

Case Series

UNCOMMON CAUSES OF MALIGNANT PERICARDIAL EFFUSION – CASE SERIES FROM A TERTIARY CARE CENTRE IN SOUTH INDIA

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ABSTRACT

Pericardial effusion is a condition that occurs when excess fluid accumulates in the pericardial space. Although it can result from different causes, one of the most alarming is malignant pericardial effusion. Malignant pericardial effusion may result from tumor infiltration of the pericardium or from the pressure of mediastinal lymph nodes obstructing the lymphatic drainage. Lung cancer, followed by breast cancer, esophageal cancer, and hematological malignancies like lymphoma are the most frequent cancer types that can result in malignant pericardial effusion. This disorder may develop as a direct invasion by a nearby primary tumor, or it may spread via the blood or lymphatic system. One of the concerning aspects of malignant pericardial effusion is that it may be the first manifestation of an underlying malignancy. Therefore, it is crucial to investigate a rapidly increasing pericardial effusion or an effusion with cardiac tamponade at presentation. Haemorrhagic pericardial fluid effusion is usually secondary to cancer metastases. Pericardial effusion can lead to complications such as cardiac tamponade, cardiovascular collapse, and death. Regardless of the cause, malignant pericardial effusion carries a poor prognosis. Early detection and treatment of cancers help prevent pericardial effusion and tamponade. Metastatic melanoma, Parotid and Endometrial carcinoma, Angiosarcoma, and T lymphoma are rare causes of pericardial effusion, and only a few cases are reported in the literature.

Here, we report these rare cases of malignant pericardial effusion. Out of these five cases, four patients had cardiac tamponade and four patients succumbed to the illness within a few months of diagnosis.

INTRODUCTION

Malignant pericardial effusion is excess fluid accumulation around the heart due to cancer. Malignant pericardial effusion is primarily associated with metastatic spread from solid tumor or hematological malignancy.^[1] The patients can be asymptomatic at presentation, or can present with cough, dyspnoea, chest pain, etc. The range of the clinical presentation can vary from an effusion that is asymptomatic to cardiac tamponade. The common carcinomas associated with pericardial effusion are carcinoma lung, breast, gastrointestinal malignancy, and B cell lymphoma.^[1] Primary cardiac tumours and pericardial tumours less commonly cause pericardial effusion.^[2] In malignant pericardial effusions, accumulation of pericardial fluid is usually due to obstruction of lymphatic and venous drainage of the heart and this raises intra pericardial pressure. This pressure elevation is influenced by the speed of fluid

accumulation, the compliance of the pericardium, and intravascular volume.^[3]

Common causes for pericardial effusion in cancer patients include metastatic spread, drug and radiation-induced pericarditis and idiopathic pericarditis.^[4] Cancer-related pericardial effusion is usually as a result of secondary tumour localization to the pericardium. In the cases of cancer patients with recurrent pericardial effusion, malignancy must be suspected even if malignant cells are absent in pericardial fluid.^[4]

In this case series, we report five distinct malignancies associated with pericardial effusion. The underlying cancers included metastatic melanoma, parotid carcinoma, endometrial carcinoma, primary cardiac angiosarcoma, and T-lymphoblastic lymphoma. Among these five patients, four developed cardiac tamponade.

Table 1 presents the relevant blood investigations and pericardial fluid analysis findings for each case.

CASE 1

A 52-year-old male was admitted with complaints of chest pain and breathlessness for the past five days. He had a history of liver melanoma, for which he underwent right hepatectomy followed by radiation therapy three years ago. He had no other known comorbidities. On admission, the pulse rate was 88/min, blood pressure was 100/60 mm of Hg, and oxygen saturation (SPO₂) was 99%. Cardiovascular system examination revealed muffled heart sounds. Chest X-ray showed cardiomegaly with pericardial effusion. Echocardiogram showed a massive pericardial effusion 4cm on the right ventricular side with right ventricular collapse during diastole, suggestive of cardiac tamponade physiology. A pigtail catheter was inserted into the pericardium, and 800 millilitres of hemorrhagic fluid was aspirated. CECT (Contrast-Enhanced Computed Tomography) of his chest showed a heterogeneously enhancing soft tissue density lesion confined within the pericardial cavity along with a moderate pericardial effusion. Cardiac MRI (Magnetic resonance imaging) was performed, which revealed a hyperintense soft tissue lesion showing diffusion restriction noted adherent to the epicardial surface of the left ventricle, with infiltration into left ventricular myocardium, and that lesion was projecting into the pericardium (Figure 1A,1B,1C).



Figure 1A: Shows the STIR Axial cardiac MRI image – Case 1

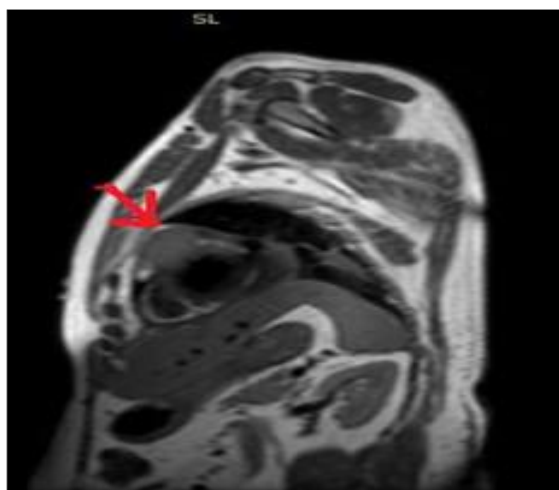


Figure 1B: T1 Sagittal image of cardiac MRI – Case 1

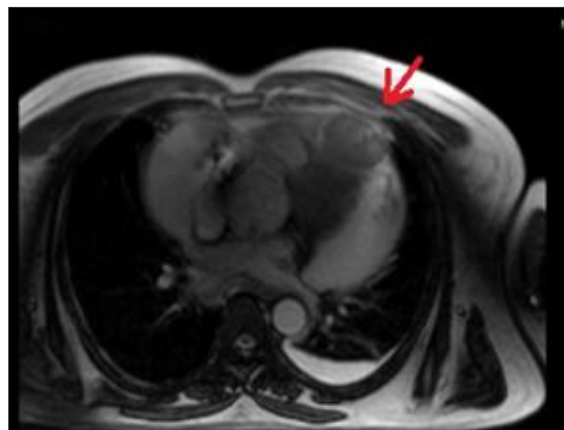


Figure 1C: T2 Axial images of cardiac MRI – Case 1

An ultrasound-guided fine needle aspiration cytology (FNAC) from the lesion was done, which showed malignant cells (Figure 2). Pericardial fluid cytology showed the presence of neoplastic cells. Cardiac mass biopsy confirmed the diagnosis of a metastatic melanoma with pericardial effusion. The patient's breathlessness worsened after 10 days. Repeat echocardiogram showed the presence of cardiac tamponade, and fluid was again aspirated. He was then taken to the radiotherapy department, where he was treated with Tab Temozolomide 100 mg for five days.

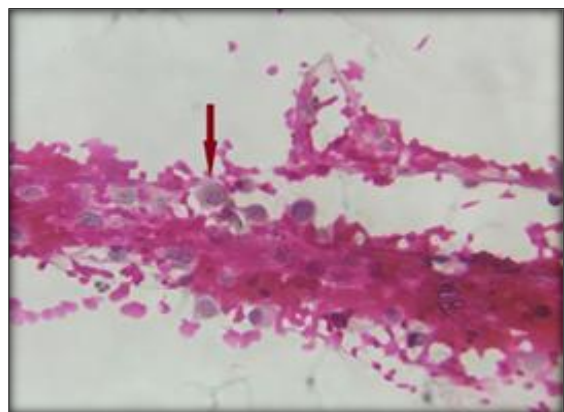


Figure 2: Malignant cells seen in the FNAC of the pericardial mass – Case 1

The pigtail catheter was removed after 20 days, and the patient was discharged. However, he was readmitted after a week with worsening breathlessness, and unfortunately, he could not be saved.

This patient was admitted with pericardial effusion together with cardiac mass, and a previous history of liver melanoma, and cardiac mass biopsy confirmed melanoma. So the diagnosis was metastatic melanoma, with pericardial effusion and tamponade.

CASE 2

A 55-year-old male, who had no prior comorbidities, initially presented with a right parotid swelling that had been increasing in size over one year. The parotid mass caused difficulty in opening the mouth. FNAC from the lesion showed adenocarcinoma of the

parotid. An MRI of the region showed parotid gland swelling in the superficial lobe of the right gland with deep lobe infiltration. The patient underwent extended radical parotidectomy and clearance of the right 1b and 2a lymph nodes with a primary closure. After the surgery, he completed a two-month course of radiotherapy.

The patient was readmitted 3 months after surgery due to breathlessness and back pain. His vital signs at presentation were pulse rate 92 per minute, blood pressure 90/60 mm Hg, respiratory rate of 28/minute, and oxygen saturation 90%. CT (Computed Tomography) chest showed pleural effusion on the right side and moderate pericardial effusion. He was treated with Tab. Lenvatinib. Since his breathlessness was not relieved with regular medications, he was readmitted. At the time of admission, he was dyspneic, and heart sounds were muffled. His electrocardiogram (ECG) revealed low-voltage complexes, and echocardiogram showed cardiac tamponade physiology (Figure 3). The patient was immediately shifted to the cardiac ICU, a pigtail catheter was inserted and 800 millilitres of blood-stained pericardial fluid was drained. His pericardial fluid analysis showed a positive cytology. This patient, who had parotid adenocarcinoma, presented with massive pericardial effusion, tamponade, and a positive cytology in pericardial fluid. Hence, a diagnosis of adenocarcinoma parotid with malignant pericardial effusion was made.



Figure 3: Echo showing pericardial effusion with RV diastolic collapse – Case 2

Despite multiple episodes of pericardiocentesis, his condition worsened, and he eventually required mechanical ventilation. Unfortunately, he could not be revived.

CASE 3

A 63-year-old female was admitted with breathlessness and cough for the past month. She had a history of endometrial carcinoma, T3N1 stage 3, one year ago. She had undergone hysterectomy, bilateral salpingectomy, right ovariectomy, and pelvic lymph node dissection. She received chemotherapy, but she was not on regular follow-up. On

examination, pulse rate-110/minute, blood pressure-100/60 mm of Hg, and respiratory rate-28/minute. Upon admission, she was dyspnoeic with SPO2 less than 90%, so she was admitted to the ICU. She had pallor and grade 3 finger clubbing. The cardiovascular system examination showed muffled heart sounds and elevated JVP. Chest x-ray showed a large pericardial effusion, and ECG showed low-voltage complexes. Echocardiogram performed in the ICU showed a large pericardial effusion with cardiac tamponade. Pericardiocentesis was performed, draining more than 800 ml of haemorrhagic fluid. CECT chest didn't show anything apart from pericardial effusion (Figure 4). Her pericardial fluid cytology was positive for neoplastic cells. So the patient with a history of endometrial carcinoma presented with large pericardial effusion and cardiac tamponade with positive cytology. Hence, the diagnosis of carcinoma of the endometrium with malignant pericardial effusion was made. The patient was treated with chemotherapy. However, after one month of treatment, the patient expired.

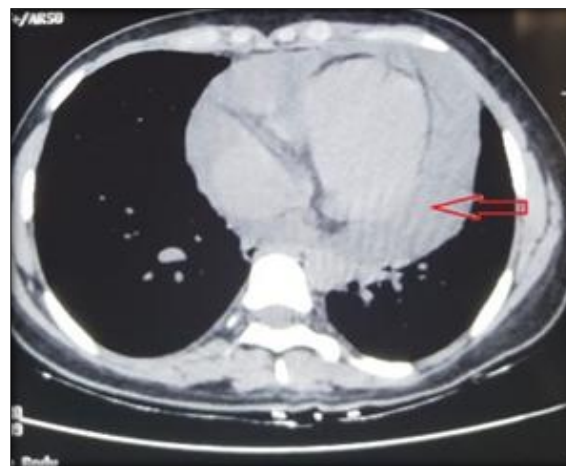


Figure 4: CT chest showing pericardial effusion - Case 3

CASE 4

A 51-year-old male presented to an outside hospital 5 months ago with complaints of fever for three days, vomiting, and presyncope for one day. He was found to be hypotensive. ECG revealed atrial tachycardia with 2:1 AV block, for which he underwent cardioversion. Echocardiogram showed moderate pericardial effusion. In the following days, the effusion progressed to cardiac tamponade, and he underwent pericardiocentesis and was drained of 600 ml of hemorrhagic fluid. Suitable investigations and imaging ruled out infectious, malignant, and rheumatologic causes of pericardial effusion. Considering the high prevalence of tuberculosis, ATT was started. He presented to our hospital three months later with progressively worsened dyspnoea. Echocardiogram done at our hospital showed a mass measuring 3.6cm x3.4 cm seen on the anterior surface of the right atrium, and another cystic mass of

approximately 16.1cm x 6.41 cm is seen along the lateral border of the right atrium and right ventricle side, compressing both chambers with large pericardial effusion. CECT chest and abdomen showed a cardiac mass lesion involving the pericardial cavity with infiltration of the right myocardium, possibly primary pericardial malignancy. Imaging also showed lung, liver, and vertebral metastases. Cardiac MRI was also taken for further characterisation, which demonstrated a malignant mass arising from the right atrium with infiltration of the pericardium, probably cardiac angiosarcoma (figure 5). But cytology of pericardial fluid, cytology of pleural fluid, or USG-guided liver biopsy didn't yield any malignant cells. A pericardial biopsy was planned, but unfortunately, the patient expired before the procedure could be performed. Considering the imaging appearances, primary cardiac angiosarcoma was kept as the most probable diagnosis.

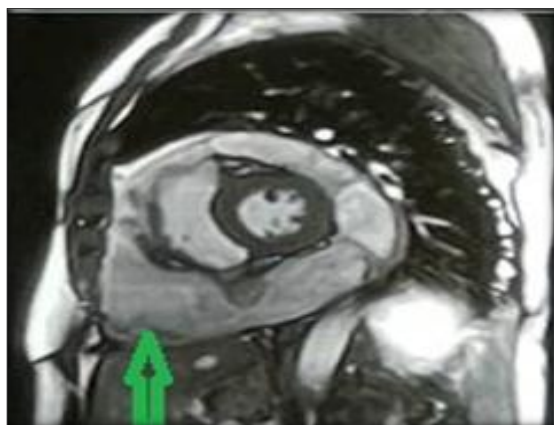


Figure 5: Cardiac MRI image of Angiosarcoma – Case 4

CASE 5

A 26-year-old male who was working abroad presented with a history of headache and cough for the past 10 days. The patient also had breathlessness and chest pain for the past week. He had a history of polytrauma one year back and an implant on his leg. His vitals were pulse rate of 76/minute, blood pressure of 130/80 mm of Hg, and oxygen saturation

of 96%. Further examination showed muffled heart sounds. ECG showed low-voltage complexes. His system examination revealed diminished breath sounds on the left side. Chest X ray showed a mediastinal mass with pericardial effusion (Figure 6). His contrast-enhanced CT chest showed a large anterior mediastinal mass with moderate pleural effusion on the left side and mild pericardial effusion, mostly suggestive of lymphoma. Echocardiogram showed moderate pericardial effusion 6 mm on the right ventricular side. His blood investigations are shown in Table 1. All tumour markers were negative. Cardiology opinion taken for pericardial effusion and pericardiocentesis was not advised as there were no signs of tamponade. Ultrasound-guided biopsy taken from the mediastinal mass revealed T lymphoblastic lymphoma. Furthermore, immunohistochemical examination of the mass showed positive for CD5 and Tdt. Cardiac MRI could not be performed as he had an implant on his leg. The patient was started on chemotherapy with Cyclophosphamide, Etoposide, Vincristine, and Prednisone (CEOP) regimen. The patient was advised to undergo a serial echocardiogram to monitor the pericardial effusion. The diagnosis is malignant pericardial effusion caused by T lymphoblastic lymphoma.



Figure 6: Chest X Ray of the patient with cardiomegaly and mediastinal mass - Case 5

Table 1:

Parameter	Case 1	Case 2	Case 3	Case 4	Case 5
Hemoglobin (g/dL)	10.8	14.7	10.2	12.5	14.3
Total Leucocyte Count (cells/mm ³)	12570	12100	13010	9600	12200
Platelet Count (cells/mm ³)	177000	235000	210000	161000	347000
Random Blood Glucose (mg/dL)	143	156	158	153	123
Total Bilirubin/Direct Bilirubin	0.8/0.3	1.2/0.8	1.1/0.7	1.1/0.4	0.9/0.2
Total Protein (g/dL) / S. Albumin (g/Dl)	6.8/3.9	7.1/4.2	6.2/3.2	6.4/ 3.4	6.8/3.5
SGOT/SGOT (IU/L)	31/50	45/63	73/65	45 / 55	15/41
Blood Urea(mg/dL) / Serum Creatinine(mg/dL)	38/1.1	19/0.54	23/1.2	27/1.1	22/1.1
Na (mEq/L) / K(mEq/L)	125/3.6	123/4.5	126/4.1	135 / 4.1	138/4.8
Tumour Markers (CEA, Ca 19-9, AFP, Beta HCG)	Negative	negative	Negative	Negative	Negative

ANA	Negative	Negative	Negative	Negative	Negative
Pericardial Fluid					
Total Cell Count (cells/mm ³)	280	110	76	3500	Not done
Protein (g/dL)	4.9	3.8	2.1	5	
Glucose(mg/dL)	19	98	64	62	
LDH (U/L)	1921	46	62	437	
ADA (U/L)	12.4	24	12.6	6	
CBNAAT	Negative	Negative	Negative	Negative	
Cytology	Negative for malignant cells	Positive for malignant cells	Positive for malignant cells	Negative for malignant cells	

Normal laboratory values: Hb 13-17 g/dL , Total Leucocyte Count: 4000-10,000 cells/mm³ , Platelets: 150000-400000 cells/mm³, Random Blood Glucose <140 mg/dL Total Bilirubin: 0.1-1.2 mg/dL, Direct Bilirubin : SGOT: 5-40 IU/L, SGPT: 5-40 IU/L, Serum Creatinine: 0.8-1.3 mg/dL, Blood Urea: 5-20 mg/dL, Total Protein-6-8.3 g/dL, S.Albumin-3.5-5.5 gm/dL, Serum Sodium - 135 to 145 mEq/L, Serum Potassium - 3.5 to 5.5 mEq/L

Pericardial fluid normal values-Total C- 0-50 cells/mm³, Protein-1.7-4.6g/dL, Sugar- 80-150mg/dL, LDH- 70-140 U/L, ADA- 0-30 U/L

ESR-erythrocyte sedimentation rate, SGOT- Serum glutamic oxaloacetic transaminase, SGPT- Serum glutamic pyruvic transaminase, Na – Serum Sodium, K – Serum Potassium, ANA – Antinuclear Antibody, CEA -Carcinoembryonic antigen, Ca 19-9 - cancer antigen 19-9, AFP -Alpha fetoprotein, Beta HCG - beta-human chorionic gonadotropin, ADA - Adenosine deaminase LDH -Lactate dehydrogenase, CBNAT -Cartridge Based Nucleic Acid Amplification Test.

DISCUSSION

The aetiology of pericardial effusion is vast, ranging from idiopathic causes to infections, malignancy, chronic renal failure, and autoimmune diseases. Among malignant causes, lung carcinoma is the most common, accounting for approximately thirty-three percent to fifty percent of cases.^[5] Most of the non-cardiac tumours causing malignant pericardial effusion are asymptomatic at presentation and are often only discovered during autopsy.^[1] The primary mechanism of malignant pericardial effusion is typically the obstruction of venous and lymphatic drainage of the pericardium.^[5] According to a study by Teresa et al, lung, breast, and hematologic cancers are responsible for 38 percent, 23 percent, and 18 percent of malignant pericardial effusions, respectively.^[6] The remaining 21% are attributed to adenocarcinoma of unknown primary, thymoma, ovarian carcinoma, mesothelioma, testicular carcinoma, osteogenic sarcoma, and malignancies of the gastrointestinal and genitourinary tracts.^[6] Pericardial effusion can occasionally be the initial presentation of an underlying malignancy. In approximately 9% of patients, pericardial effusion is the first manifestation of cancer, while in 4% of cases, the pericardium is the first site of metastasis from a known primary malignancy.^[7]

Pericardial effusion can present with a wide range of symptoms, though it may also be entirely asymptomatic. Most patients experience symptoms such as dyspnea, palpitations, orthopnea, chest pain, cough, malaise, weakness, fatigue, hemoptysis, peripheral edema, and vomiting. The most common signs include pulsus paradoxus, elevated jugular pressure, tachycardia, decreased heart sounds, peripheral edema, hypotension and pericardial rub. In cases of cardiac tamponade, the classic clinical findings—collectively known as Beck's triad—include hypotension, distended neck veins, and muffled heart sounds.

The typical ECG changes include low-voltage complexes and electrical alternans. The gold standard for diagnosing pericardial effusion is transthoracic echocardiography. Echocardiogram shows right atrial systolic collapse and right ventricular early diastolic collapse in cardiac tamponade.^[8] Cardiac CT and MRI may also be employed to provide more detailed anatomical visualization and are particularly useful in differentiating tumors from normal myocardium.

Biochemical analysis of pericardial fluid is recommended to help determine the aetiology of the effusion. Cytological examination of the fluid has shown variable sensitivity ranging from 54% to 92%.^[9] In a study by Ben-Horin et al, cytology demonstrated a sensitivity of 51%.^[9] Management of pericardial effusion depends on the patient's overall prognosis and may include pericardiocentesis, sclerotherapy, balloon pericardiotomy, or cardiothoracic surgery.^[8] Patients with malignant pericardial effusion generally have a poor prognosis, as the underlying malignancy is often advanced at the time of diagnosis.^[8]

CASE 1

Metastatic melanoma can cause 4.4 % of cardiac metastases. The most common site of malignant melanoma is skin, but it can metastasize to many organs, including heart.^[10] The rarity of cardiac metastasis as an initial presentation makes it difficult to diagnose. It is due to haematological spreading of the neoplasm and can appear in all four heart chambers. The right atrium is mostly involved.^[11] Metastatic melanoma can invade the myocardium and pericardium, but the endocardial layer is rarely affected.^[10] B R J Aerts et al reported a case of cardiac metastasis of malignant melanoma.^[10]

CASE 2

Parotid carcinoma rarely causes pericardial metastasis; a few cases have been reported in the

literature. This patient showed pericardial effusion and tamponade in a surgically removed parotid carcinoma. Barbetakis et al described a case of surgically removed parotid carcinoma that presented with cardiac tamponade later.^[3] M El Fortia also described a case of pericardial effusion and tamponade due to adenocarcinoma of the parotid.^[12]

CASE 3

Pericardial metastasis rarely occurs in Endometrial Carcinoma and a smaller number of cases were reported in the literature.^[13] Patients have a poor prognosis in endometrial carcinoma with pericardial metastasis. Liu G et al reported endometrial carcinoma with malignant pericardial effusion.^[13] Mizuguchi et al reported a large pericardial effusion in post-surgical patient with endometrial mixed carcinoma.^[14]

CASE 4

Among neoplasms involving the heart and pericardium, metastatic lesions are more frequently encountered than primary cardiac tumors. The prevalence of primary cardiac tumors is quite rare, estimated to range from 0.0027% to 0.003%.^[15] Among the malignant primary tumors of the heart, angiosarcoma is the most common.^[16] Other malignant tumors involving the pericardium include mesotheliomas, lymphomas, and primitive neuroectodermal tumors.^[17]

In a study conducted at the Royal Brompton Hospital in London, benign tumors—particularly myxomas—were found to account for over 70% of all cardiac tumors.^[18] Imaging modalities such as CT and MRI play a crucial role in the characterization and assessment of these lesions. The imaging findings in our patient were strongly suggestive of a primary cardiac angiosarcoma, although the patient unfortunately passed away before a histopathological diagnosis could be established. Primary cardiac angiosarcoma typically presents with features of heart failure, pericardial effusion, or arrhythmias. It is a highly invasive tumor that is often diagnosed at an advanced stage, as was the case with our patient.^[16] In a study conducted by Yan Chen et al, all 12 reported cases of cardiac angiosarcoma originated from the right side of the heart, which is consistent with our findings.^[19] The prognosis for cardiac angiosarcoma remains poor due to challenges such as incomplete surgical resection and limited response to chemoradiation therapy.^[19]

CASE 5

This patient presented with a rare case of pericardial effusion in T-cell lymphoblastic lymphoma. CECT scan of the chest showed the presence of a mediastinal mass. Biopsy from the mediastinal mass showed features consistent with a lymphoblastic lymphoma, which was confirmed as T-cell lymphoblastic lymphoma on histological and immunohistological examination. A T-cell lymphoblastic lymphoma (T-LBL) is an infrequent subtype of adult Non-Hodgkin's lymphoma with an incidence of only 2%.^[20] T-LBL may present as a mediastinal mass, but its presentation as malignant

pericardial effusion and cardiac tamponade is rare.^[21] Malignant pericardial effusion associated with T-lymphoblastic lymphoma is a sign of advanced malignancy and poor prognosis.^[22] The differential diagnosis of mediastinal masses includes thymoma, thymic carcinoma, Hodgkin's lymphoma (nodular sclerosis subtype), primary mediastinal B-cell lymphoma with sclerosis, Burkitt lymphoma, Extranodal NK/T-cell lymphoma, blastoid variant of mantle cell lymphoma, and germ cell tumors.. However, in this case, the biopsy of the mediastinal mass was T lymphoblastic lymphoma, which was further confirmed by positive immunostaining of tumor cells to T-cell markers such as CD-5 and Tdt. Malignant pericardial effusion is associated with an extremely poor prognosis. In this case series, four patients with malignant pericardial effusion progressed to develop cardiac tamponade. All four required pericardiocentesis, but unfortunately, each of them succumbed to the illness within a few months of diagnosis. One additional case had only mild pericardial effusion, which did not require any intervention.

CONCLUSION

Pericardial effusion is a relatively common but potentially serious manifestation of malignancies. While tumors such as metastatic melanoma, parotid carcinoma, endometrial carcinoma, T-cell lymphoma, and angiosarcoma are rare causes of pericardial effusion and cardiac tamponade, they should still be considered in the differential diagnosis.

Early detection and timely management of these malignancies may help prevent the development of pericardial complications and improve overall patient outcomes. Clinicians should maintain a high index of suspicion for these less common etiologies, particularly in cases with unexplained or recurrent pericardial effusion.

The treatment of malignant pericardial effusion should be individualized, taking into account the patient's clinical condition, the type and stage of the underlying malignancy, and other relevant prognostic factors. However, therapeutic options remain limited, and malignant pericardial effusion is frequently associated with poor prognosis and high mortality.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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