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Case Report

Intracardiac amorphous tumor presenting in a patient with homocystinuria; a case report with literature review ☆,☆☆

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ABSTRACT

Homocystinuria is a rare genetic disease with autosomal recessive pattern. It is reported to be highest in Arabian descend and could cause thrombosis, but mainly peripherally. Cardiac amorphous tumor has been recognized in the past 20 years and it is also a very rare cause primary benign tumor of the heart. Most of the cases reported to be associated with end-stage renal disease. Homocystinuria associated with Cardiac Amorphous tumor is extremely rare. Up to our knowledge, there has been only one other case has been reported. Our patient is a 14-year-old female known case of homocystinuria presented with dyspnea and leg edema. On workup was found to have a mass in the right atrium extending to superior vena cava and inferior cava. Surgery undertaken on cardiopulmonary bypass partial resection of the mass was done and result came back as cardiac amorphous tumor. We assume the cause of this sinister complication of her primary illness is calcification of thrombus as stated in literature. And also recommend further studies regarding issue on hand.

Introduction

Among autosomal recessive diseases, homocystinuria (HCU) is a relatively rare condition. HCU prevalence varies based on ethnicity—it is as low as 0.02:100,000 in Asians, 0.2:100,000 in Africans, and 0.72:100,000 in most Europeans. Currently, there is a ratio of 1:100,000-200,000 in the United States, and it rises to 1:20,000 in the Gulf region for countries such as Qatar, where it is 1:1800 [1–3]. Recent research from the United States

Abbreviations: CAD, cardiac amorphous tumor; HCU, homocystinuria; CT scan, computed tomography scan; MRI, magnetic resonance imaging; RV, right ventricle; PA, pulmonary artery; IVC, inferior vena cava; SVC, superior vena cava; RA, right atrium.

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indicates that the number is highly underestimated, and the actual number is 10 times higher [3].

This condition results from an inborn error of metabolism caused by an insufficient amount of cystathionine beta-synthase enzyme. As a result, blood and urine levels of homocysteine and methionine are increased [2]. This elevation increases the risk of developing thromboembolic events. Due to an elevated level of homocysteine in the blood, HCU is considered to be an inheritable thrombophilia. An elevated homocysteine level in the blood alters endoplasmic signaling, thereby causing endothelial dysfunction [2,4].

Hyperhomocysteinemia and HCU may contribute to the development of atherosclerosis and plaques. The first report of this disease was published in 1964 [5]. Reynolds et al. first described cardiac calcified amorphous tumors (CATs) in 1997 [6]. CAT is a rare non-neoplastic intracavitary primary heart tumor characterized by calcification and calcium nodules within an amorphous fibrinous matrix. Those with a history of thrombosis are at risk for developing such a condition [6]. The likelihood of developing this condition is higher among patients with end-stage renal disease [7].

There is a lack of understanding in the literature regarding the connection between the 2 entities mentioned above. In our case, the patient is a known case of homocystinuria who was recently diagnosed with an amorphous cardiac tumor.

Case report

A 14-year-old female diagnosed with homocystinuria in 2014 presented with progressive shortness of breath for the past 8 months. After visiting multiple specialty centers, she was referred to our department at the Sulaimaniyah Teaching Hospital, As-Sulaimaniyah, Iraq. In addition to orthopnea, bilateral lower leg swelling, and fascial swelling, her condition progressively worsened.

The medical and surgical history of the patient indicates that she suffered a right radial fracture when she was 3 years old. Additionally, she had undergone a tonsillectomy. As well as nearsightedness, she has been diagnosed with lens displacement; she has been wearing glasses for the past 5 years. As a result of her condition, she is taking pyridoxine and folic acid.

It has been reported that she has a strong family history of HCU, as 2 of her sisters and 1 of her brothers suffer from the same disease. She denied any history of invasive lines, including central lines.

An examination revealed engorged neck veins, axillary lymphadenopathy, long slender hands, and leukonychia. An examination of the chest revealed bilaterally decreased air entry. There was pitting edema in the lower limbs. An ophthalmological examination revealed amblyopia. Her mental state and intelligence were intact.

On imaging, her chest X-ray revealed calcifications in the right atrium and superior vena cava (SVC) (Fig. 1A). An echocardiogram revealed a mass that extended from the right innominate vein into the right atrium and SVC. Contrast computed tomography (CT) scan of the chest showed an intracavitary hyperdense mass in the SVC and right atrium

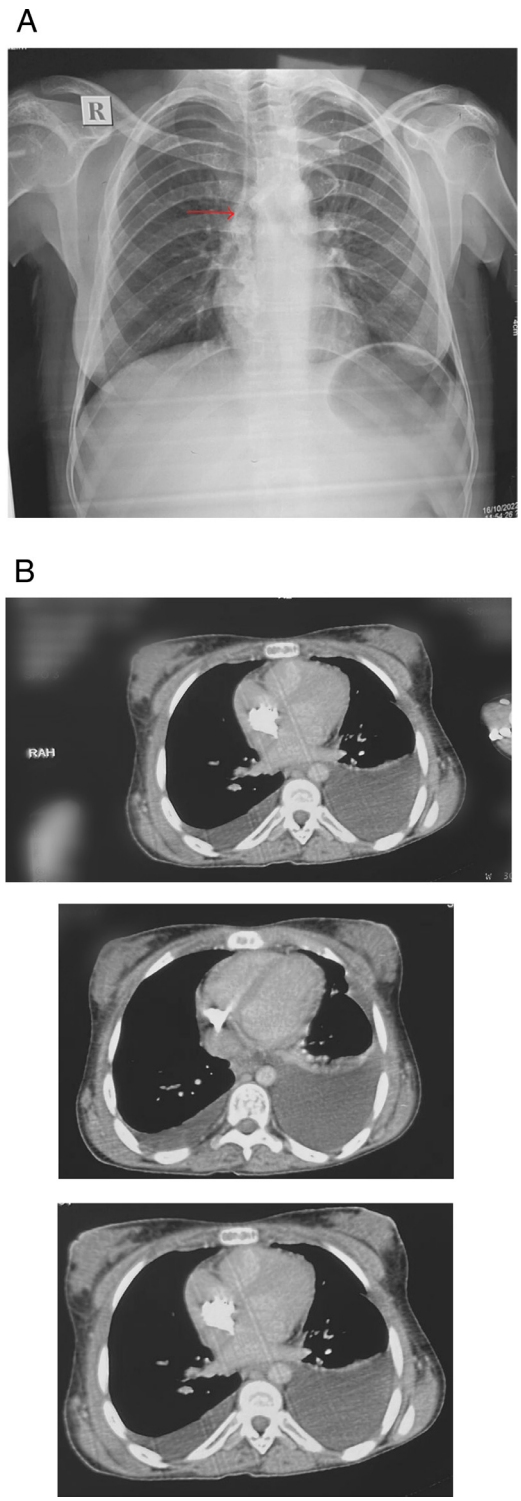

Fig. 1 – (A) Chest X-ray shows heterogeneous opacity in the right mediastinum (arrow). (B) CT scan shows RA and SVC calcified lesion and bilateral pleural effusion. CT, computed tomography; RA, right atrium; SVC, superior vena cava.

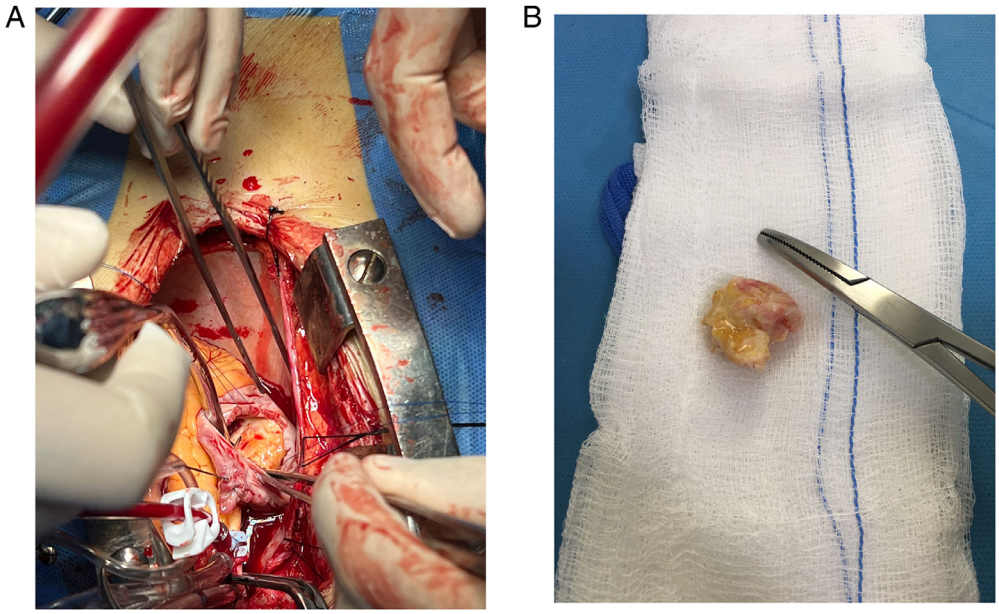

Fig. 2 – (A) shows the tumor inside RA and on the orifice of IVC. (B) Resected tumor specimen. RA, right atrium; IVC, inferior vena cava.

(Figs. 1B). Cardiac magnetic resonance imaging (MRI) showed a hypointense lesion on both T1- and T2-weighted images suggesting it was an intramural thrombus.

The patient was prepared for surgery on cardiopulmonary bypass through sternotomy. Intraoperative findings revealed a cord-like SVC. Due to heavy calcification, direct cannulation of the SVC and inferior vena cava (IVC) was not possible. The patient was put under deep hypothermic circulatory arrest after atrial cannulation (Fig. 2A), and the right atrium was opened. The mass stretched from the SVC orifice attached to the interatrial septum, coronary sinus, and septal leaflet of the tricuspid valve to the IVC orifice in the right atrium. In both the IVC and SVC, the orifices were cleared. However, the mass could not be removed entirely. The resected specimen was sent for histopathological examination (Fig. 2B).

The patient was transferred to the ICU and kept there for 1 day. After 2 days in the surgical ward, the patient was discharged home. The result of the biopsy came back as an amorphous cardiac tumor. A follow-up of 10 days postoperation showed that the patient was doing well and her symptoms were improving.

The diagram shows a hand drawing of the mass and involved structures (Fig. 3).

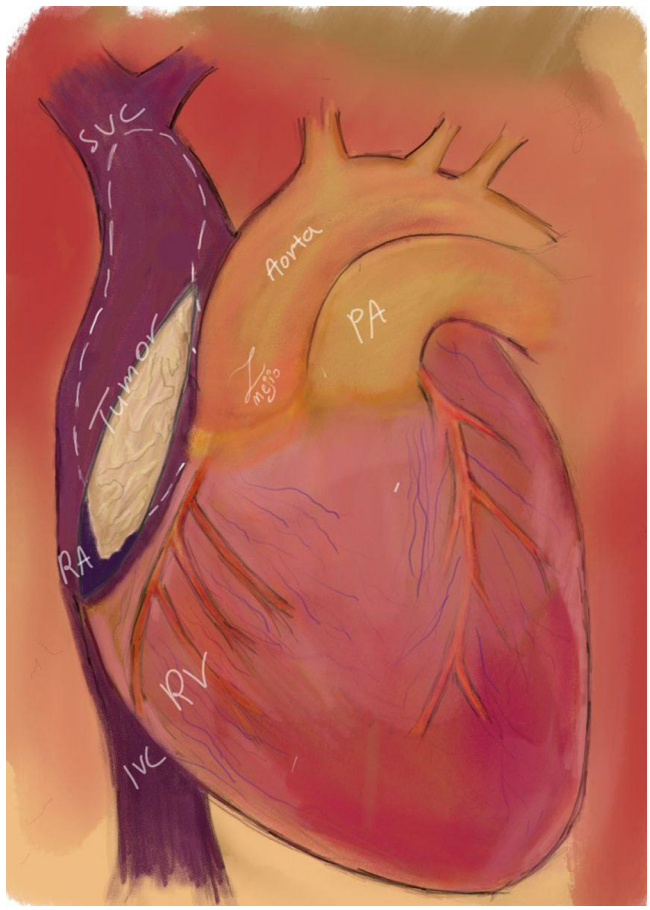

Fig. 3 – A sketch drew by one of the authors to show site of the tumor.

Discussion

Based on the response to therapy with pyridoxine (vitamin B6), HCU can be divided into 2 types. In infancy, they may be normal, or they may exhibit nonspecific signs such as failure to thrive [8]. The condition may be mistaken for Marfan syndrome due to their thinness and tall stature, as well as its arachnodactyly and Marfanoid characteristics [8]. Chil-

dren may experience cardiovascular and cardiac complications later in life, with thrombotic events ranging from 13% to 78%. According to Mudd et al., 25% of children with homozygous HCU developed thrombotic events [9]. In the responsive type, the annual risk is 4%-8%, while in the nonresponsive type, it is 6%-10% [9].

According to Mandel et al. [10], venous thromboembolism risk is greatly increased in Arab and Israeli families since HCU and factor V Leiden deficiency are concordant. Our patient is of Arab descent.

It is important to discuss a subtype referred to as the vascular subtype, which indicates that very high levels of homocysteine cause late-onset venous thrombosis [11]. In this study, a family with 3 sisters with hyperhomocysteinemia developed single or multiple venous thromboembolic episodes [11].

CAT has only been reported in the literature in the past 2 decades, but reports about similar lesions date back to when they were known as calcified pseudotumors. As a result, it is likely that this condition is underreported in the literature. There is a lack of understanding of the pathology of such tumors. Several theories have been proposed. There is a theory that ordinary thrombi become mummified and calcified with time, although Reynolds rejected this idea at the time since a calcified thrombus may not exhibit Lines of Zahn. Hypercoagulability and abnormal phosphate calcium metabolism are 2 other theories [6,7,12,13].

There are several different diagnoses of CAT, including myxoma and thrombi formation. The diagnosis of CAT can be challenging [6,14–16]. It may provide a clue based on clinical manifestations, such as in patients with end-stage renal disease and valvular heart disease [6]. A cardiac imaging study with echocardiography can aid in diagnosing an intracavitary calcified mass in any chamber of the heart [6], which can still be misdiagnosed as a myxoma, as suggested in Reynolds' original series. The transthoracic echocardiography may also reveal an entity called a swinging CAT, which tends to embolize. CT scans and MRIs can be used to assess CATs that show partially calcified hypodense or diffusely calcified masses. A significant finding is the presence of large foci of calcification in partially calcified CATs, together with low-weighted T1 and T2 images on MRI [16]. The diagnosis is established by a pathological examination of the specimen, which reveals fibrin degeneration and calcific nodules. Most cases of CAD are treated surgically through resection, with a survival rate of up to 95% in the literature [6].

As far as we are aware, there has only been one report of HCU presenting with CAT. A 13-year-old boy with a history of HCU was diagnosed with right atrial CAT and referred for surgery [17].

Conclusion

Based on a comprehensive literature review, we concluded that the relationship between HCU and CAT is not completely understood. It is likely that this is a symptom of a hypercoagulability disease which may lead to thrombosis and further complications. HCU is known to cause atherosclerosis and may contribute to the calcification of thrombi.

Considering that HCU is a treatable disease, we recommend further research into this issue. Such complications can be avoided by treating HCU early.

Authors' contribution

In this case, Diar is the surgeon responsible for collecting the required data, while Yad is the author responsible for writing and finalizing the manuscript. Zryan assisted with manuscript writing and sketched the figure illustrating the tumor site, Arian assisted with data collection, Razhan reviewed the manuscript for grammar and sentence structure, and Han was the pathologist who diagnosed the specimen and wrote the pathology report. The final draft was accepted by all authors.

Ethical statement

An ethical approval has been obtained from the hospital's Ethical Committee.

Patient consent

The patient's guardians (in this case her parents) provided written consent to the Cardiac Center's legal committee and the surgeon in charge to publish this case and show photos that include investigations and intraoperative images.

If the journal so requests, these are available for review.

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