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Long-term Follow-up of Cardiac Calcified Amorphous Tumor in Three Thalassemia Patients

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ABSTRACT

Introduction: Cardiac Calcified Amorphous Tumors (CATs) are rare non-neoplastic heart intracavitary mass lesions. Cardiac CATs may arise in any heart chamber and are characterized histopathologically by diffuse calcium infiltration. The recommended treatment of choice is complete resection of the mass through surgery. Herein, three cases with thalassemia were presented with significant CATs that remained asymptomatic during close observation without any surgical interventions.

Case Presentation: The three patients suffered from thalassemia. One of them had a calcified mass (3.8 × 0.74 cm) in the right ventricle in the vicinity of ventricular trabeculations, which prolapsed into the tricuspid valve orifice that resulted in moderate to severe tricuspid regurgitation without the development of any stenosis. Another case had an irregular calcified mass (2.3 × 0.75 cm) in the roof of the left atrium. The third case had a large calcified mass with a mobile component in right ventricular trabeculation. Surgical resection of the mass was recommended in all the cases, but they were closely monitored without surgical intervention. During the five-year follow-up, they remained totally asymptomatic and had no cardiovascular or cerebral events.

Conclusions: Immobile CATs in patients with thalassemia can be asymptomatic. Hence, they can be closely monitored and surgical intervention can be delayed for many years.

1. Introduction

Cardiac Calcified Amorphous Tumors (CATs) are rare and infrequent non-cancerous intracardiac mass lesions with similar presentations to other cardiac masses (1). The clinical diagnosis of CAT is quite difficult and therapeutic challenges are another problem. The treatment of choice is complete surgical resection (2). Herein, three cases of thalassemia have been reported with significant CATs that remained asymptomatic during close observation without surgery.

2. Case Presentation

First case: The first case was a 47-year-old woman with a history of major thalassemia under continuous blood transfusion therapy. Her hemoglobin was 8.5 mg/dL prior to transfusion. The results of the tests for renal, thyroid, and parathyroid function were normal. Routine transthoracic echocardiography showed a calcified mass (3.8 × 0.74 cm) in the right ventricle attached to ventricular trabeculations with prolapse into the tricuspid valve orifice, resulting in moderate to severe tricuspid regurgitation (Figure 1). The right atrium was normal in size. Cardiac Magnetic Resonance (CMR) imaging showed a multi-fragmented Right Ventricular (RV) mass that was iso-signal to low signal in the Steady-State Free Precession (SSFP) sequence, which was attached to the RV mid to apical trabeculation (with at least two components measured about 23×5 mm and 15 × 5 mm). The mass had a strongly high signal intensity in the STTR/T2 weighted sequence. However, the mass did not have any gadolinium enhancement in the late-enhancement sequence and was without any perfusion in the first pass perfusion sequence. The characteristics of the mass were compatible with a cardiac CAT. The right ventricle was mildly dilated without hypertrophy and had normal systolic function (Right Ventricular Ejection Fraction (RVEF = 54%). There was no myocardial iron overload.

Second case: The second case was a 28-year-old man with a history of major thalassemia on chronic transfusion therapy. His hemoglobin was 9 mg/dL before transfusion. Other laboratory data were within the normal range.

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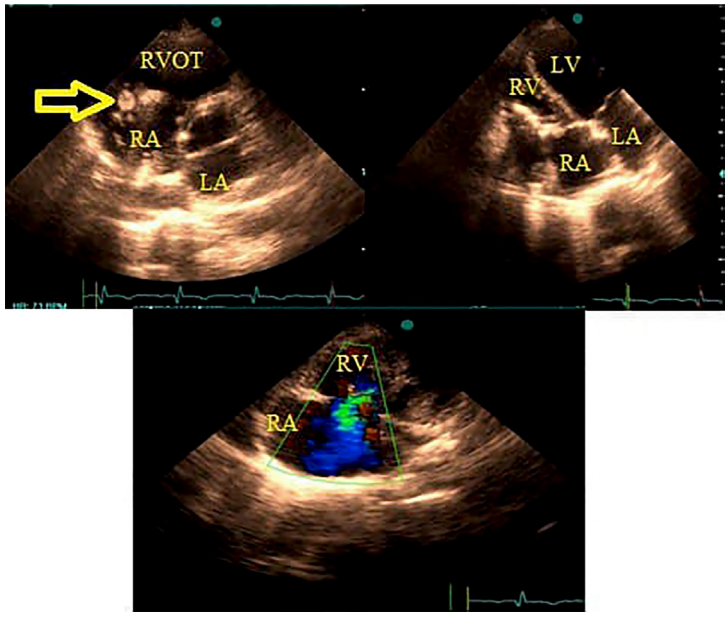

Figure 1. The Arrow Points to the Calcified Amorphous Tumor in the Right Ventricle Attached to Ventricular Trabeculations with Prolapse into the Tricuspid Valve Orifice, Which Resulted in Moderate to Severe Tricuspid Regurgitation.

Routine transthoracic echocardiography showed a calcified irregular immobile mass (2.3 × 0.75 cm) in the posterolateral aspect of the left atrium. A small calcified spot was also detected on the inter-atrial septum at the fossa ovalis region. The left atrium was moderately enlarged in size. The biventricular function was normal without any noticeable valvular abnormalities. There was a mild pulmonary arterial hypertension (Figure 2). CMR data confirmed the presence of a left atrial mass lesion, suggesting a cardiac CAT. No myocardial iron overload was detected.

Third case: The last case was a 21-year-old man with intermediate thalassemia referred with gradually aggravated dry coughs for the last four months, sputum without hemoptysis, and intermittent fever in the setting of pneumonia. On his past medical history, splenectomy was noticeable. He had received regular blood transfusions up to two months ago. He was taking cefixime and hydroxyurea. On admission, he had dyspnea with NYHA functional class II/III. He also had sinus tachycardia with a heart rate of about 120 beats per minute and his body temperature was 38 ºC. Other vital signs were stable. On physical examination, splenomegaly and decreased respiratory sounds at the left lung lobe were noticeable. No infection source of fever was found. The laboratory data showed elevated white blood cell count (15300/m3) and no bacteria growth in blood and urinary cultures. The results of inflammation-related tests such as C-reactive protein and erythrocyte sedimentation rate were within the normal range. The pro-BNP level was elevated (779.5 mg/dL, reference value: < 125 mg/dL). Moreover, transthoracic echocardiography demonstrated mild systolic dysfunction, mild left ventricular diastolic dysfunction, normal left ventricular size, and moderate RV enlargement with mild to moderate systolic dysfunction. Furthermore, pulmonary artery hypertension due to

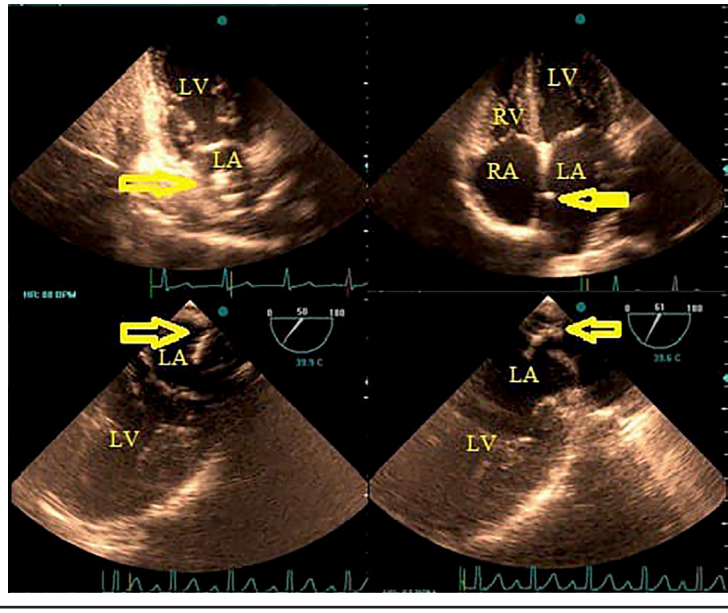

Figure 2. The Arrow Points to the Calcified Amorphous Tumor in the Left Atrium and Inter-Atrial Septum at the Fossa Ovalis Region.

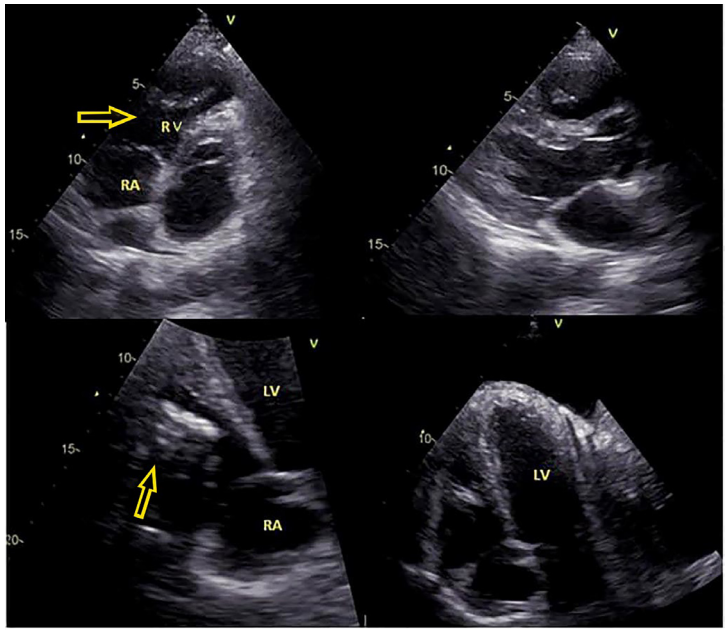

Figure 3. The Arrow Points to the Calcified Amorphous Tumor in the Right Ventricular Trabeculations.

moderate tricuspid regurgitation, small pericardial effusion, and left-sided pleural effusion were detected. There was also a large calcified mass with a mobile component in RV trabeculation (sized about 5 × 1.87 cm) (Figure 3). The mass was mostly compatible with a cardiac CAT. Due to dyspnea, tachycardia, and pulmonary arterial hypertension, cardiac CT Angiography (CTA) was performed to rule out pulmonary throboembolism. The results revealed a dilated main pulmonary artery, chronic pulmonary embolism in the right lower lobar and most bilateral segmental arterial branches accompanied by web-like luminal densities, and chronic left postero-basal segmental branch occlusion. Minimal left postero-basal sub-pleural consolidation with mild left-sided pleural effusion were noticed, as well. Color Doppler sonography showed normal flow and compressibility in the peripheral veins.

The surgical resection of the mass was recommended for all cases. However, the researchers preferred to observe them closely with the optimization of thalassemia treatment, because of the increased risk of cardiac surgery in thalassemia cases as well as the possibility of recurrence of calcific masses. The cases were regularly followed up with acceptable echocardiography and CMR findings. Fortunately, the first and second cases did not show any side effects during the follow-up. However, the third case was visited due to having serious symptoms after the deliberate discontinuation of all medications, which returned to normal after the resumption of medications. After a five-year medical follow-up, all cases are asymptomatic now.

3. Discussion

Imbalanced phosphocalcic metabolism has been proposed as the main contributing mechanism to the development of cardiac CATs in the setting of End-Stage Renal Disease (ESRD). However, the role of this abnormality in the setting of thalassemia has not yet been widely evaluated (3). There are reports regarding the genetic background in the development of unwanted calcification (4, 5). Ectopic calcification has also been reported in the setting of Pseudoxanthoma Elasticum (PXE) and PXE-like cases due to the activation of fibroblasts, smooth muscle cells, and pericytes (6). Similarly, there are reports of ectopic calcification affecting different organs such as the cardiovascular system in thalassemia (7). However, the prevalence of cardiac CATs has been found to be low in a variety of patients with thalassemia. Nonetheless, the impact of fibroblast gene alterations on ectopic calcification is unclear and needs further investigations.

In the categorized definition of intra-cardiac masses, CATs have been recognized as benign tumors (8). This particular pathological mass is a rare benign cardiac mass with similar manifestations to other cardiac tumors mostly related to the embolization of calcified fragments or flow obstruction such as syncope and dyspnea (9). The precise diagnosis of CATs is made by surgical resection. In the case of asymptomatic patients, however, such imaging modalities as echocardiography, CMR imaging, and CT scan are helpful (10, 11). If clinically suspicious immobile cardiac CATs are present and patients are asymptomatic, close observation and postponing the surgical operation are recommended, especially in thalassemia cases. Furthermore, adequate blood transfusion and iron chelation therapy may slow the growth of calcified masses, because they can control and modulate chronic oxidative stress conditions.

3.1. Conclusions

CATs with immobile features in patients with thalassemia can be managed by close observation and postponing the surgical intervention. This can be considered a piece of advice in the thalassemia cases who are reluctant or high risk for surgical interventions.

3.2. Limitations of this Study

The pathological examination of these masses was not evaluated and the diagnosis of CATs was just based on the echocardiography and CMR data.

3.3. Ethical Approval

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3.4. Informed Consent

The informed consent form was signed and uploaded.

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Authors' Contribution

M.P.: data collection and analysis, M.B.: drafting and revision of the manuscript and study supervision.

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The authors declare that there is no conflict of interest.

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