INTRODUCTION

In Tanzania, tuberculosis is among the most common and important diagnoses in a patient presenting with constitutional symptoms and changes on plain radiography. We report a 32-year-old man initially diagnosed as tuberculosis based on symptoms and imaging. Further workup revealed a rare but aggressive metastatic angiosarcoma.

An angiosarcoma (AS) is an aggressive, rare malignant endothelial cell tumor of lymphatic or vascular origin that can arise in the liver, breast, spleen, bone, or heart, but frequently they are multicentric.1,2 Metastasis occurs in more
than half of all patients, most involving the lung that usually presents with multiple pulmonary nodules and diffuse alveolar hemorrhage.3-5

Patients with primary disease or metastasis to the lung are often misdiagnosed due to nonspecific symptoms manifestation and its rare nature of the illness and hence delays diagnosis and a poorer prognosis.5

Angiosarcomas have insidious growth, and they may be asymptomatic until the disease is advanced.6 Clinical features of angiosarcomas depending on sites and structures involved and on the extent of the disease. These patients may present with disseminated intravascular coagulation, bleeding, anemia, thrombocytopenia, pathologic fractures, compression of adjacent neurovascular structures, or hepatic dysfunction.7 Patients with soft tissue angiosarcomas usually present with a moderately paced growing mass in the extremities.8

In the low-grade form, angiosarcoma may resemble a hemangioma, while the aggressive form may have overlapping features.9 The tumor can present at any age; recent cases have been reported in a 5-year-old child and an elderly of 97 years.10

Since 1879, when Langhans and colleagues reported the first angiosarcoma in the spleen,11 the exact etiology of these tumors has never been established; however, several risk factors have been implicated and include exposure to environmental chemical toxins and foreign bodies, radiation therapy, chronic lymphedema, human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS), and chronic use of calcium channel blockers.1,5,6,12-14

Long-term use of anabolic steroids has also been linked with the development of angiosarcomas.14,15

The differential diagnosis of angiosarcoma includes melanoma, pyogenic granuloma, fibrosarcoma, liposarcoma, Kaposi sarcoma, and metastatic cancer with unknown primary site.

The site of disease involved and staging guide the choice of imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emitted tomography (PET). The treatment options are minimal, especially with the aggressive nature of the disease. To date, there is no single or combined definitive therapy which confers long-term favorable outcome with metastatic disease.16

2 | CASE PRESENTATION

A 32-year-old man presented to our Internal Medicine department from a primary health care facility having been initiated on antituberculous medications based on his symptoms and chest x-ray findings (Figure 1) without improvement. He reported having a 4-month history of constitutional symptoms that were associated with atypical left-sided chest pain. He denied a history of headache, visual disturbance, convulsions, loss of consciousness, or abdominal pain.

Two weeks before attending our department, he was seen at the ophthalmology clinic with a 6 weeks history of small, painless, but itching mass on the left lower lid. Examination at this clinic found him to have a nodule on the right lower eyelid arising from the inferior tarsal conjunctiva with skin-colored to erythematous, measuring 3 × 3 cm. Excision biopsy of the nodular mass was done for histopathological evaluation.

At the time of admission, this patient was healthy with stable baseline vital signs. He had a left perinostril mass measuring 1 × 1 cm, which bled easily to touch. On chest examination, he had nontender left anterior chest wall swelling at the level of the third rib. The mass was firm and mobile, measuring 8 × 8 cm. There were crackles on the left infra-scapular area. We took an incisional biopsy from the anterior chest swelling. This patient was admitted to the medical wards and stayed for 4 weeks.

Hematological parameters revealed an elevated erythrocyte sedimentation rate of 79 mm/h, rest of blood cell lines, urea, creatinine, electrolytes, and liver function tests were normal. The HIV infection serology and sputum for TB tests (Acid Fast Bacilli and GeneXpert® MTB/RIF) were all negative. The chest x-ray revealed bilateral diffuse pulmonary nodular lesions and prominent lobulated right cardiac margin suggestive of middle mediastinum mass with metastatic pulmonary lesions. Contrasted chest CT (Figure 2A) was performed and showed soft tissue heterogeneously enhancing lobulated mediastinal mass extending into the right atrium (RA) with associated diffuse pulmonary and pleural nodular lesions. At the same time, head CT (Figure 3A) disclosed ring-enhancing lesions with surrounding edema involving the right frontal lobe consistent with metastatic lesions. Contrasted
abdominal-pelvic CT (Figure 2B) was performed 2 weeks later and displayed multiple enhancing hypodense hepatic lesions with the scanned part of chest showing increased pulmonary nodules and pleural effusion (done 2 wks later).

Transthoracic echocardiography (Figure 4) demonstrated a large anterior mass that was compressing and infiltrating the right atrium. Also noted were multiple right atrial masses with one mobile mass moving through tricuspid valves leaflets. Masses were of variable sizes largest measuring and heterogeneous echogenicity causing mid-right atrium and tricuspid valve pseudostenosis with a significant mean pressure gradient of 12.9 mm Hg. The rest of the echo study was normal with preserved left ventricular ejection fraction (LVEF) of 70%.

While in the ward, he developed shortness of breath with a respiratory rate of 25 bpm, heart rate of 102 bpm, but maintained normal saturation on room air of 93%. We had a concern about probable pulmonary embolism based on the clinical background and echocardiographic findings. He was, in the meantime, started on a full dose of unfractionated heparin with reasonable improvement from his shortness of breath.

The histopathological results of the excised conjunctival mass and incisional biopsy on the left mammary area showed features suggestive of angiosarcoma (Figure 5).
Due to the evidence for advanced metastasis, the patient and the relatives were involved in the discussion of the possible treatment options available. However, the family requested to be discharged for home-based palliative care. Unfortunately, the patient demised 1 week after discharge from the hospital.

3 | DISCUSSION

Angiosarcomas are a rare type of malignancy that involves the lining of blood vessels and lymphatics, with a propensity to invade local and distant organs, including the heart, lungs, lymph nodes, soft tissue, liver, bone, and skin. These tumors are highly aggressive with early metastasis and poor prognosis. Due to its nonspecific symptoms and aggressive nature, by the time of clinical presentation, the disease is usually advanced, which poses a challenge in establishing the diagnosis and discerning the primary origin, which might explain the misdiagnosis of tuberculosis with our patient. Because of this nonspecific presentation, symptoms are therefore related to the specific organ involved, local tumor invasion, or metastasis.

Symptoms and signs of angiosarcomas depend on the structure involved. Pulmonary angiosarcoma symptoms are
nonspecific, ranging from cough, hemoptysis, dyspnea, chest pain, and weight loss. At the same time, cardiac involvement presents mainly with arrhythmias, features of heart failure, pericardial effusion, hypotension, and syncope depending on the structure involved. Our patient presented with a myriad of these symptoms.

The imaging modality is dictated by the extent and specific organs that are involved. Pulmonary angiosarcoma features are variable and atypical. Shimabukuro et al reported 31 cases of CT features of primary pulmonary angiosarcomas and reported the most frequent finding to be the pulmonary nodules (87%), as was the case in our patient. Other features were infiltrations, ground glass appearance, pleural effusions, and invasion of other organs.

In cardiac angiosarcomas, echocardiography and MRI scan form a major component in the workup with echocardiography reported to have 97% sensitivity in detecting cardiac tumors. Other advantages of echocardiography include—it is inexpensive, noninvasive, widely available, and can reveal tumor location, extent, and cardiac function. Its limitations are the inability to characterize different tissue types and their reliance on the operator experience. However, CT and MRI are superior to cardiac ultrasound, with CT scan being able to provide information on the vascular anatomy of the mass. On the other hand, MRI has better tissue characterization and lack of ionizing radiation.

Like in our patient, when the heart is involved, it extensively infiltrates cardiac structures and may extend through the heart wall to involve adjacent structures.

Transthoracic echocardiography (TTE) aids in detecting the tumors and its size, identify the site of attachment, and the pattern of tumor movement, as was noted in our patient. It is inexpensive, noninvasive, and widely available even in the resource-limited centers. TEE has a much higher resolution for differentiating between benign and malignant tumors.

Chest x-ray is not diagnostic of cardiac angiosarcomas but can unmask cardiomegaly, which is the most common finding, widened mediastinum, hilar adenopathy, focal cardiac mass, pulmonary consolidation, or pericardial effusion. On the other hand, similar to our patient, the CT scan findings may reveal multifocal or solitary lesions demonstrating a predominant, highly vascular right atrial mass that involves the cardiac chambers which may be nodular and irregular; and PET can help in the diagnosis, staging, and follow-up.

Like in most mesenchymal tumors, biochemical parameters do not help much in the diagnostic workup; however, histopathology and immunohistochemistry may still confirm the diagnosis. Immunohistoexpression of vascular markers, such as ERG, CD31, CD34, and FLI1, that we could not test may also aid in achieving the correct diagnosis.

A multidisciplinary approach is advisable with surgical resection in localized disease, which cannot be achieved in most cases due to the vascular nature of the disease. With a 5-year survival rate of <50%, treatment options are limited and carry a poor prognosis. Some authors advocate an aggressive treatment approach involving both surgical resection and radiotherapy. While several agents such as adriamycin, ifosfamide, cyclophosphamide, vincristine, dacarbazine, and paclitaxel are used in the management of these patients, there is still some debate on the role of adjuvant chemotherapy and the choice of agents.

4 | CONCLUSION

To the best of our knowledge, this is the first report of metastatic angiosarcoma with cardiac and pulmonary involvement in Tanzania. Angiosarcoma though rare but may be misdiagnosed as tuberculosis or any other form of diseases that are common in developing countries. Misdiagnosis leads to a delay in the correct diagnosis and exposure to the inappropriate medication and eventually untimely death. The integration of careful and extensive history, physical examination, multi-imaging modality, histopathology, and multidisciplinary approach should form the basis of diagnosis and management to avoid misdiagnosis of similar cases in resource-limited settings.

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CONFLICT OF INTEREST

The authors have nothing to disclose.

AUTHOR CONTRIBUTIONS

MI, LN, and LBM: conceptualized and drafted the manuscript. MI, NM, LT, CN, BC, HM, LM, IN, and LBM: involved in patient evaluation and follow-up. NM, CN, and HK: provided radiology images and assessments. LM: collected biopsies. LT: provided histology slides and assessments. All authors: contributed to the writing and revision of the manuscript.

CONSENT

Written consent was obtained from this patient.

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