Radiology Case Reports 19 (2024) 1722–1728

Available online at www.sciencedirect.com

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journal homepage: www.elsevier.com/locate/radcr

Case Report

Rare case of cardiac angiosarcoma and alveolar hemorrhage in an adolescent patient initially suspected COVID19 infection: A case report and literature review ☆,☆☆,★,★★,†

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ARTICLE INFO

Article history:
Received 26 December 2023
Revised 11 January 2024
Accepted 18 January 2024

Keywords:
Cardiac mass
Angiosarcoma
Alveolar hemorrhage
Diffuse alveolar hemorrhage
Thoracic computed tomography
Case report

ABSTRACT

Primary cardiac tumors are a rarity, and sarcomas emerge as the prevailing form of primary malignant cardiac tumors across age groups, encompassing both children and adults. Within this category, angiosarcoma stands out, constituting around 31% of all primary malignant cardiac tumors. Primary cardiac angiosarcoma displays a notably aggressive nature, characterized by early systemic metastasis, and is accompanied by a generally unfavorable prognosis.

We describe a case concerning a previously healthy teenage girl who displayed persistent constitutional symptoms and hemoptysis for 15 days. Subsequent investigation uncovered alveolar hemorrhage, ultimately linked to a cardiac angiosarcoma. The difficulty in this instance arose from the vague nature of the initial symptoms, posing a challenge to promptly and accurately diagnose the condition.

This case highlights the aggressive nature of primary cardiac angiosarcoma. The vague initial symptoms underscore the need for early detection and optimized treatment to improve the generally unfavorable prognosis associated with this condition. Increased awareness and a multidisciplinary approach are crucial in addressing the diagnostic and therapeutic challenges posed by primary cardiac angiosarcoma.

☆ Acknowledgments: We thank all the people who contributed to the realization of this work.
☆☆ Competing Interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.
★ Funding: This study had no funding from any resource.
★★ Authors' contributions: All authors have contributed to this work and have read and approved the final version
† Availability of data and materials: All relevant data generated and analyzed during this study are included in this published article. If it needs any additional information, it is available from the corresponding author on reasonable request.
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https://doi.org/10.1016/j.radcr.2024.01.045

Introduction

Cardiac tumors are uncommon in children, encompassing both primary and secondary types, with a prevalence ranging from 0.0017% to 0.28% in autopsy studies and an incidence of 0.14% during fetal life [1]. Malignant tumors constitute approximately 20% to 30% of all primary cardiac neoplasms, with sarcoma being the predominant type in both pediatric and adult cases. Among malignant cardiac tumors, angiosarcoma holds the highest occurrence at 31%, followed by rhabdomyosarcoma at 21% [2]. Angiosarcoma, a rare malignant vascular tumor, demonstrates a lower incidence in adults compared to children and adolescents. It predominantly affects middle-aged adult males, although there are reports indicating a higher incidence in females for primary cardiac sarcomas [3]. Due to its rarity, only a limited number of case reports are available, highlighting its highly aggressive nature, early systemic metastasis, and poor prognosis. Diagnosing this disease poses challenges, often resulting in delays due to the absence of specific symptoms. A conclusive diagnosis relies on histopathological examination [4]. The management of cardiac angiosarcoma remains a subject of debate, lacking standardized treatment regimens.

This review presents an unusual case involving a female adolescent patient with a right atrial mass and alveolar hemorrhage, ultimately identified as a malignant cardiac tumor with lung metastasis. This atypical presentation deviates from the expected epidemiological patterns. Our paper was written according to the CARE guidelines [5].

Case presentation

A 16-year-old girl presented to the emergency room with a recent 15-day history of asthenia and anorexia, accompanied by a cough, intermittent hemoptysis, and exertional dyspnea. She denied any fever, night sweats, weight loss, chest pain, palpitations, joint pain, rash, or urinary complaints. Her medical history revealed a 4-year history of untreated iron deficiency anemia. There was no history of toxic habits, air pollution, and her family history was negative for autoimmune diseases.

Upon physical examination, her respiratory rate was 16 breaths per minute, heart rate was 100 beats per minute, blood pressure was 100/70 mmHg, body temperature was 37.0°C, and percutaneous oxygen saturation was 90% on ambient air, necessitating oxygen therapy to maintain saturation at 94%. Skin and mucous pallor with subicterus and crackling sounds on pulmonary auscultation were noted. Chest X-ray revealed bilateral alveolo-interstitial opacities, more pronounced in the right lung (Fig. 1). Biologically, she presented with a hemoglobin level of 7 g/dL (reference range 12.1-15.1 g/dL), indicative of hypochromic and microcytic anemia, ferritin at 40 ng/mL (reference range 24-307 ng/mL), white blood cell count at 6400 elem/mm^3 (reference range 4500-11,000/mm^3) with eosinophils at 900 elem/mm^3 mm^3 (reference range 30-350/mm^3), and platelets at 350,000 elem/mm3 (reference range 150,000-450,000/mm^3). Coagulation studies showed a prothrombin time of 50% (reference range 85%-100%), fibrinogen at 500 mg/dL (reference range 200-400 mg/dL), and C-reactive protein at 15 mg/L (reference range 0,3-1 mg/dL). Indirect bilirubin was elevated at 32 μmol/L (reference range 3.4-12.0 μmol/L), with schizocytes and decreased haptoglobin, suggesting associated hemolysis. Renal and liver function, urine analysis, and procalcitonin were normal. Despite negative COVID-19 tests, a chest CT scan revealed frosted glass areas with Crazy Paving patterns, indicative of alveolar hemorrhage, and a heterogeneous mass in the right atrium (Figs. 2.1 and 2.2). The transthoracic echocardiogram revealed a mobile, heterogeneous, nonvascularized mass originating from the lateral portion of the free wall of the right atrium. One part of the mass occupied the majority of the atrial cavity, while an extracardiac component projected towards the right ventricle associated with pericardial effusion, without concurrent valve disease or ventricular dysfunction (Fig. 3). Initially, the patient was suspected to have a diffuse alveolar hemorrhage secondary to pulmonary capillaritis associated with the cardiac mass. Subsequent investigations, including normal protein electrophoresis, borderline positive antinuclear antibodies, negative antiribonucleoprotein antibodies, antibasement membrane antibodies, cytoplasmic antineutrophil antibodies, antiphospholipid antibodies, complement and cryoglobulin levels, and tumor markers (CA 15.3, CA19.9, CA 125, and AFP), ruled out autoimmune causes of alveolar hemorrhage. HIV serologies were negative, and infectious parameters, including those related to COVID-19, were also negative, eliminating an infectious cause. Additionally, a cerebral and abdomino-pelvic CT scan, conducted as part of the extended assessment, did not reveal another secondary location. We diagnosed the case as diffuse pulmonary hemorrhage and initiated treatment with 240mg/day of methylprednisolone for 1 week, which was subsequently reduced to 50 mg/day orally. Additionally, 2 units of erythrocyte suspension were administered twice. A regression of pulmonary hemorrhage was observed and confirmed by chest CT scan, leading to an improvement in the patient's condition. We diagnosed the case as diffuse pulmonary hemorrhage and initiated treatment with 240 mg/day of methylprednisolone for 1 week, which was subsequently reduced to 50 mg/day orally. Additionally, 2 units of erythrocyte suspension were administered twice. A regression of pulmonary hemorrhage was observed and confirmed by chest CT scan, leading to an improvement in the patient's condition. After 2 weeks of clinical progress, we opted for surgery via a median sternotomy. During the operation, tumor tissue covering the right atrium, the entire anterolateral pericardium, and extending over the right ventricle was discovered. The tumor was fragile and necrotic, prompting a complete excision with atrium reconstruction. An anatomopathological study revealed a vascular neoplasia (Fig. 4A). Subsequently, immunohistochemistry was performed, showing positivity for platelet endothelial cell adhesion molecule (CD31) (Fig. 4B). These findings were consistent with cardiac angiosarcoma, confirming the definitive diagnosis.

However, 1 week postsurgery, bilateral infiltrations were identified on the chest X-ray. Unfortunately, the patient's general condition deteriorated, ultimately leading to her demise during this hospitalization period.

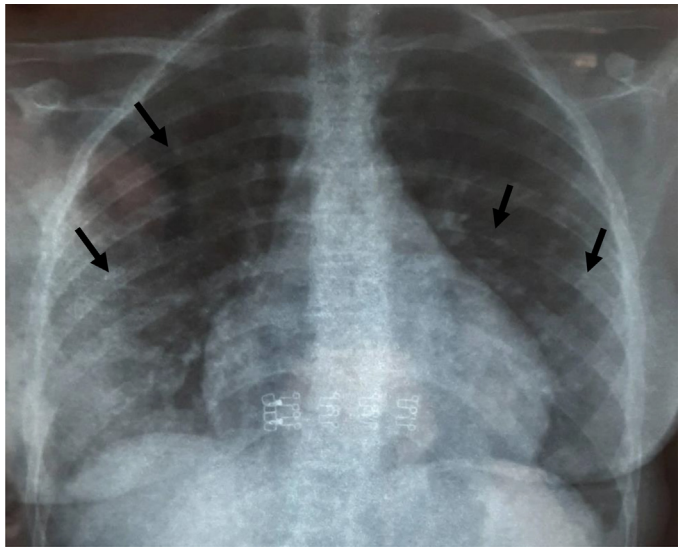

Fig. 1 – Chest x-ray showing bilateral alveolo-interstitial opacities more marked in the right lung (arrows) with an overflow from the lower right arch.

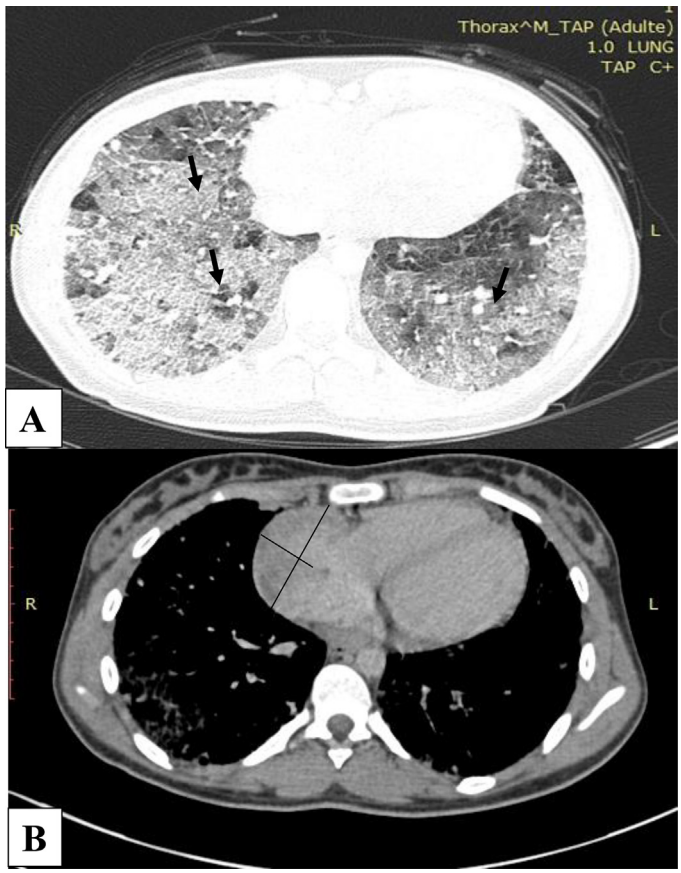

Fig. 2.1 – Chest CT showing: (A) Frosted glass areas diffusing predominantly at the bases, with scattered hyperdense pulmonary opacities evoking an alveolar hemorrhage(arrows). (B) Heterogeneous mass in the right atrium measuring 60*37 mm in transverse diameter and 60 mm in height.

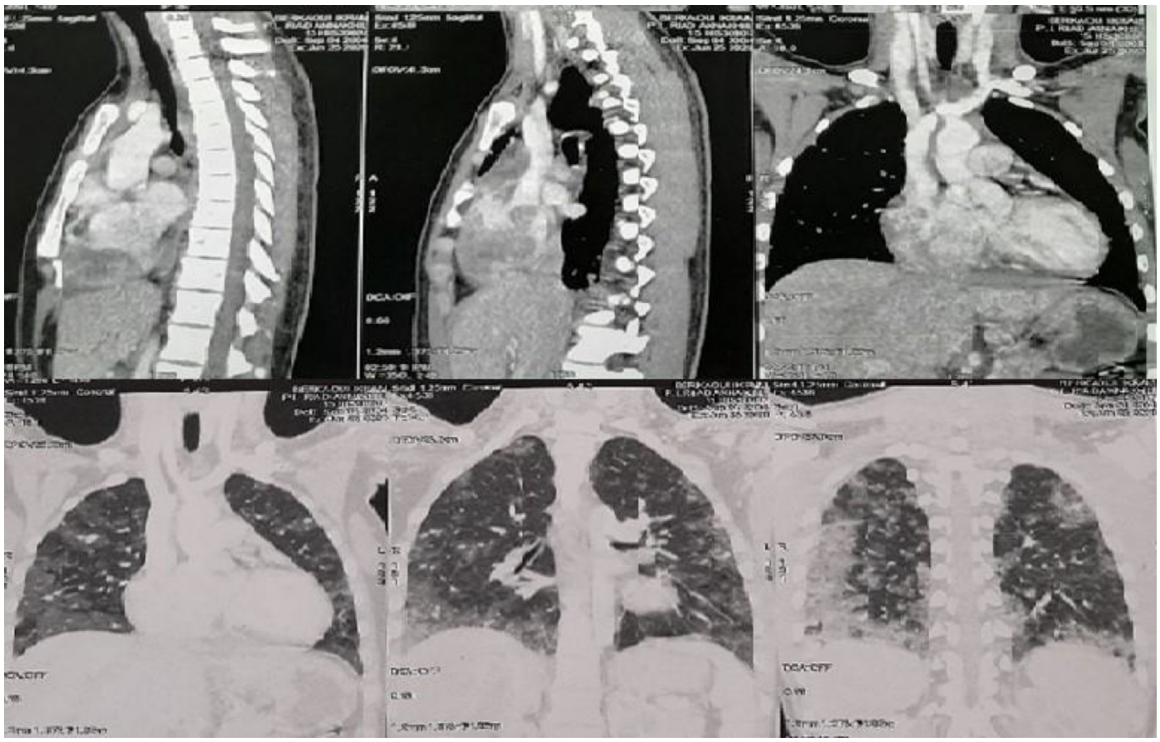

Fig. 2.2 – Coronal and sagittal CT scan sections illustrating the extent of the mass and extension of the pulmonary involvement.

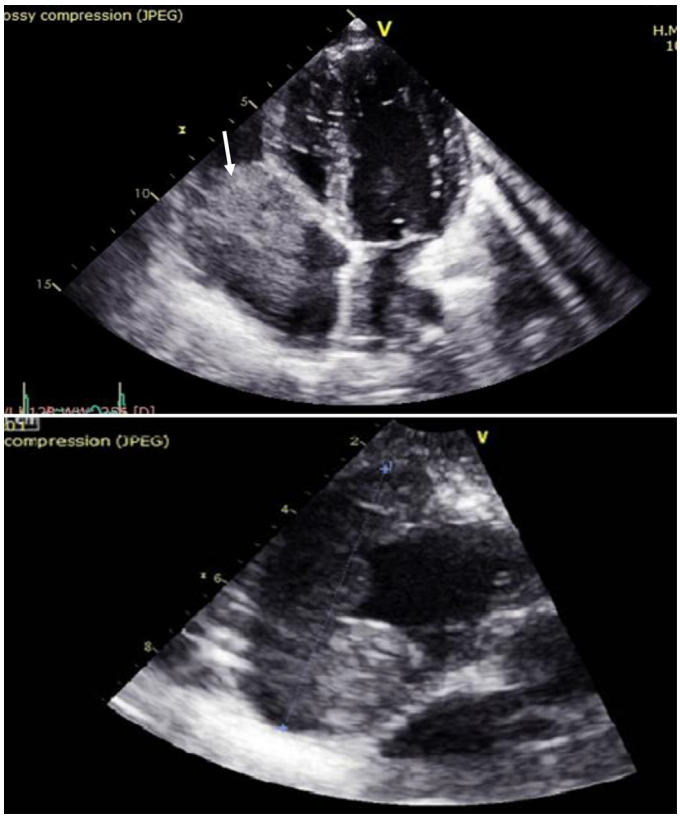

Fig. 3 – Heterogeneous mass that arises from the free wall of the right atrium (arrow) with an extra cardiac part which projects towards the right ventricle associated with pericardial effusion.

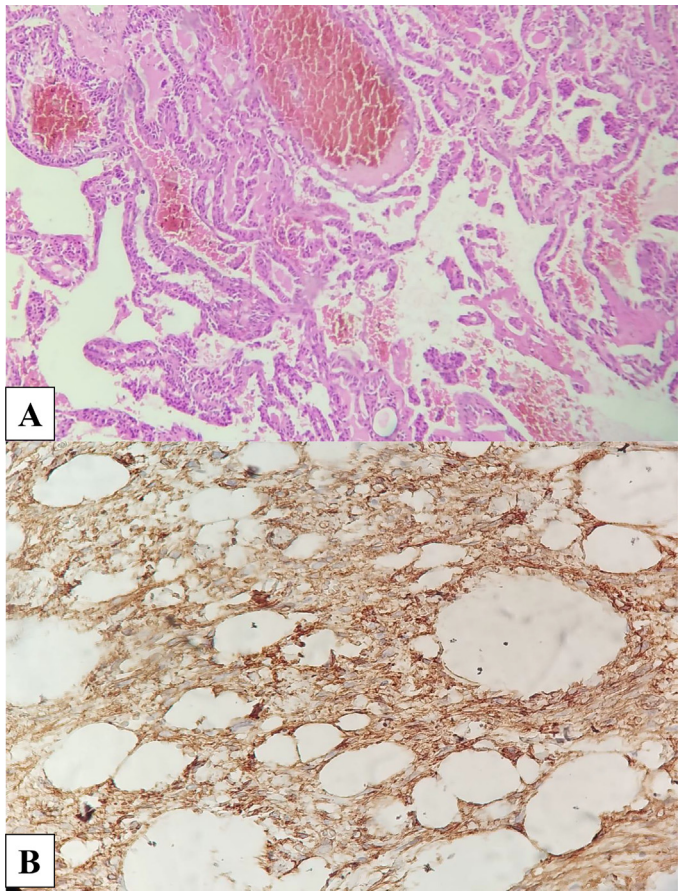

Fig. 4 – (A) Tumoral proliferation with vascular channel lined by atypical endothelial cells (HE x100) (B) Immunohistochemical staining revealing a high expression by the tumoral cells of the endothelial marker CD31 demonstrating the endothelial origin of the neoplastic cells (IHC x 200).

Discussion

Among malignant cardiac tumors in children, metastases are 10-20 times more common than malignant primary tumors. They are commonly located in the pericardium, right heart, and left heart and vary depending on the primary malignancy. Sarcomas are the most common primary malignant tumors in both children and adults, constituting 75% of primary malignant cardiac masses [6]. They are predominantly located in the atrium, or ventricle, and myocardium [7]. Undifferentiated sarcoma, angiosarcoma, and rhabdomyosarcoma are the most common sarcomas in children [1]. Angiosarcomas are highly aggressive tumors consisting of irregularly shaped vascular channels lined by anaplastic epithelial cells with sizable areas of necrosis and hemorrhage. These tumors typically arise from the right atrium in approximately 75% of cases, filling this chamber and then infiltrating the pericardium, tricuspid valve, right ventricle, and right coronary artery [8]. The invasion of the ventricular septum or ventricular walls makes complete excision impossible. Metastases develop in 47% to 89% of patients, most commonly to the lungs, bone, colon, and brain [9]. As sarcomas infiltrate extensively, the prognosis is poor and uniformly fatal. While no direct attribution has been established between secondhand smoking exposure and the occurrence of cardiac angiosarcoma, some studies describe that exposure to vinyl chloride monomer at high environmental concentrations can cause liver angiosarcoma [10], but no literature concerns the cardiac location. The clinical presentation is nonspecific and depends on the size and location of the cardiac tumor. Children or adults with cardiac tumors may specifically present with atrial localization, manifesting as superior vena cava syndrome and peripheral edema. On the other hand, those with ventricular localization can develop arrhythmias, heart failure, heart murmurs, valvular insufficiency, dyspnea, and hemoptysis, as observed in our case, or, rarely, may experience sudden death [11]. Abnormal electrocardiographic findings can occur, ranging from asymptomatic conduction disturbances to fatal arrhythmias [11]. Our patient presented with anemia and pulmonary symptoms related to diffuse alveolar hemorrhage. In the classical presentation, the most common causes are vasculitis, such as Wegener's granulomatosis or microscopic polyangiitis, and connective tissue diseases, including systemic lupus. Diffuse pulmonary hemorrhage is a rare presentation of angiosarcoma, especially in young adults or adolescents, manifesting as a crazy paving pattern on thoracic computed tomography (CT) [12]. The crazy paving pattern is defined as thickened inter-

lobular septa and intralobular lines superimposed on diffuse ground-glass attenuation, named for its resemblance to stone pavement streets. This pattern is classically noted as a finding in COVID-19 infection [13], which was initially considered in our case report due to the pandemic context. However, repeated PCR and serology ruled out the diagnosis. The evaluation of a cardiac mass typically begins with echocardiography. On transthoracic echo, angiosarcomas typically appear as anechoic nodular or lobulated masses in the right atrium, often accompanied by pericardial effusion or direct pericardial extension. Transesophageal echo allows for distinguishing the tumor from a thrombus and assessing its location and anatomical relationship with the valves. Computed tomography reveals a grossly hemorrhagic tumor, often presenting a heterogeneous appearance due to scattered areas of nonenhancing necrosis [14]. Invasion into adjacent structures at the time of diagnosis is common, with pericardial and pleural effusions readily observed [14]. Cardiac magnetic resonance imaging (MRI) further characterizes the mass, facilitating diagnosis and providing information for preoperative planning. On T1-weighted imaging, it appears as isointense lesions with multiple nodular areas of high intensity [15]. Late gadolinium enhancement characteristics of the tumor show heterogeneous enhancement or a large necrotic core without enhancement [15]. Ultimately, histopathological analysis of the material obtained by biopsy or surgical resection is necessary for a correct diagnosis and staging, guiding appropriate therapy initiation. The standard therapy involves a combination of surgery, chemotherapy, and radiation therapy, as recommended by the Soft Tissue Sarcoma Committee of the Children's Oncology Group [16]. Complete surgical resection is the most crucial prognostic factor, but subtotal resection may also alleviate symptoms in selected cases [16]. In cases of incomplete surgical resection, chemotherapy, and radiotherapy can be employed, with high doses of radiation potentially improving local tumor control [17]. Chemotherapy for cardiac angiosarcoma is controversial, with doxorubicin and ifosfamide being the most eligible agents, along with cyclophosphamide, taxanes, vincristine, and dactinomycin. Combination therapy with doxorubicin and ifosfamide has shown effectiveness in treating metastatic soft-tissue sarcomas, including angiosarcoma, regardless of origin [18]. In our case, despite the high lethality of angiosarcomas of the heart, we conclude, based on our experience, that surgery was indicated to clarify the diagnosis, provide palliation, and improve short-term survival. Nevertheless, the prognosis remains poor, with mean survival ranging from 2 to 55 months, a median survival of 14 months after surgical resection, and a mean survival of 3.8 ± 2.5 months without surgical resection [19].

Conclusion

This case report serves as a means to draw attention within the professional community to consider primary cardiac lesions in adolescent patients presenting with diffuse alveolar hemorrhage or nonspecific symptoms. Early recognition based on such cases can significantly contribute to extending the survival of these patients and ensuring a better quality of life through timely intervention.

Patient consent

Written informed consent was obtained from the patient's parents (legal guardian) for publication and any 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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