Case Report

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A unique presentation of pericardial epithelioid angiosarcoma with multifaceted complications

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Introduction and importance: Angiosarcomas are rare tumors of endothelial origin and may arise in any organ. Epithelioid angiosarcomas are a subtype of angiosarcoma that are rapidly progressive and typically fatal.

Case presentation: The authors report a case of a 25-year-old previously healthy female who presented initially for dyspnea and palpitations, on further evaluation she was found to have large bilateral pleural effusions and cardiac tamponade.

Clinical discussion: Pericardiocentesis and thoracentesis were performed alongside biopsies that revealed atypical cellular proliferation. Fluorodeoxyglucose-positron emission tomography (FDG-PET) showed avid uptake in the anterior mediastinum, perivascular, paratracheal, subcarinal and pleural lymph nodes with large FDG uptake in the bilateral pleural effusion. Mediastinoscopy was done and biopsies showed an overtly malignant, epithelioid neoplasm with foci of vaso-formation; Keeping with high-grade epithelioid angiosarcoma of the pericardium. She received six cycles of weekly paclitaxel, but imaging for abdominal pain incidentally showed evidence of metastasis to the liver and spine so she was switched to Adriamycin-Ifosfamide for which she received one cycle so far. Her hospital course was complicated by high-output pleural effusions, chylothorax, left atrial thrombus formation and an intensive care unit stay for septic shock.

Conclusion: Pericardial epithelioid angiosarcoma has been reported rarely in the literature. The authors aim to report a case of extensive metastatic pericardial epithelioid angiosarcoma in a young patient; which we believe can be an addition to the literature of a malignancy associated with poor prognosis and no definitive proven treatment regimen.

Keywords: case report, chylo-pneumothorax, pericardial epithelioid angiosarcoma, pleural effusion, tamponade

Introduction

Primary cardiac tumors are rare and far less common than metastatic diseases; they often involve the right side more often and may involve the pericardium[1]. Cardiac angiosarcomas constitute a third of all primary cardiac tumors and are the most common malignant primary cardiac tumor[2].

Epithelioid angiosarcoma is a subtype of cardiac angiosarcoma that is associated with an aggressive course, poor prognosis and high mortality rate[3].

Pericardial angiosarcoma can initially be insidious, but soon it clinically manifests as dyspnea, chest pain, cough and fatigue. Its complications can range from pericardial effusions, tamponade, pericarditis and other symptoms associated with adjacent structural invasion[4].

We present a case of a 25-year-old female who was diagnosed with pericardial angiosarcoma that metastasized to the ribs and liver. It was complicated by massive pleural effusions, cardiac tamponade, chylothorax, pneumothorax and pneumomediastinum with esophageal ulcer that could represent a metastatic disease.

Pericardial epithelioid angiosarcoma is a rare entity, and to our knowledge, it has previously been reported only in 4 case reports. We believe our case describes an unusual, complicated presentation of a surviving patient with epithelioid angiosarcoma. And we hope it can be a useful addition to the scarce literature of a rare and challenging malignancy that is associated with poor prognosis and survival.

Case presentation

A 25-year-old female college student with no past medical history, no family history of malignancies or occupational exposures presented to another hospital with dyspnea and palpitations, her dyspnea started 2 weeks prior to presentation on exertion and at rest, palpitations started 1 week prior to presentation, there was no associated paroxysmal nocturnal dyspnea, lower extremity edema or chest pain, no fever or chills, she was found to have large bilateral pleural effusions and cardiac tamponade, pleural

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fluid analysis showed a PH of 7.5, LDH of 195, glucose 95 mg/dl and a protein of 25 g/l, subsequently, bilateral chest tubes were inserted and she underwent pericardiocentesis as a treatment for her cardiac tamponade which resolved and did not reoccur. Biopsies were taken from the pleura and pericardium, which revealed atypical cellular proliferation. Fluorodeoxyglucose-positron emission tomography (FDG-PET) revealed avid radiotracer uptake in the anterior mediastinum, perivascular, paratracheal, subcarinal and pleural lymph nodes/lesions with standardized uptake value (SUV) max up to 8, mild FDG uptake in the pericardial effusion keeping with disease involvement, large FDG uptake in the bilateral pleural effusion. Two weeks after her initial presentation she was transferred to our institution for continuity of care.

Upon presentation, she was cachectic, ill, appearing with sinus tachycardia. Physical examination revealed decreased breath sounds bilaterally. Blood tests were only significant for albumin of 23 g/l, liver and renal chemistries were normal. CT chest without contrast revealed bilateral massive pleural effusions with underlying air space disease with trace pericardial effusion (Fig. 1).

Transthoracic echocardiography further confirmed the massive pleural effusions causing moderate right ventricular compression without IVC dilatation, a normal left ventricular function with a small pericardial effusion.

Diagnostic and therapeutic thoracocentesis with bilateral pigtail catheter insertion was done. Studies showed exudative pleural effusion with atypical cells on cytology. A repeat CT scan with contrast was done after drainage, showing decreased bilateral effusion and the development of small bilateral pneumothoraxes and a large left atrial thrombus. Bilateral pleural catheters were inserted for recurrent bilateral hemopneumothoraxes with a high output of 2–5 l per day with frequent monitoring and anticoagulation for the left atrial thrombus (Fig. 2).

She underwent mediastinoscopy with a biopsy of the mediastinal mass, paratracheal and supraclavicular lymph nodes.

The histopathology sections included show an overtly malignant, epithelioid cell with purple cytoplasm, vesicular nuclei, and prominent nucleoli (Fig. 3A). In regions the tumor shows dissecting growth pattern through a background of fibrous tissue, and there are foci morphologically suggestive of vaso-formation (Fig. 3B); the tumor was found to harbor a SMARCA4 mutation. Of note, the presence of a point mutation does not necessarily imply the tumor is SMARCA4-deficient, and immunohistochemistry demonstrates retained expression of SMARCA4 and INI1 (Fig. 3C).

Immunohistochemistry is entirely negative for pan-CK, SOX2, SALL4, CK5, p40, PAX8, NUT, SOX10, CD34, CD99, WT-1 and ETV4. However, consistent with the morphologic evidence of vaso-formation, the tumor shows a diffuse expression of ERG (Fig. 3D) and CD31 (Fig. 3C). confirming the diagnosis of high-grade epithelioid angiosarcoma.

Two weeks after starting chemotherapy with weekly paclitaxel, the patient had melena for a couple of days, for which gastroscopy showed a deep ulcer semi-circumferential in the distal esophagus extending over a length of 10 cm with raised borders mainly at the distal end suggestive of a malignant process (Fig. 4).

Mild active oozing was seen but was not amenable to endoscopic treatment, her melena was managed conservatively with proton pump inhibitors.

She received six doses of weekly paclitaxel, after which a CT angiography of the abdomen showed incidental hypodense hepatic round lesions, lytic spine lesions consistent with metastases (Fig. 5).

Her case was reviewed in a tumor board conference, in the shadow of disease progression, her chemotherapy was changed to Adriamycin-Ifosfamide (one cycle received so far).

HIGHLIGHTS

- Angiosarcomas are rare tumors of endothelial origin and may arise in any organ. Epithelioid angiosarcomas are a subtype of angiosarcoma that are rapidly progressive and typically fatal.
- We report a case of a 25-year-old previously healthy female who presented initially for dyspnea and palpitations, on further evaluation she was found to have large bilateral pleural effusions and cardiac tamponade. Pericardiocentesis and thoracentesis were performed alongside biopsies that revealed atypical cellular proliferation.
- FDG-PET showed avid uptake in the anterior mediastinum, perivascular, paratracheal, subcarinal and pleural lymph nodes with large FDG uptake in the bilateral pleural effusion.
- Mediastinoscopy was done and biopsies showed an overtly malignant, epithelioid neoplasm with foci of vaso-formation; Keeping with high-grade epithelioid angiosarcoma of the pericardium.
- She received six cycles of weekly paclitaxel, but imaging for abdominal pain incidentally showed evidence of metastasis to the liver and spine so she was switched to Adriamycin-Ifosfamide for which she received one cycle so far.
- Her hospital course was complicated by high-output pleural effusions, chylothorax, left atrial thrombus formation and ICU stay for septic shock.
- Pericardial epithelioid angiosarcoma has been reported rarely in the literature. We aim to report a case of extensive metastatic pericardial epithelioid angiosarcoma in a young patient; which we believe can be an addition to the literature of a malignancy associated with poor prognosis and no definitive proven treatment regimen.

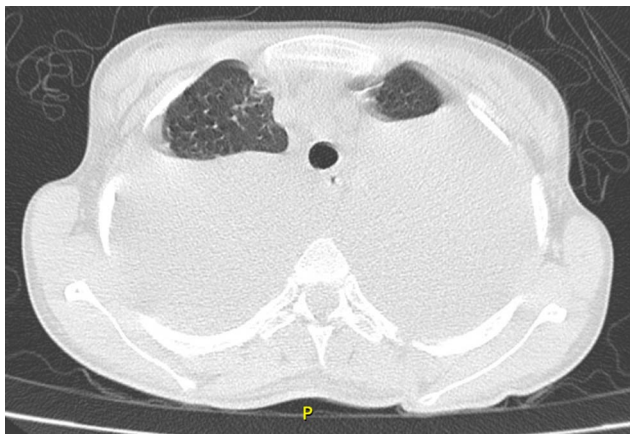

Figure 1. Showing computed tomography chest without contrast upon admission showing large bilateral pleural effusion.

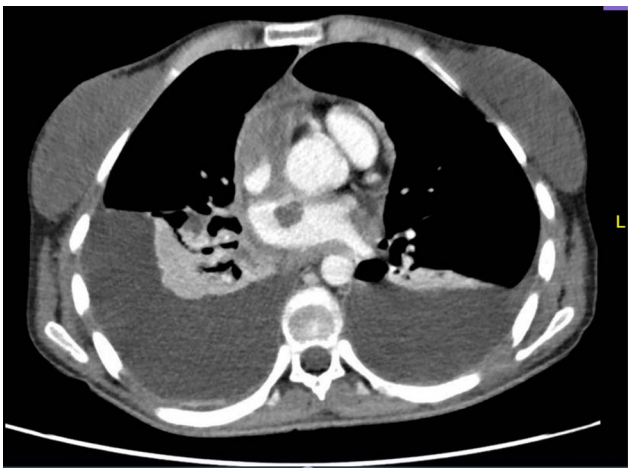

Figure 2. Computed tomography scan with contrast showing decrease in size of bilateral pleural effusion and a left atrial thrombus.

Through her hospitalization, the patient felt down with episodes of depression that were addressed by her family member's presence, support and our palliative care psychologist service.

The patient is still alive and well seven months after her first presentation, currently in the intensive care unit with respiratory failure.

Discussion

Angiosarcoma is an exceptionally rare malignancy, representing 1–2% of soft tissue sarcomas, where only one person in a million is diagnosed with this disease in the U.S. each year. Angiosarcomas most frequently (60%) occur in cutaneous lesions, commonly found in the head and neck region. Additionally, angiosarcomas can manifest in other areas such as soft tissues, visceral organs, bone, and the retroperitoneum[5]. Pericardial epithelioid angiosarcoma is an exceptionally rare malignancy, characterized by aggressive behavior and a propensity for late-stage diagnosis[6]. Our case report adds to the limited literature on this entity, as only four previous case reports have been documented in the medical literature to be pericardial epithelioid angiosarcoma[6–8]. Patients can present with different chief complaints, from chest pain, dyspnea, palpitations, to pericardial effusion, congestive heart failure, and cardiac tamponade upon presentation[4–6]. Pericardial angiosarcomas predominate in the younger population, peaking in the fourth and fifth decades of life[8]. Our patient, a 25-year-old female consistent with the predominant age of onset, presented with a one-

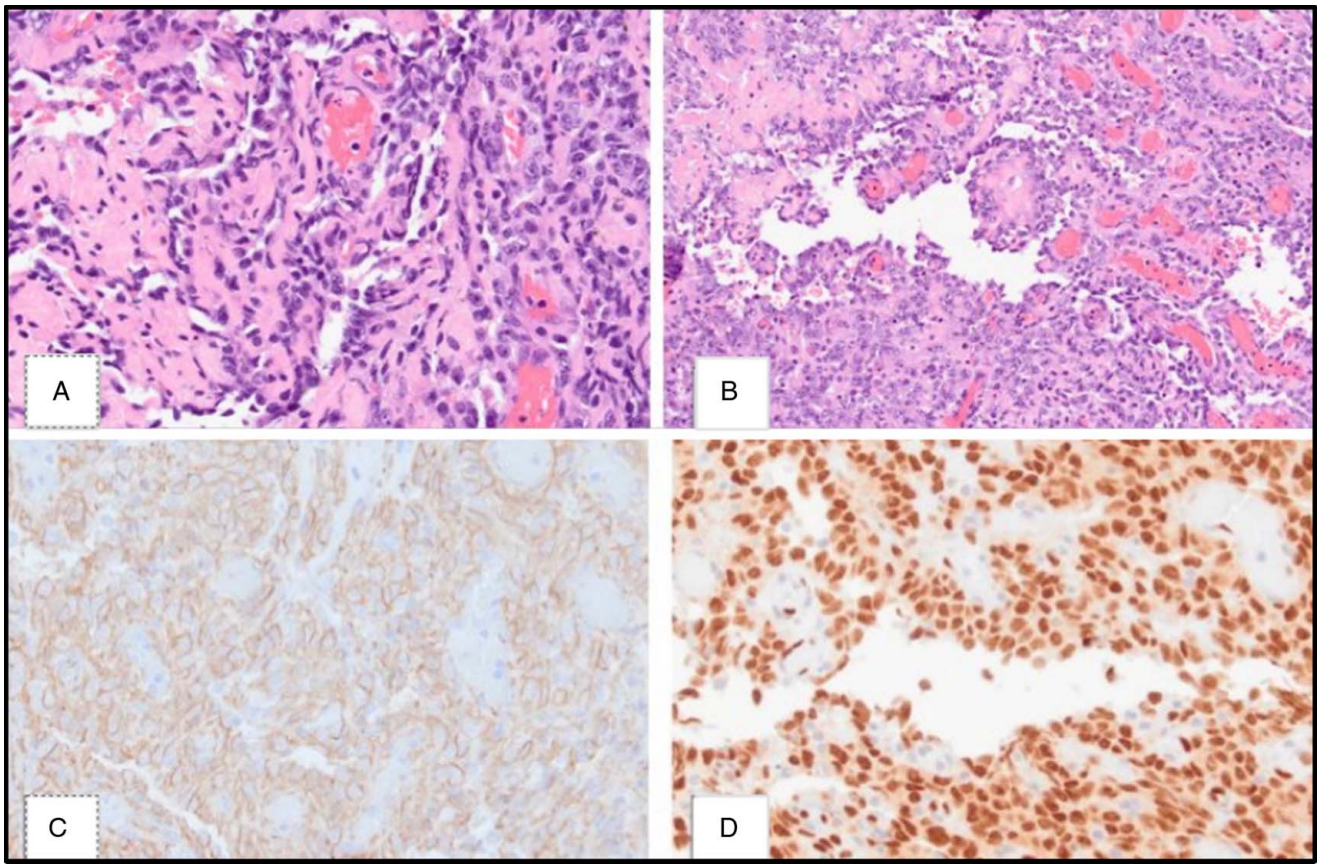

Figure 3. (A) Shows histopathology sections of overtly malignant epithelioid cells with purple cytoplasm, vesicular nuclei, and prominent nucleoli. (B) In some regions, the tumor shows a dissecting growth pattern through a background of fibrous tissue, and there are foci that are morphologically suggestive of vasoformation. (C) Immunostaining for CD 31 was positive. (D) The ERG immunostain shows nuclear positivity.

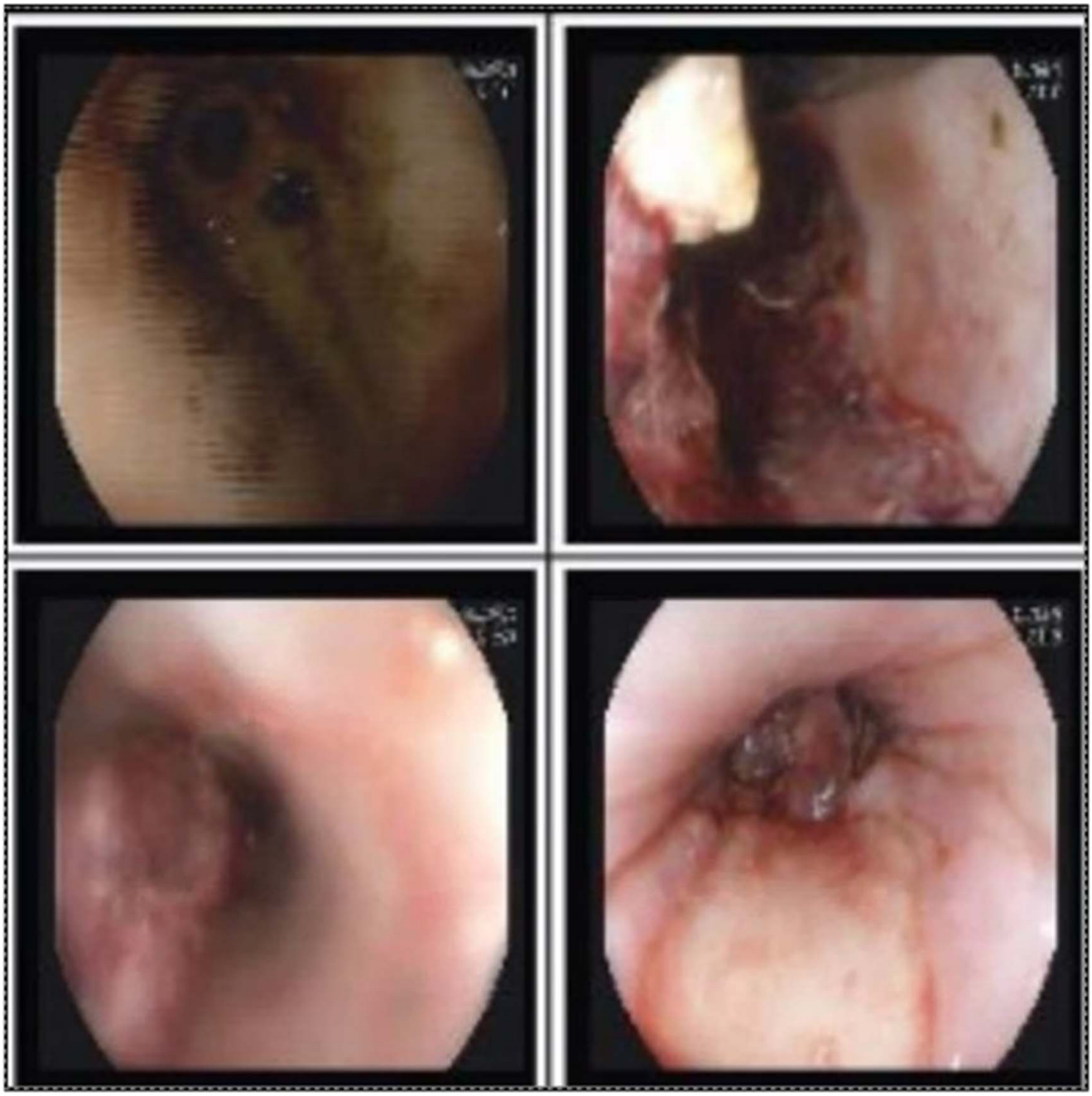

Figure 4. Shows gastroscopy yielding a deep ulcer, semi-circumferential in the distal esophagus extending over a length of 10 cm with raised borders mainly at the distal end suggestive of a malignant process.

month history of progressively worsening, moderate dyspnea at rest, and found to have marked bilateral pleural & pericardial effusion. As expected, exudative fluid was the result of the tap; however, yield for malignant cells remains low for this type of sarcoma[8]. Pan-CTs with PET-CT scan showed a heterogeneous anterior mediastinal mass measuring 3×2.3 cm, with a left supraclavicular ill-defined soft tissue abnormality measuring 1.8×1.4 cm. Diagnosis remains challenging, as despite all the advances in imaging, tissue biopsy with a detailed immunohistochemical staining pattern remains essential for diagnosis. In the four published cases, 2 were CD34 positive, 3 were vimentin positive, and 3 were positive for CD31 (none reported ERG staining, 2 unreported for vimentin and 1 unreported for CD31)[6–8]. Remarkably, our patient was the only reported case to exhibit a very high-output chylo-pneumothorax, with an estimated daily drainage of ~2–5 l throughout the past 6 months. The interplay between the pericardial tumor and the thoracic lymphatic system likely contributes to this phenomenon. Given the rarity of pericardial epithelioid angiosarcoma, there is no established standard of care. In our case, we opted for paclitaxel-

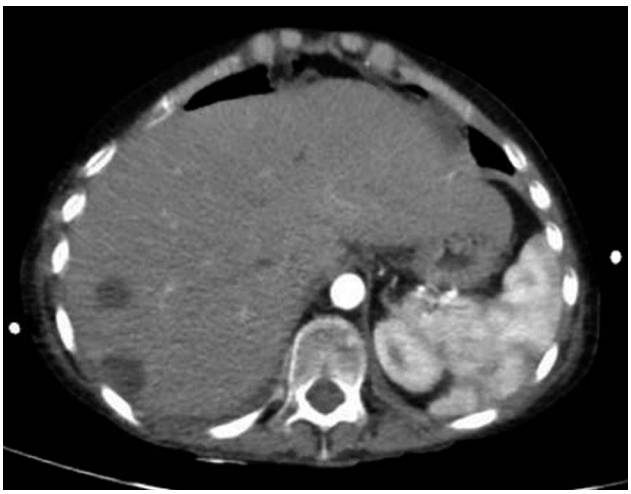

Figure 5. Shows an abdominal computed tomography angiography yielding two incidental hepatic nodules suspicious for metastasis.

based chemotherapy, considering its Anthracycline-based regimens exert anti-angiogenic properties and are associated with a response rate of 16–27% and median survival of up to 12 months[9,10]. Retrospective data indicates that anthracycline and taxanes have a similar survival benefit, despite the lack of a prospective trial comparing their efficacy in treating angiosarcomas. Because the tumors are vascular, early interest in anti-VEGF therapy is on the rise. Immune-checkpoint inhibitors like anti-PD-1 monoclonal antibodies (e.g. pembrolizumab and nivolumab) as well as CAR-T therapy have shown encouraging results for soft tissue sarcomas; however, they have not yet been studied in epithelioid angiosarcomas[8–11]. Evidently, despite the multiple cycles of chemotherapy the patient is receiving, her disease is progressing, and her prognosis remains dismal. The role of adjuvant radiotherapy and chemotherapy remains anecdotal in the treatment of patients with primary cardiac sarcoma. Collaboration with a multidisciplinary team, including oncologists, cardiothoracic surgeons, and interventional radiologists, remains crucial.

Our case report has several possible limitations. First, given the rarity of pericardial epithelioid angiosarcoma, treatment decisions are based on limited evidence. Despite the theoretical angiogenic properties associated with anthracyclines, its use on this rare entity is not established. The absence of prospective trials limits our ability to determine optimal treatment strategies. Second, opting for taxanes therapy alone limits this case report's value in adding to the emerging evidence of anti-VEGF therapy on epithelioid angiosarcomas. Third, of the scant cases reported in the literature, none reported on ERG staining, two unreported for vimentin, and one unreported for CD31, making immunohistochemical comparison of such cases relatively limited. Finally, it remains unclear as to at what stage of tumor invasion does the entity exhibit the reported high-output chylo-pneumothorax.

Conclusion

The insidious onset of symptoms underscores the need for heightened suspicion in patients with unexplained dyspnea. The definitive diagnosis was established through tissue biopsy, revealing the characteristic histopathological features of epithelioid angiosarcoma.

As we accumulate more cases of pericardial epithelioid angiosarcoma, collaborative efforts are essential to elucidate optimal treatment strategies. Prospective studies and international registries can provide valuable insights into disease behavior, prognostic factors, and novel therapeutic approaches.

In conclusion, our case report contributes to the growing body of knowledge surrounding this rare malignancy. By sharing our experience, we hope to enhance awareness, guide clinical decision-making, and improve outcomes for future patients with pericardial epithelioid angiosarcoma.

Collaboration with a multidisciplinary team, including oncologists, cardiothoracic surgeons, and interventional radiologists, remains crucial.

Reporting statement

This Case report has been reported in line with the SCARE 2023 criteria[12].

Ethical approval

Not applicable.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

M.A. contributed to the conception and design of work. M.C. and O.A. contributed to manuscript write-up. O.F. and A.T. contributed with revision and provided expert opinion.

Conflicts of interest disclosure

The authors declare no potential conflict of interest with respect to the research, authorship and publication of this article.

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