Primary Cardiac Tumors in Infancy: A Case Report and Literature Review

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ABSTRACT

Sudden death in infants due to primary cardiac tumors is extremely rare. Herein we describe a case of an 8-month-old male infant, without any previous medical history, who died in a hospital in the city of Medellín-Antioquia, Colombia. The family stated that approximately 15 minutes after he received a bottle, the baby became cyanotic and subsequently lost consciousness. He was taken to the hospital immediately; however, he arrived lifeless. As this was a sudden death case, the child was referred to the Institute of Legal Medicine and Forensic Sciences in the city of Medellín to clarify the cause, manner, and mechanism of death.

The forensic autopsy revealed a eutrophic infant with central and peripheral cyanosis, without signs of trauma, and the internal examination found a single cardiac tumor in the anterior wall of the left ventricle. The mass was white and whorled; histological evaluation diagnosed a fibroma.

The manner of death was natural due to a cardiogenic shock caused by a primary tumor. *Acad Forensic Pathol.* 2017 7(1): 112-118

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INTRODUCTION

Primary cardiac tumors are rare in the pediatric population. When they do occur, most of these tumors are considered benign, with easily recognizable features. The most common variant is rhabdomyoma, followed by fibromas and teratomas. Published medical literature has also described vascular tumors, myxomas, and lastly, the pericardial teratoma, which comprises a minor percentage.

We present a 8-month-old male infant who suffered a sudden death due to a primary cardiac tumor within the anterior wall of the left ventricle; histopathologic sections revealed a fibroma.

CASE REPORT

A young male infant, 8 months old and without previous medical history, suddenly died in April 2009. The mother stated that at approximately 10:30 pm the baby received a bottle and 15 minutes later became cyanotic and lost consciousness. The infant arrived at the hospital at 11:16 pm, unconscious and with acral and central cyanosis. There, physicians began external monitoring and basic life resuscitation efforts; however, his condition did not improve as he was unresponsive to stimuli, audible heart and lung sounds could not be auscultated, and his pupils were fixed and dilated. Resuscitation efforts were then suspended and the infant was pronounced dead.

As this was a case of sudden death of an infant, it was decided to have a medicolegal autopsy performed. The infant was taken to the National Institute of Legal Medicine and Forensic Sciences in Medellín, Colombia in order to establish the cause, mechanism, and manner of death.

The medicolegal autopsy identified the body as that of a eutrophic (i.e., adequate nutritional status), male infant with generalized cyanosis without any external malformations or signs of trauma. A milky liquid was noted to be exiting the mouth and nose.

The infant's weights and measures were normal for age.

The internal examination revealed an intact pericardium without hemorrhage. The heart weighed 74 g and there was a deformity due to a well-circumscribed intramural mass in the anterior and inferior wall of the left ventricle (**Image 1**).

Cardiovascular examination was performed following the lines of blood flow of the heart revealing a non-patent foramen ovale, a tricuspid valve circumference of 5 cm, pulmonary valve circumference of 3.5 cm, mitral valve circumference of 4.5 cm, and an aortic valve circumference of 3 cm. There was a mass in the anterior and inferior wall of the left ventricle measuring 4.7 x 3 x 3.5 cm, causing a large wall deformity and compressing the intraventricular space (**Image 2**).

The mass was well-circumscribed, off-white, and whorled with a firm consistency (**Image 3**).

Detailed inspection of the other organs, including histopathologic and neuropathology examinations, found no other lesions, anatomical defects, or additional important gross and microscopic findings that would have contributed to the death of the infant. Toxicology studies were negative. Microbiology and metabolic studies were not performed.

At the completion of the autopsy, the heart was preserved for fixation and sections for microscopic examination were obtained. Histological evaluation of the tumor revealed a nonencapsulated neoplasm composed of bland fibroblasts and collagen, without atypia, and infiltrating and displacing the normal underlying myocardium (**Image 4**). A diagnosis of fibroma was made.

DISCUSSION

Primary cardiac tumors are infrequent amongst all age groups. The incidence varies between 0.0017 to 0.28% with more than 90% having a benign histology. The most common variant in the pediatric population is rhabdomyoma (45-70%) and 60% of these cases are in patients with tuberous sclerosis. The next most frequently encountered primary tumors include fibromas (6-25%), teratomas (2-10%), vascular tumors, myxo-

mas, and finally the pericardial teratoma, which comprises a minor percentage (1).

Cardiac tumors, including fibromas, can cause multiple symptoms including those associated with outflow obstruction, interference of the function of the valves, arrhythmias, syncopal episodes, and sudden death. The clinical presentation is related to the size and location of the tumor. The signs and symptoms encountered occur in the following frequency: asymptomatic (63%), murmur (10%), arrhythmias (9%), seizures (5%), cyanosis, respiratory distress and cardiac insufficiency (4%), family history of tuberous sclerosis (3%), hydrops fetalis (2%), polyhydramnios (1%), and cerebral embolism (0.9%) (1-4).

Sudden death occurs from cardiac tumors when they involve critical structures in the heart. It has been described to occur unexpectedly in individuals in good health and without symptoms and in those who show slight symptoms of illness 24 hours prior to death. Sudden infant death syndrome is diagnosed with a prevalence between 0.17 and 1.5 per 1000 live births, followed by undiagnosed neoplasms (primary cardiac tumors and primary neoplasms of the nervous system), along with occult cardiac anomalies, intracranial hemorrhage, and infections (5). The mechanism of death from primary cardiac tumors is by obstruction of the atrioventricular orifices (outflow tract obstruction) (2), anomalies of the cardiac conduction system, and myocardial infarcts by emboli (5).

Image 1: Incision through the lateral left ventricle wall. Intramural mass within the anterior and inferior wall of the left ventricle.

Image 2: Internal view, depicting the anterior and inferior left ventricle wall with a well-circumscribed mass.

Image 3: Cross-section of intramural mass within the anterior wall of the left ventricle.

Rhabdomyomas comprise 45% of primary cardiac tumors in infants and 53% of the benign primary cardiac tumors in the pediatric population. They are associated with tuberous sclerosis (Bourneville disease) in 60–75% of cases. Tuberous sclerosis is an autosomal dominant neurocutaneous syndrome that manifests with mental retardation, seizures, benign tumors in the brain and other organs, and hypopigmentation of the skin with presence of the disease also in one of the family members (2, 6, 7).

Histologically, rhabdomyomas are comprised of large polygonal cells with cytoplasmic vacuoles full of glycogen. The mass is lobulated, white and often small with a shiny or aqueous cut surface; a few hemorrhages and calcifications are commonly found. Multiple small tumors may be present and often occur in the

Image 4: Microscopic findings: bland fibroblasts and collagen (H&E, x40).

left ventricle or in the interventricular septum. When there are multiple tumors, this is often associated with tuberous sclerosis and presents as an outflow tract obstruction. A large number of these tumors spontaneously regress particularly if they occur in the first two years of life. The mechanism responsible for regression, according to the literature, is apoptosis (2).

Cardiac fibromas are solitary, well-circumscribed intramural lesions that are homogenous white in color; they represent 6-25% of pediatric primary cardiac tu-

mors. These tumors originate from fibroblasts of the connective tissue and the majority are located in the free wall of the left ventricle or the intraventricular septum. Histological examination shows an unencapsulated neoplasm composed of fusiform cells without atypia that infiltrate and displace the normal underlying myocardium. There may be areas of calcification and occasional foci of necrosis or areas of cystic degeneration due to its large growth. While histologically benign, these do not spontaneously regress, unlike rhabdomyomas. Depending on its size, these can ob-

struct blood flow within the heart, interfere with the function of the valves, and compromise the conduction system, leading to ventricular arrhythmias, syncope, or sudden death. Fibromas require early surgical treatment and those that do receive this early treatment have a good prognosis (3, 8-10).

Fibromas can occur in the autosomal dominant disorder, Gorlin-Goltz syndrome (characterized by basal cell carcinomas) in 3-5% of cases (10, 11).

Pericardial teratomas are benign tumors that usually present with pericardial hemorrhage or hydrops fetalis. Histologically, elements from all three germ layers may be identified along with multicystic areas and calcifications. These are surgically managed with a high rate of survival occurring after treatment. Even though they have been reported to recur, they are stable or may even regress (1).

Cardiac myxomas are the most common adult primary cardiac tumor. These soft, pale polypoid masses commonly form in the left atrium at the fossa ovale and often lead to valvular obstruction and arrhythmias. Microscopically, they are comprised of stellate cells with eosinophilic cytoplasm and indistinct cell borders within a myxoid stroma with variable fibrosis and calcifications identified. Most of these cases are sporadic, however, 10% are associated with Carney syndrome (12, 13).

Fetal echocardiography and magnetic resonance imaging (MRI) are techniques utilized to diagnose cardiac tumors in utero while echocardiography, cardiac catheterization, and magnetic resonance angiography have greater diagnostic efficacy in the postnatal period. Magnetic resonance imaging supplements the echocardiogram when the results obtained are suboptimal and permits a detailed assessment of the tumor, a better characterization of the tissue, and narrows the differential diagnosis on histopathologic analysis (14). Additionally, it provides a better assessment of the tumor's size, mural wall infiltration, and whether there is extension into the great vessels. The majority of the clinicians prefer echocardiogram in pediatric population, while the MRI has a fundamental role in

the adult (1, 11). These imaging techniques provide clinicians the opportunity to surgically intervene prior to cardiovascular compromise, thus preventing sudden death.

The treatment for cardiac fibromas may require non-radical surgical resection for those patients that present with outflow obstruction and arrhythmias; however, the preferred approach is follow-up echocardiograms in asymptomatic patients, as these characteristically spontaneously regress (9). Some fibroma tumors are managed conservatively, especially when the tumor is large (15).

CONCLUSION

Primary cardiac tumors are tumors that originate in the heart; these are rare in infancy. The majority of these tumors are benign (90-97%) and the effect they have on hemodynamics depends on their size and location. Of these tumors, fibromas are the second most common variety encountered amongst infants only after rhabdomyomas. Fibromas usually present as a solitary unencapsulated lesion located in the free wall of the left ventricle or in the septum. While these are histologically benign, spontaneous remission is a rare occurrence. Although they do not invade, they can become very large in size thus compromising proper hemodynamics and increasing mortality risk (1). Early diagnosis is possible with the help of imaging; however, the majority of patients are asymptomatic. Therefore, sudden death may be the first and only sign of their presence (5). This occurs after compromising the outflow tract when in the left ventricle or when the conduction system is involved, creating a fatal ventricular arrhythmia.

The incidence, prevalence, and mortality associated with these tumors amongst other causes of sudden death is unknown. Upon further analysis, research revealed very few cases reported within the national and international literature. The presented case is an illustration of a young infant without previously known medical history with a primary cardiac tumor that presented with sudden death.

In order to determine the cause of a sudden and unexpected death in an infant, correlation of the pre- and postnatal history along with the perimortem circumstances and any findings of the medicolegal autopsy that explain the physiopathological process that lead to death are required. We also emphasize the importance of the role of radiologic imaging techniques, such as fetal echocardiogram, that provide early diagnosis prior to symptoms suggestive of endstage cardiovascular compromise appear and aids in the histopathologic differential so that early surgical intervention can be made, if necessary, thus preventing sudden death from these tumors.

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