symptoms in pericardial effusive
disease. The etiology of pericardial effusion often remains
unknown but may be caused by malignancies that are
mostly metastatic, complications of myocardial infarction,
infections or iatrogenic. Differentiating between primary
cardiac malignancies and other causes of pericardial

FIGURE 2 | Figure showcasing the timeline of events.
effusion should be accomplished using non-invasive imaging, CAG, cytological and ideally histological investigation of pericardial effusion and tissue specimen, respectively (4).

Primary cardiac tumors are extremely rare with an autopsy incidence of <0.06% (1, 2) of which one quarter turns out to be malignant. Angiosarcoma is the most common primary cardiac malignancy (5) and has been first reported in 1934 by Barnes et al. (6). Cardiac angiosarcomas are aggressive tumors and are often fatal and metastases are found in the majority of patients (66–89%) at time of diagnosis (7).

Angiosarcomas are soft-tissue sarcomas of endothelial cell origin that may show features of vascular and/or lymphatic differentiation. The majority of angiosarcomas arise in the RA (8) in contrast to intimal or unclassified sarcomas, which typically arise from the left atrium or inter-atrial septum (9). Common sites of extension are the right coronary artery, myocardium of the LV and RV, superior and inferior caval vein, pericardium, and mediastinum.

Early diagnosis of cardiac angiosarcoma is difficult. Non-specific symptoms and disease rarity often prevent clinicians from inclusion in the initial differential diagnosis (2).
Previous cases have described angiosarcomas as irregular lobulated masses extending into the pericardium and adjacent vessels and have demonstrated non-invasive imaging modalities to be useful (10).

CAG is generally recommended to rule out coronary artery disease and dissection (4). Pericardiocentesis is indicated in case of hemodynamic compromise (4), and to obtain material for cytological examination, although initially rarely yielding a conclusive diagnosis of angiosarcoma (11).

Histological investigation is often needed to finally diagnose angiosarcoma and tissue specimen can be obtained via thoracotomy or imaging-guided biopsy, although biopsies are often non-diagnostic while carrying considerable procedural risk. In the current European guidelines, a diagnostic epicardial/pericardial biopsy is a class IIA/B indication and only recommended after more than 3 weeks of illness (4).

Because cardiac angiosarcomas are rare, no evidence-based guidelines exist for its treatment. Complete surgical resection is indicated in case of a solitary lesion and if resection preserves cardiac integrity (12). Unfortunately, this is often not possible (12) because of its diffuse infiltrative nature. There is insufficient evidence that chemotherapy, radiotherapy or cardiac transplantation may improve survival (13, 14). As a result, prognosis of cardiac angiosarcomas remains poor with survival ranging from 6 to 9 months after diagnosis (13).

Cardiac angiosarcoma turned out to be a devil in disguise in our case and we were misled by the non-diagnostic results of the initial pericardiocentesis, CAG, and imaging results. Only after repeat and exploratory surgery, the diffuse venous pericardial hemorrhages with localized thrombi typical of angiosarcoma were discovered. At that time, the angiosarcoma was already disseminated with focal transmural invasion and only palliative options remained.

In retrospect, pathologically confirming angiosarcoma would have been possible several days earlier (day 12) if we had considered biopsy (either surgical or image-guided) immediately after transfer to our center. Whether this would have changed the outcome is doubtful, given that the tumor was already widely disseminated. Though, earlier diagnosis may have omitted repetitive surgery.

With the present case we would like to stress the importance of considering cardiac angiosarcoma as a potential diagnosis in recurrent pericardial effusion, even when malignant cells are absent in the pericardial fluid and macroscopic lesions on non-invasive imaging cannot (yet) be seen. An atypical clinical course of recurrent pericardial effusion may be typical for angiosarcoma of the heart.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

UN and SB contributed to conception and design of the study and wrote the first drafts of the manuscript. AV, PS, AH, RD, and MP wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2021.755106/full#supplementary-material

Supplementary Video 1 | Chamber cine CMR video.

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