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CASE REPORT

Sudden unexpected death due to inflammatory myofibroblastic tumor of the heart: a case report and review of the literature

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Abstract Inflammatory myofibroblastic tumor (IMT) or inflammatory pseudotumor is a rare primary cardiac tumor that may result in sudden death. We report a sudden unexpected death due to occlusion of the coronary arteries by IMT arising from the left coronary cusp of the aortic valve. An 8-year-old child suddenly woke up from his sleep with complaint of severe chest pain to his parents, and shortly he became unresponsive. He expired 40 min later in the hospital despite resuscitation efforts. The postmortem examination revealed a 2.5×2×1-cm mass composed of multiple entangled slender cylindrical fronts, filling the coronary sinus and obstructing the coronary ostia. The patient had complained of recurrent chest pains about 2 weeks prior to his death. Echocardiogram was conducted on the patient but did not recognize the mass. Histological examination of the mass established the diagnosis of primary cardiac IMT. The detailed pathological findings are described. In addition, the literature is reviewed, and pathogenesis, clinical presentation, and the importance of forensic autopsy examination are discussed.

Keywords Inflammatory myofibroblastic tumor · Heart · Sudden unexpected death · Forensic autopsy

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Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare entity with distinctive fibroinflammatory and even pseudosarcomatous appearance. Although the best known and common site of IMT is the lungs and gastrointestinal tract, it has been now identified at multiple extrapulmonary anatomic sites, particularly the soft tissue and solid organs of children and young adults [1–5]. IMT rarely involves the heart. When it does, however, it is potentially fatal and may result in sudden death [6, 7]. Although the cardiac involvement of IMT was first reported in 1975 [8], sudden death associated with cardiac IMT has rarely been reported in the medical literature. We present a case in which clinically unrecognized IMT involved the left coronary cusp of the aortic valve, thereby causing obstruction of the coronary arteries and resulting in sudden cardiac death.

Case report

Case history

An 8-year-old male child suddenly woke up at 4:00 am from his sleep with complaint of a severe chest pain to his parents. While his mother was calling the medical emergency service, he became unresponsive. He was found in full cardiac arrest by emergency medical services at 4:28 am. The patient was resuscitated but the attempt was unsuccessful. He was pronounced dead in the hospital at 5:01 am.

According to his mother, he had first complained of a severe chest pain while he was playing soccer 18 days prior to his death. The patient stated that the pain was burning in nature with no dizziness or shortness of breath. Two days later, he experienced the same mid-sternal chest pain again when he was running. On the 11th day since the initial chest pain, he was evaluated by a cardiologist. It was noted that he had a grade 2+/6 vibratory systolic ejection murmur heard best midway between his left mid-sternal border and apex. This murmur varied considerably with his respiratory cycle and position, as well as activity. Electrocardiogram showed a normal sinus rhythm with normal intervals, including a normal QT, corrected for heart rate. Echocardiogram reported a structurally normal heart with excellent biventricular function and no focal segmental motion wall abnormalities. Of note, it appeared that his circumflex coronary artery may come off posteriorly from the aorta off the noncoronary cusp rather than the left main coronary artery. Seven days later, he had a stress exercise test and repeat echocardiogram. The EKG tracing revealed a ST segment depression in leads II and III, as well as questionably in some of his mid-precordial leads. He experienced chest pain during the stress exercise test. The repeat echocardiogram showed that his circumflex coronary artery arose from the right coronary artery and coursed behind the aorta. Further workup was recommended; however, the patient died the next day.

According to the investigation, he was born at term by normal spontaneous vaginal delivery after an uncomplicated pregnancy with a birth weight of 7 lb 10 oz. He had a healthy sibling. There was no family history of congenital heart disease or sudden unexpected death at an early age. A forensic autopsy was requested due to the nature of sudden unexpected death with uncertain cause of death.

Autopsy findings

Autopsy revealed that the child was well developed and well nourished. His body weighed 41 kg, and was 132 cm in height with body mass index of 23.5. External examination of the body did not show any evidence of significant trauma.

Internal examination revealed that the heart weighed 170 g. There were normal epicardial fat and normal cardiac chamber dimensions. A 2.5×2×1-cm polypoid mass was attached to the left coronary cusp of the aortic valve. The mass was composed of multiple entangled slender cylindrical fronds, some with serpiginous to helical configurations, filling the left coronary sinus and occluding the left main coronary ostium; one frond extending to the right coronary sinus and obstructing the right coronary ostium (Fig. 1). The other valves and endocardium were grossly unremarkable. There was no gross myocardial fibrosis or necrosis. The proximal left anterior descending coronary artery and the proximal left circumflex coronary artery were totally occluded by the tumor extending from the aortic sinus (Fig. 2). In addition, the left circumflex coronary artery arose from the proximal right coronary artery and coursing posterior to the aorta.

Histological examination of the mass, with hematoxylin and eosin stain and Movat stain, showed interlacing fascicles of atypical spindle cells with vesicular nuclei and prominent nucleoli in a proteoglycan-rich matrix (Fig. 3). Rare mitotic figures and tumor giant cells were present. There was focal adherent fibrin-platelet thrombus on the tumor surface. Sections of the myocardium showed focal contraction band necrosis, but no evidence of any older ischemic cardiac changes noted. Immunohistochemistry studies with multiple stains were conducted on the mass. The mass stained positive for smooth muscle actin (SMA) in spindle cell components (Fig. 4) and CD 34 positive in small vessel endothelial cells. Actin, Pancytokeratin/Kermix, and desmin D33 were negative.

There was no evidence of any abnormalities in other organ systems. Postmortem toxicological analysis was negative for drugs and alcohol.

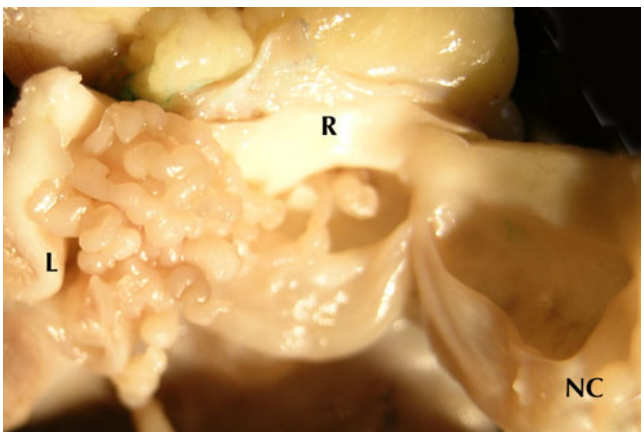

Fig. 1 A 2.5×2×1-cm polypoid mass was attached to the left coronary cusp of aortic valve, filling the left coronary sinus and obstructing the left main coronary ostium; one frond extending to the right coronary sinus and obstructing the right coronary ostium. *R* right sinus, *L* left sinus, *NC* noncoronary sinus of Valsalva

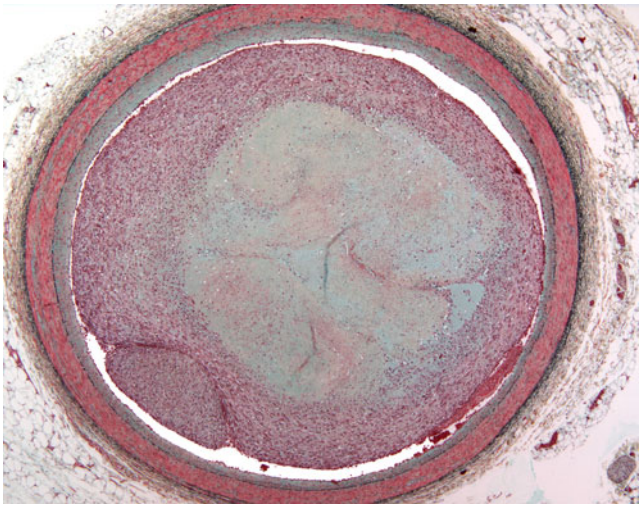

Fig. 2 The proximal left anterior descending coronary artery was completely occluded by the tumor. (H & E stain; original magnification ×4)

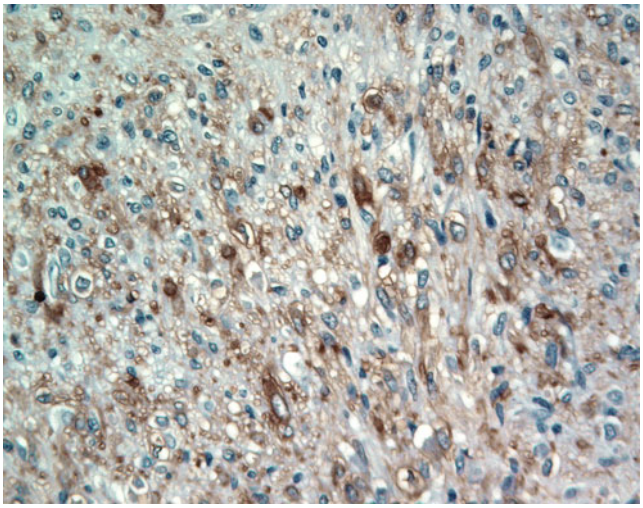

Fig. 4 The tumor stained positive for SMA in spindle cell components (SMA stain; original magnification ×40)

Discussion

Primary cardiac tumors are uncommon; the prevalence, reported from autopsy studies of patients of all ages, varies from 0.0017% to 0.28% [9–11]. The most frequent type of primary cardiac tumor in children is rhabdomyoma, whilst the myxoma is the most common primary tumor in adults [10–12]. Although the majority of the primary cardiac tumors are benign and noninvasive, they may have significant hemodynamic and conductive consequences depending on their location and size. Sudden unexpected death due to primary cardiac tumors is very uncommon with atrioventricular nodal tumor reported as the most common intracardiac lesion causing sudden death [13, 14].

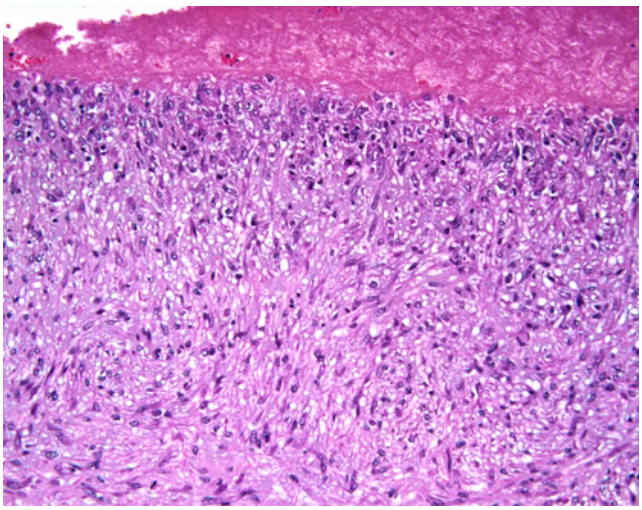

Fig. 3 Histological section of the tumor showed interlacing fascicles of atypical spindle cells with vesicular nuclei and prominent nucleoli. There was focal adherent fibrin-platelet thrombus on the tumor surface (H & E stain). Original magnification ×20

A case of sudden death due to pulmonary embolism from right atrial myxoma has been reported [15]. Sudden death due to cardiac IMT has rarely been reported in the medical literature. To our best knowledge, this case is the third reported cardiac IMT to cause sudden unexpected death [16, 17] and the first to result in death due to coronary embolization. In the presented case, ischemic cardiac arrhythmia due to occlusion of the coronary arteries with IMT arising from the left coronary cusp of aortic valve was determined as the cause of death. The anomalous left circumflex coronary artery arising from the proximal right coronary artery was an additional incidental finding.

Cardiac IMTs mostly occur in children and young adults, and have involved various sites; the right atrium and right ventricle are more predominant [6, 7, 18]. Cardiac IMT occurs primarily as an endocardial-based mass with a common gross appearance of polypoid, broad-based structures projecting into the lumen, often with surface fibrin [7]. IMTs may be firm, fleshy, or gelatinous, with a white or tan cut surface. Calcification, hemorrhage, and necrosis are identified in a minority of cases [19]. The histological features of the cardiac IMT are characterized by interlacing architecture of college fibers with spindle cells that have vesicular nucleoli and indistinct eosinophilic cytoplasm in a proteoglycan-rich matrix. Admixed with the tumor is a variably prominent chronic inflammatory infiltrate [20]. Rarely, IMT may undergo histological evolution to a morphologically higher-grade lesion with increased cellularity, marked nuclear atypia, frequent mitosis, atypical mitotic figures, and/or necrosis [1, 7, 20]. In this case, the tumor stained positive for SMA in spindle cell components and CD 34 positive in small vessel endothelial cells. Generally, immunohistochemistry does not play a major role in confirming the diagnosis due to the variable

expression and lack of specificity of myofibroblastic markers. It has been reported that approximately 50% of IMTs are positive for ALK, with reactivity in several large series ranging from 36% to 71% [20, 21].

The pathogenesis of IMT remains unclear, although the tumors were thought to be an abnormal and exaggerated immunological response by proliferated spindle cells and primary myofibroblasts to injury, inflammation, and infection [5, 6]. The recent classification of the World Health Organization recognizes the uncertainty of the biological nature of IMT, whether it is reactive or neoplastic [22]. Clinically, IMTs generally behave in an indolent manner and generally do not recur after compete surgical excision [5], but local recurrence and malignant transformation have been reported in a small subset of patients [1, 4]. There has been only one recurrent cardiac IMT reported [23]; no metastasis has been reported.

The clinical symptoms of IMT include varying degrees of fever, weight loss, anemia, thrombocytopenia, hypergammaglobulinemia, and elevated erythrocyte sedimentation rate [7]. Cardiovascular manifestations are highly variable, ranging from no symptoms to syncope, chest pain, transit ischemic attack, symptoms caused by peripheral emboli to the cerebral, systemic, and coronary arterial circulations, and ischemic arrhythmia leading to sudden death [7, 16, 17]. The cardiovascular symptoms are determined by many factors, including tumor location, size, growth rate, tendency for embolization, and degree of invasiveness. In the presented case, the tumor was attached to the left coronary cusp of the aortic valve, composed of multiple entangled slender cylindrical fronds, floating in the left coronary sinus, which led to partial or transient coronary blockage until the tumor completely occluded the coronary arteries. The patient experienced recurrent mid-sternal chest pain about 2 weeks prior to his death. Each time the pain occurred during exertion such as playing soccer, running, or during a stress exercise test. The pathogenesis of the recidivating mid-sternal pain may have resulted from transient myocardial ischemia due to reduction of the coronary perfusion by partial or transient coronary tumor blockage and increase of cardiac blood oxygen demand by physical activity. The sudden death was caused by fatal ischemic arrhythmia due to total occlusion of the coronary arteries.

Cardiac IMT is generally considered biologically benign with favorable prognosis [6, 7]. Currently, surgical resection of the tumor remains the definitive treatment and has a satisfactory outcome [6]. Because cardiac IMT can be potentially fatal, early clinical diagnosis is critical. In general, clinical diagnosis of primary cardiac tumors can be made by echocardiography. It has been reported that echocardiography has high sensitivity and specificity for clinical identification of primary cardiac tumors and is the preferred initial modality, but CT and MR imaging add very specific information in the evaluation of primary cardiac neoplasms [24, 25]. In the presented case, repeated echocardiogram had missed the diagnosis of the cardiac IMT although it had identified the anomalous left circumflex coronary artery arising from the proximal right coronary artery. The unique use of standard echocardiography as diagnostic technique may miss diagnosis of cardiac IMT, therefore CT with contrast and MR imaging should be also recommended in patients who are young and have abnormal EKG tracing with no clear causes and in patients with poor echocardiographic image quality to improve diagnostic accuracy.

In conclusion, we presented an autopsy case of sudden unexpected death due to clinically unrecognized/missed cardiac IMT that arose from the left coronary cusp of the aortic valve and had occluded coronary arteries. The diagnosis of the cardiac IMT was established by postmortem pathological examination. Forensic autopsy is further proved to be the gold standard to identify the cause of death in individuals who die suddenly and unexpectedly. Because cardiac IMT is potentially fatal and may cause sudden death, and because cardiac IMT is generally benign and surgical resection has favorable prognosis, thorough clinical investigation should be conducted in identifying this rare condition. In individuals especially children or young adults who have chest pain with unexplained causes, an intracardiac tumor including IMT must be taken into consideration.

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