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Case reports

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Ventricular fibrillation and arrhythmia associated with cardiac fibromas involving both ventricles in a 1.5-year-old girl

Daniel Farkaš[1] · Mária Pisarčíková[2] · Peter Vasovčák[3] · Anna Crhová[3] · Alžbeta Ginelliová[1] · Lucia Mistríková[4] · Lucia Fröhlichová[5] · Silvia Farkašová Iannaccone[6]

[1] Medico-Legal and Pathological-Anatomical Department of Health Care Surveillance Authority, Košice, Slovakia; [2] Department of Pediatric Anesthesiology and Intensive Medicine, Children's University Hospital and Pavol Jozef Šafárik University, Košice, Slovakia; [3] Laboratory of Molecular Biology, Agel Nový Jičín, a.s., Nový Jičín, Czech Republic; [4] Department of Heart Surgery, East Slovak Institute of Cardiovascular Disease, Košice, Slovakia; [5] Department of Pathology, Louis Pasteur University Hospital, Košice, Slovakia; [6] Department of Forensic Medicine, Faculty of Medicine, Pavol Jozef Šafárik University, Košice, Slovakia

Abstract

This article reports the autopsy findings of a 1.5-year-old girl with no history of previous hospital admission who suddenly collapsed at home. After 45 minutes of resuscitation efforts, the cardiac activity was restored. During hospitalization, she had ventricular arrhythmia and extremely elevated cardiac troponin levels. Internal examination and immunohistochemistry revealed cardiac fibromas of the right and left ventricles and extensive hypoxic myocardial damage. The right ventricular fibroma demonstrated interdigitating and entrapped myocardium visible at the edges and within the central portion of the tumor. The left ventricular fibroma originated in the subepicardial region and propagated towards the endocardium.

Keywords
Cardiac tumors · Cardiac fibroma · Ventricular tachycardia · Ventricular arrhythmia · Osseous metaplasia of the central fibrous body · Gorlin-Goltz syndrome

Introduction

Cardiac fibroma is a benign tumor of the heart that occurs primarily in infants and children and may be congenital [1]. Presenting symptoms include heart failure, pericardial effusion, syncope, cyanosis, chest pain [1, 2], ventricular tachycardia [3, 4], arrhythmias, sudden death [1, 5], and heart murmurs [2]. This article reports the autopsy findings of a 1.5-year-old girl who presented to the hospital with ventricular tachycardia and arrhythmia after she suddenly collapsed at home.

Case report

The child (height 85 cm, weight 18 kg, body mass index 23.5 kg/m^2) was delivered by cesarean section following an uneventful first pregnancy. At birth, she weighed 4.65 kg and measured 50 cm. Due to the above-average size and head circumference, she underwent echocardiography, which revealed normal dimensions of the heart. Follow-up echocardiography was not carried out due to the coronavirus disease 2019 (COVID-19) pandemic. Past medical history included common childhood illnesses and normal screening test results. There was no history of previous hospital admissions.

The night before admission to the hospital, the child did not sleep well and woke up multiple times. In the early morning hours, she was restless. Later that day, she suddenly lost her balance and became unresponsive while standing upright. She

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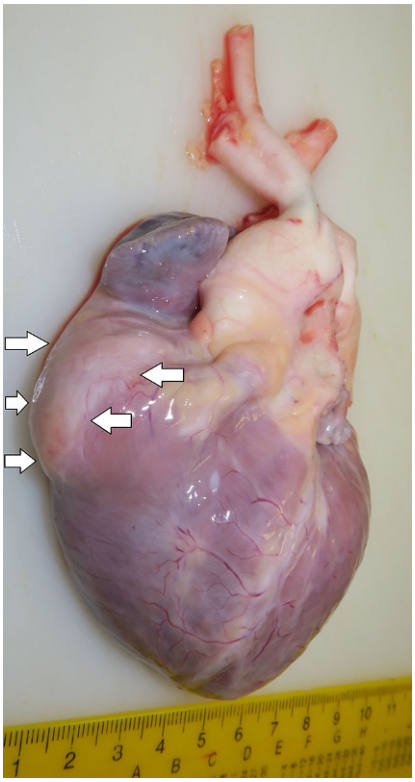

Fig. 1 ▲ Tumor of the right ventricular anterolateral wall (*arrows*)

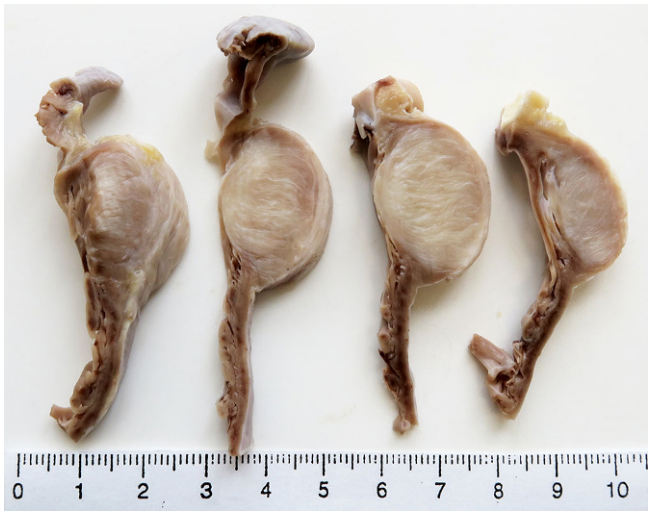

Fig. 2 ◀ Sections of the anterolateral wall of the right ventricle with a tumoriform lesion

suffered no injuries because her father caught her in his arms. Bluish discoloration of the face was evident. There was no sign of convulsions. The father provided cardiopulmonary resuscitation until an ambulance arrived. Upon arrival, the child was unconscious with a Glasgow coma scale of 3, oxygen saturation of 60%, and unmeasurable blood pressure. The initial electrocardiogram revealed ventricular fibrillation and after 45 min of resuscitation the cardiac activity (sinus rhythm) was restored. Upon arrival at the hospital the child was unconscious without spontaneous breathing and had tachycardia and an oxygen saturation of 97%. She was placed on mechanical ventilation during the entire hospitalization and was mostly hypotensive. Arrhythmias repeatedly occurred during hospitalization. Examinations during hospitalization revealed turricephaly, macrocephaly, hypertelorism, saddle nose, and frontal bossing. Laboratory results demonstrated severe metabolic acidosis. Bedsides, echocardiography (carried out using outdated equipment) did not reveal any significant changes in the heart. Initial head computed tomography revealed diffuse cerebral edema with tonsillar herniation. There was no sign of lytic or cystic lesions of the skull or dental anomalies. Chest radiograph demonstrated focal thickening and bifid ribs of the right second, third and fourth ribs. Significantly elevated cardiac troponin (cTnT) levels (1120 ng/l, 7731 ng/l, and 7213 ng/l during hospitalisation) were detected in the blood (the normal range of cTnT is between 3 and 14 ng/l). The patient died within 4 days of admission due to cerebral and pulmonary edema and unspecified cardiac arrhythmia.

An autopsy was performed 4 h after death. External and internal examination of the body revealed no sign of trauma. The heart measured 6 × 7 × 4 cm and weighed 92 g. A firm, white, bulging mass involving the right ventricular anterolateral wall was visible (**Fig. 1**) close to the right coronary artery. The endocardial surface of the right ventricle showed a grey-white patch with poorly defined borders. Multiple sections of the anterolateral wall of the right ventricle revealed a white tumoriform lesion with a whorled and trabecular pattern (**Fig. 2**) measuring 2.5 × 2.5 × 2 cm and weighing approximately 11 g. Gross findings of the heart included another solid, white, 0.1 cm deep lesion the size of 0.7 cm located at the bottom of the left ventricular anterior wall (**Fig. 3**). The cut surface of the ventricles and interventricular septum demonstrated a mottled myocardium with areas in which the damage was present through the entire wall. Coronary arteries had a normal pattern of origin and distribution. Other findings of note included severe cerebral and pulmonary edema with pneumorrhagia.

Hematoxylin and eosin-stained sections of the heart (atria and ventricles) showed foci of myofibrillar degeneration, general eosinophilia of the myocardial fibers, loss of nuclear basophilia of the cardiomyocytes, minimal leukocyte reaction and areas of recent hemorrhage. The non-encapsulated tumoriform lesion of the right ventricle consisted of interlacing bundles of collagen arranged in fascicles and separated by islands of entrapped myocardium exhibiting a striated appearance (**Fig. 4**). The lesion showed minimal spindle cell proliferation of bland fibroblasts. No mitosis or nuclear pleomorphism was identified. Elastic fibers were only detected in hypocellular areas composed of increased collagen. The diagnosis of cardiac fibroma was based on immunohistochemical analysis, which showed that the tumor was positive for vimentin and negative for desmin, smooth muscle actin, and beta-catenin.

Elastica-Van Gieson-stained sections taken from the anterior wall of the left ventricle showed an increased amount of collagen with myocardial interdigitation and entrapment due to infiltrative growth of the tumor (**Fig. 5**). The immunohistochemical profile of the tumoriform lesion was identical to that of the right ventricular fibroma. Immunohistochemistry showed desmin depletion (**Fig. 6**) in areas of hypoxic myocardial damage previously detected in the hematoxylin

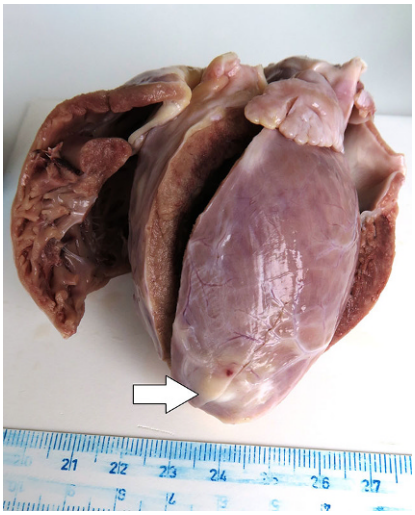

Fig. 3 ▲ Fibroma of the left ventricular anterior wall (*arrow*)

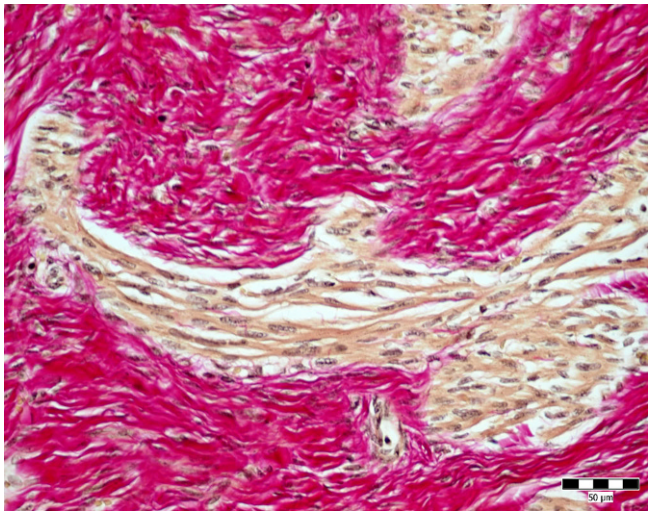

Fig. 4 ◀ Fibroma of the right ventricle with entrapped and separated islands of myocardium (elastica-van Gieson, magnification x400)

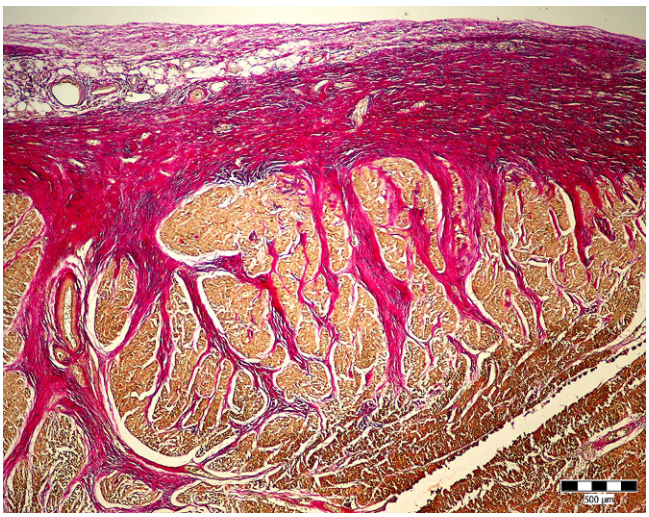

Fig. 5 ◀ Left ventricular fibroma originating in the subepicardial region (elastica-van Gieson, magnification x40)

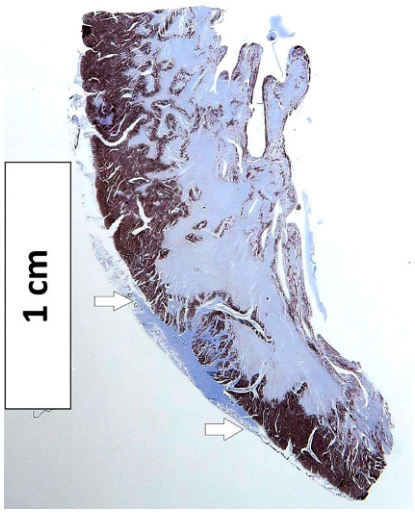

Fig. 6 ▲ Histotopogram of the left ventricular fibroma. Desmin depletion in the areas of hypoxic myocardial damage (*arrows*) (Desmin)

and eosin-stained sections. Sporadically, hypertensive vascular changes of the coronary artery branches were observed in close proximity to the fibroma of the right ventricle. The right coronary artery showed a recanalized thrombus. Osseous metaplasia of the central fibrous body was present in close proximity to the atrioventricular node. Histologic examination of the brain confirmed extensive hypoxic brain injury. Death was attributed to global post-hypoxic cardiac damage and severe cerebral edema following resuscitation after cardiac arrest.

Postmortem genetic analysis was performed on DNA extracted from formalin-fixed, paraffin-embedded tissue of the heart. Targeted sequencing performed using Illumina NextSeq 550 system (Illumina Inc., Hayward, CA, USA) revealed a pathogenic mutation in the protein patched homolog 1 (*PTCH1*) gene (NM_000264.3), c.2513_2516del, associated with Gorlin-Goltz syndrome.

Discussion

Primary cardiac tumors are rare, with a prevalence of 0.0017–0.28% in the autopsy series [6]. The incidence of cardiac tumors during fetal life has been reported to be 0.14% [6]. The first documented case of cardiac fibroma was that of Luschka in 1855, who found such a tumor in a 6-year-old boy who died of diphtheria [7]. Cardiac fibromas comprise less than 5% of primary tumors of the heart [2] and represent the second most common tumor of the heart in children after rhabdomyoma [8, 9]. They are exceptionally rare in adults [6] and may be associated with Gorlin-Goltz syndrome (multiple nevoid basal cell carcinomas, mandibular cysts, fused ribs, calcification of the falx cerebri, odontogenic keratocysts) [10, 11]. Fibromas can be asymptomatic or present with significant arrhythmias, ventricular tachycardia being the most common type [12]. In this case, upon arrival of the ambulance, the patient had ventricular tachycardia at the time of initial resuscitation. Arrhythmias repeatedly occurred during hospitalization. The differential diagnosis should include left ventricular aneurysm, endo-

cardial fibroelastosis, anomalous coronary arteries, hypertrophic subaortic stenosis, and pulmonary stenosis [2, 13]. Screening techniques available for the diagnosis of cardiac fibroma include ultrasound, echocardiography, and magnetic resonance imaging [12]. Cardiomegaly and calcification within the cardiac silhouette are visible on a plain chest x-ray. In this case, the patient received standard medical care. The occurrence of cardiac arrhythmias was unpredictable. The patient was admitted to the hospital with an infaust prognosis due to extensive hypoxic brain injury. Cardiac fibromas most commonly arise in the interventricular septum, followed by the left and right ventricular free walls [1]. Cardiac fibromas are almost always solitary [6, 8, 9], although multiple tumors have been reported [14] as in this case. Although most fibromas are intramural lesions [9] this case showed a fibroma of the left ventricle originating in the subepicardial region and growing towards the endocardium. The size of fibromas may vary from 2.5 to 10 cm, and they may display solid or infiltrative growth patterns [1, 6, 13]. Microscopically, the amount of collagen increases with age, whereas the degree of cellularity decreases with age [1, 8]. Fibromas occurring in the interventricular septum can lead to compression of the atrioventricular node, cartilaginous metaplasia of the central fibrous body [5], and infiltration of the His bundle [8, 15]. In this case report, a large fibroma of the right ventricle caused mechanical overload and increased stress on the central fibrous body presenting as focal osseous metaplasia. At the age of 1–2 years, the normal female heart weighs 43–55 g [16]. At autopsy, the heart weighed 92 g. After deducting the weight of the tumor (approximately 11 g), the heart was still significantly enlarged, weighing 81 g. Chronic mechanical overload of the heart subsequently led to increased heart weight. Even though fibromas are typically benign tumors [1], in some cases the borders of the lesion may infiltrate the adjacent cardiac muscle [8, 9] leading to myocardial interdigitation and entrapment. In this case report, the edges of both lesions were irregular, with entrapped and separated islands of the myocardium. These microscopic findings should be taken into consideration when developing a surgical treatment plan for patients with cardiac fibromas of various sizes. The differential diagnosis of a cardiac mass should also include non-neoplastic cardiac lesions [12, 17]. Due to its rarity, the optimal management strategy for pediatric patients with cardiac fibromas remains unclear. Surgical treatment for cardiac fibroma depends on the size and location of the tumor and its clinical features [2, 18, 19]. The first successful excision of a left ventricular fibroma in a 2-year-old boy was performed in 1959 [20]. In this case, we found that desmin depletion in cardiomyocytes strongly correlated with high levels of troponin in the blood. With increasing levels of troponin, a more prominent desmin depletion in cardiomyocytes can be observed. Due to the presence of clinical features and autopsy findings (facial and rib abnormalities, cardiac fibromas) associated with Gorlin-Goltz syndrome [21, 22], post-mortem genetic testing was performed. The presence of *PTCH1* mutation confirmed the presumptive diagnosis.

Conclusion

This case report demonstrates the gross and microscopic features of cardiac fibromas of the right and left ventricle in a 1.5-year-old female with the presence of *PTCH1* mutation confirmed post-mortem. Other than that, our case presents a rare co-occurrence of cardiac fibromas involving both ventricles, subepicardial location of the left ventricular fibroma, and histological findings involving the coronary arteries (hypertensive vascular changes, recanalized thrombus), and the central fibrous body (osseous metaplasia).

Corresponding address

Alžbeta Ginelliová
Medico-Legal and Pathological-Anatomical Department of Health Care Surveillance Authority
P. O. Box 014, Ipeľská 1, 043 74 Košice, Slovakia
e.ginelli@gmail.com

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Declarations

Conflict of interest. D. Farkaš, M. Pisarčíková, P. Vasovčák, A. Crhová, A. Ginelliová, L. Mistríková, L. Fröhlichová and S. Farkašová Iannaccone declare that they have no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case. Additional written informed consent was obtained from all individual participants or their legal representatives for whom identifying information is included in this article. The investigations were carried out according to the specifications of the Central Ethics Committee of the Federal Medical Council.

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Zusammenfassung

Kammerflimmern und Herzrhythmusstörungen assoziiert mit biventrikulären Herzfibromen bei einem 1,5-jährigen Mädchen

In diesem Artikel wird über die Autopsiebefunde eines 1,5-jährigen Mädchens ohne vorherige Krankenhauseinweisung berichtet, das plötzlich zu Hause zusammenbrach. Nach 45-minütigen Reanimationsbemühungen war die Herzaktivität wiederhergestellt. Während des Krankenhausaufenthalts litt sie unter ventrikulären Arrhythmien und extrem erhöhten kardialen Troponinspiegeln. Klinische Diagnostik und Immunhistochemie ergaben ein Herzfibrom des rechten und linken Ventrikels und einen ausgedehnten hypoxischen Myokardschaden. Das Fibrom des rechten Ventrikels zeigte ineinandergreifendes und eingeschlossenes Myokard, das an den Rändern und innerhalb des zentralen Teils des Tumors sichtbar war. Das linksventrikuläre Fibrom entstand in der subepikardialen Region und breitete sich zum Endokard aus.

Schlüsselwörter
Herztumoren · Herzfibrom · Ventrikuläre Tachykardie · Ventrikuläre Arrhythmie · Knochenmetaplasie des zentralen Faserkörpers · Gorlin-Goltz-Syndrom