Metastatic angiosarcoma of unknown primary site misdiagnosed as extrapulmonary tuberculosis

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Abstract

In Tanzania, Tuberculosis is among the most common and important diagnoses in a patient presenting with constitutional symptoms and lung opacities on plain radiography. We report a 32-year-old male who was misdiagnosed as extrapulmonary tuberculosis based on symptoms and imaging. Further workup revealed a rare but aggressive metastatic angiosarcoma.

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Key Clinical Message

The integration of correct history and physical exam, multimodality imaging, and histopathology, should be part of the diagnostic panel to avoid misdiagnosis of angiosarcoma in resource-limited settings, where many other diseases can mimic signs and symptoms of this disease.

Introduction

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 common clinical manifestation and little clinical suspicion index of the illness, which often leads to late diagnosis and a poorer prognosis [5].

Angiosarcomas have insidious growth, and they may be asymptomatic until the disease is well advanced [6]. Clinical features of angiosarcomas depend on sites and organs involved. The patient 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 haemangioma. In contrast, 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 like 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].

Case Presentation

A 32-year-old male with no significant medical history presented to our Internal Medicine department with a history of constitutional symptoms that were associated with atypical left-sided chest pain, which led to the diagnosis of extrapulmonary tuberculosis based on symptoms and chest radiography findings (Fig. 1). He was kept on antituberculous drugs for two weeks without improvement. He denied a history of headache, visual disturbance, convulsions, loss of consciousness, or abdominal pain. He denied a history of headache, visual disturbance, convulsions, loss of consciousness, or abdominal pain.

Two weeks before the diagnosis of extrapulmonary tuberculosis, he was attended at the ophthalmology clinic with a six weeks history of a moderately growing mass on the left lower lid that was painless and itching. On local examination, there was a nodule on the right lower eyelid arising from the inferior tarsal conjunctiva with skin-colored to erythematous, measuring 3cm x 3cm. Excision biopsy of the nodular mass was done for histopathological evaluation.

On examination, he was not wasted with stable baseline vital signs. He had a left peri-nostril mass measuring 1 cm x 1 cm, which bled easily to touch. On chest examination, he had non-tender left anterior chest wall swelling at the level of the third rib. The mass was firm and mobile, measuring 8 cm x 8 cm. There were crackles on the left infra-scapular area. The incisional biopsy was taken from the anterior chest swelling on the left mammary area.

Hematological parameters revealed an elevated erythrocyte sedimentation rate of 79 mm/hr, 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) were negative. The chest x-ray revealed bilateral diffuse pulmonary nodular lesions and prominent lobulated right cardiac margin features suggestive of middle mediastinum mass with metastatic pulmonary lesions. Contrasted Chest CT (Fig. 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 while Head CT (Fig. 3a) showed ring-enhancing lesions with surrounding edema involving the right frontal lobe consistent with metastatic lesions. Contrasted abdominal pelvic CT (Fig. 2b) was performed two weeks later and showed multiple enhancing hypodense hepatic lesions with the scanned part of the chest, showing increased pulmonary nodules consistent with rapid disease progression. There was also bone involvement (Fig. 3b)

Transthoracic echocardiography (Fig. 4) revealed 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 heterogenous echogenicity causing mid-right atrium and tricuspid valve pseudostenosis with a significant mean pressure gradient of 12.9 mmHg. The rest of the echo study was normal with preserved left ventricle ejection fraction (LVEF) of 70%.

This patient was admitted to the medical ward. 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 echo 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 (Fig. 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 one week after discharge from the hospital.

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 [1,17,18]. These tumors are highly aggressive with early metastasis and poor prognosis[17–19]. Due to its nonspecific symptoms and aggressive nature, by the time of clinical presentation, the disease is usually advanced [5,20], 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[17–19].

Symptoms and signs of angiosarcomas depend on the structure involved. Pulmonary angiosarcoma symptoms are non-specific, ranging from cough, hemoptysis, dyspnea, chest pain, and weight loss[10,17]. At the same time, cardiac involvement presents mainly with arrhythmias, features of heart failure, pericardial effusion, hypotension, and syncope depending on the structure involved[10,21]. Our patient presented with a myriad of these symptoms.

The imaging modality is dictated by the extent and specific organs that are involved. Pulmonary angiosarcomas 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 [22].

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[23].

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 [10,23].

Transthoracic echocardiography (TTE) aids in detecting the tumors and its size, identify the site of attachment, and the pattern of tumor movement [22,23], 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[23].

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 [12,23]. 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[23–25]; and PET can help in the diagnosis, staging, and follow-up [26,27].

Like in most mesenchymal tumors, biochemical parameters do not help much in the diagnostic workup; however, histopathology and immunochemistry may still confirm the diagnosis. Immunoexpression of vascular markers, such as ERG, CD31, CD34, and FLI1, that we could not test may also aid in achieving the correct diagnosis [28].

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 less than 50%, treatment options are limited and carry a poor prognosis. Some authors advocate an aggressive treatment approach involving both surgical resection and radiotherapy [29]. 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 [30,31].

Conclusion

To the best of our knowledge, this is the first report of metastatic angiosarcoma with cardiac and pulmonary involvement in Tanzania. The integration of correct history, physical examination, multimodality imaging, and histopathology, should be part of the diagnostic panel to avoid misdiagnosis of angiosarcoma in resource-limited settings, where many other diseases can mimic signs and symptoms of this disease.

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Conflict of interest

The authors have nothing to disclose.

Author Contributions

MI and LBM: conceptualized and drafted the manuscript. MI, NM, LT, CN, BC, HM, LM, IN, LN, 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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