SUDDEN CARDIAC DEATH IN AN YOUNG ADULT.

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Abstract:

Sudden cardiac death (SCD) in young adults is an uncommon event, yet it is devastating to families who lose a child so suddenly and unexpectedly. Sudden cardiac death is end result of a number of cardiovascular diseases. Although coronary artery disease accounts for a majority of these deaths across all ages, many other etiologies contribute to this when it occurs in the young (age < or = 35 years), where coronary artery disease is far less common. Here we are reporting a case of sudden cardiac death in young adult as a result of hypertrophic cardiomyopathy (HCM), who was apparently normal. Importance of complete, meticulous autopsy and histopathological examination is stressed. With this case we have reviewed and discussed sudden death due to hypertrophic cardiomyopathy.

Key words: sudden cardiac death, hypertrophic cardiomyopathy, autopsy

Introduction

Sudden cardiac death (SCD) contributed to about half of the cardiovascular deaths in rural South India. SCD contributed to 17% of the total deaths excluding accidental deaths.[1] A generally accepted definition of SCD is *natural death due to cardiac causes*, heralded by abrupt loss of consciousness within *1 hr* of the onset of acute symptoms, in an individual who may have known *preexisting* heart disease but in whom the *time* and *mode* of death are *unexpected.*[2]

Up to 80% of all SCDs in the United States are due to the consequences of coronary atherosclerosis. The cardiomyopathies account for another 10 to 15% of SCDs, and all the remaining diverse etiologies cause only 5 to 10% of all SCDs.

The inherited arrhythmia syndromes are more common causes in adolescent and young adults. Other than theses syndromes, such as hypertrophic cardiomyopathy (HCM), risk of SCD begins to increase after puberty, with increase in the level of physical activity.

HCM is the most common cause of SCD in young athletes.[3,4,5] McCaffrey et al[4] reviewed 7 studies and found hypertrophic cardiomyopathy (HCM) responsible for 24% of the deaths in athletes, whereas coronary artery abnormalities were present in 18% of patients. The review by Maron et al[3] found HCM or "possible HCM" to account for 46% of all deaths, with coronary artery anomalies leading to an additional 19% of SCD cases. Other studies have found HCM responsible for nearly half of all deaths.[5,6]

One study found that the incidence of sudden cardiac death in young competitive athletes declined in the Veneto region of Italy by 89% since introduction of routine Hypertrophic Cardiomyopathy Screening of athletes.[7] As of

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2010, however, studies have shown that the incidence of sudden cardiac death, among all HCM patients, has declined to one percent, or less.[8]

Prevalence of phenotypically expressed HCM in adult general population is about 1:500. Therefore, HCM is not rare and is the most common genetic cardiovascular disease, with reports from many countries. [9]

Hypertrophic cardiomyopathy is inherited as a Mendelian autosomal dominant trait and caused by mutant trait. It is caused by mutations in any 1 of 10 genes, each encoding proteins of the cardiac sarcomere (Components of thick or thin filaments with contractile structural or regulatory functions). Three of the HCM causing mutant genes predominate, namely, β-Myosin heavy chain (β MHC the first identified), Cardiac troponin T (TnT), and myosin binding protein C. The other genes account for minority of hypertrophic cardiomyopathy cases, namely cardiac troponin I, regulatory and essential myosin light chains, titin, α-tropomyosin, α actin, and α myosin heavy chain. This diversity is compounded by intragenic heterogenicity, with more than 150 mutations identified, most of which are missense with a single amino acid residue substituted with another.[9]

Hypertrophy may be restricted to interventricular system, which along with systolic anterior movement of the mitral valve can produce dynamic obstruction to the left ventricular out flow tract. The disease may occur in familial or sporadic form. Morphological evidence of disease is seen in 25 % of asymptomatic first degree relatives of patients with HCM.[10]

Sudden and unexpected death is the most devastating and unpredictable complication of HCM, but only a minority of patients are actually at risk. Sudden death in HCM may occur without warning sign and is caused by lethal heart rhythm disturbances (called ventricular tachycardia and ventricular fibrillation) that probably originate from the disorganized heart muscle structure or from small scars. While sudden death occurs most commonly in children and young adults, the risk extends to mid-life and beyond.[11]

Hypertrophic cardiomyopathy may be initially suspected because of heart murmur, positive family history, new symptoms or abnormal electrocardiogram (ECG) pattern.

Screening of first degree relatives, including history taking and physical examination, and two dimensional echocardiography and ECG should be encouraged.

Case Report

A young adult, 21 year old, male, college student, while having his breakfast just before examination, suddenly collapsed and died on the spot. Police sent the deceased body for autopsy examination. On external examination deceased was a young adult male, moderately built and moderately nourished. No external injuries found. External examination was unremarkable. On internal examination heart was grossly enlarged weighed 420 grams and showed white plaques of different sizes on the epicardial surface. Right Ventricle and right atrium were grossly dilated. The right ventricular wall showed thin areas of less than 1 mm thickness at places. Right ventricular wall thickness was 5 mm, the pulmonary artery diameter is reduced and measured 0.8 cm, left ventricular wall thickness measured 2.2 cm near interventricular septum, thickness was 18 mm at apex and 0.8 cm at near left ventricular outflow. The lumen of the left ventricle was greatly reduced and narrow.

Coronary arteries were patent. Heart valves appear normal. Other viscera were congested. Microscopy showed the pale white patch overlying right atrium is composed of dense hyalinised collagen as a broad layer superficial to epicardial fat, blood vessels and nerves. There is no granuloma. The myocardial fibres were separated by thin collagen. Myocardial fibres showed large hypertrophic nuclei in many. Right ventricular wall in thin areas showed only collagen and minimal myocardial cells. In the thicker part of right ventricle, myocardial bundles were seen many of which show nuclear enlargement and broad fibres. Adipose tissue was seen in some of the bundles. The left ventricle and interventricular septum showed hypertrophic cardiac fibres and fibre disarray at multiple sites (Fig-01). There is increased stromal collagen in areas of fibre disruption. Coronary arteries were normal. Final cause of death was opined as sudden cardiac death in a case of hypertrophic cardiomyopathy affecting mainly left ventricle.

Discussion

Sudden death is most common mode of demise and most devastating and unpredictable complication of hypertrophic cardiomyopathy.

SCD is usually the result of a malignant ventricular arrhythmia, including asystole. Most often acute myocardial ischemia is the cause for the fatal arrhythmia contrary to the logical assumption that ischemic involvement of the conduction system should be the source of arrhythmias, it is usually the acute ischemia induced electrical instability of the myocardium, that is away from conduction system. Because of the sudden death following acute ischemia of the myocardium, microscopy will not reveal visible changes of acute myocardial infarction in majority of the cases. Critical (>75%) narrowing of coronaries or scars of old infarct are the usual indirect evidence of acute ischemic injury to the myocardium. Arrythymogenic foci are often located adjacent to scar left by old myocardial infarctions.

Hypertrophic cardiomyopathy has genetic etiology in 100% cases. It is caused by mutations in any one of the several genes that encode sarcomeric proteins like β-myosin heavy chain, Cardiac TnT, α tropomysin and myosin binding protein C, the first one being most common. Mutations to β-MHC, Myosin binding protein –C and TnT account for 70-80% of all cases. Different affected families may have distinct mutation involving the same protein. Approximate, 50 different mutations of B-MHC are known to exist. However pathway from these mutations to morphologic abnormalities is still poorly understood. The variability in the natural history of disease may be due to the presence of different types of mutations and their variable penetrance although in most cases the pattern of transmission is autosomal dominant[12].

Further understanding of the pathogenesis of HCM had lead to recent evidence suggesting that HCM may stem from a defect in energy transfer from mitochondria to the sarcomere, the site of usage of energy, leading to subcellular energy deficiency.[12]

Many shows diffusely distributed left ventricular hypertrophy, almost 1/3 have mild wall thickening localized to single segment, including the apical form. Left ventricular hypertrophy is characteristically asymmetric, with anterior septum usually predominant, although a few show a symmetric (concentric) pattern. Microscopic findings in HCM are left ventricular myocardial architecture is disorganized, composed of hypertrophic cardiac muscle cells (myocytes) with bizarre shapes and multiple intercellular connections often arranged

in chaotic alignment at oblique and perpendicular angles. Cellular disarray may be widely distributed occupying substantial portions of left ventricular wall (Average 33%) and is more extensive in young patients who die of their disease. Disorganized cellular architecture, myocardial scarring and expanded interstitial (matrix) collagen probable serve as arrhythmogenic substrates predisposing to life threatening electrical instability. This substrate is likely the source of primary ventricular tachycardia and ventricular fibrillation which appears to be the predominant mechanism of sudden death either primarily or in association with triggers intrinsic to the disease process, namely myocardial ischemia, systemic hypotension, supraventricular tachyarrythmias, or environmental variables (e.g., intense physical exertion). The majority of HCM patients (55%) do not demonstrate any of the acknowledged risk factors in this disease and it is exceedingly uncommon for such patients to die suddenly; the subset at increased appears to comprise about 10% to 20% of the HCM population.[9]

There are many potential mechanisms of sudden death to consider in the identification of high risk patients. Both impaired and accelerated atrioventricular conduction have been documented. It is well recognized that a tachycardia, whether physiologic or secondary to arrhythmia may be associated with hypotension, ischemia, symptoms of angina, or impaired consciousness.[13]

In our case there was no significant personal history related to cardiovascular disease and family history of sudden cardiac death was absent. Deceased father and brother underwent ECG and echocardiography investigations, after our advice but investigations found normal.

Histopathological findings of left ventricular hypertrophy, hypertrophic cardiac fibres and fibre disarray at multiple sites with increased stromal collagen in areas of fibre disruption confirmed diagnosis of hypertrophic cardiomyopathy.

Conclusion

Genetically transmitted conditions associated with SCD, like HCM, are of importance, since preventive measures can be adopted after genetic studies in surviving family members. Relative of HCM diagnosed patient or deceased and young athletes advised to undergo an ECG and two dimensional echocardiography investigations.

Referances

1. Madhavan SR, Reddy S, Panuganti PK et.al. Epidemiology of Sudden Cardiac Death in Rural South India - Insights from the Andhra Pradesh Rural Health Initiative. Indian Pacing Electrophysiol J. 2011:11: 93-102.

2. Fauci A S, Braunwald E, Kasper L D et al. Infectious diseases. Harrison's Principles of Internal Medicine. 17th edn. Vol 2. USA Mc Graw Hilll Company, 2008: 1708-1709

3. Maron BJ, Shirani J, Poliac LC, Mathenge R, Roberts WC, Mueller FO. Sudden death in young competitive athletes: clinical, demographic, and pathological profiles. JAMA. 1996;276: 199–204.

4. McCaffrey FM, Braden DS, Strong WB. Sudden cardiac death in young athletes: a review. Am J Dis Child. 1991: 145:177–183.

5. Maron BJ, Roberts WC, McAllister HA, Rosing DR, Epstein SE. Sudden death in young athletes. Circulation. 1980: 62:218–229

6. Maron BJ, Roberts WC, Epstein SE. Sudden death in hypertrophic cardiomyopathy: a profile of 78 patients. Circulation. 1982: 65:1388–94.

7. Barsheshet, Alon; Brenyo,Andrew; Moss,Arthur; Goldenberg,Ilan "Genetics of Sudden Cardiac Death". Current Cardiology Reports July 2011: 13 :5: 364–76

8. Corrado D, Basso C, Pavei A, Michieli P, Schiavon M, Thiene G. "Trends in sudden cardiovascular death in young competitive athletes after implementation of a preparticipation screening program". JAMA 2006: 296 :13: 1593–601

9. Barry J Maron, MD Hypertrophic Cardiomyopathy A systemic review. JAMA March 13, 2002:287:10 :1308-19

10. Shah N S. Infectious Diseases. Association of Physicians of India Textbook of Medicine. 7th edn, India. The API publishers, 2003: 492

11. Barry J Maron. Hypertrophic Cardiomyopathy, Circulation 2002 :106:2419-21

12. Kumar, Abbas, Fausto and Aster, The Heart, Robbins and Contran Pathologic Basis of Disease. 8th edn. Saunders Elsevier 2010: 558, 577

13. WJ McKenna and AJ Camm, Sudden death in hypertrophic cardiomyopathy. Assessment of patients at high risk, Circulation 1989:80:1489-92

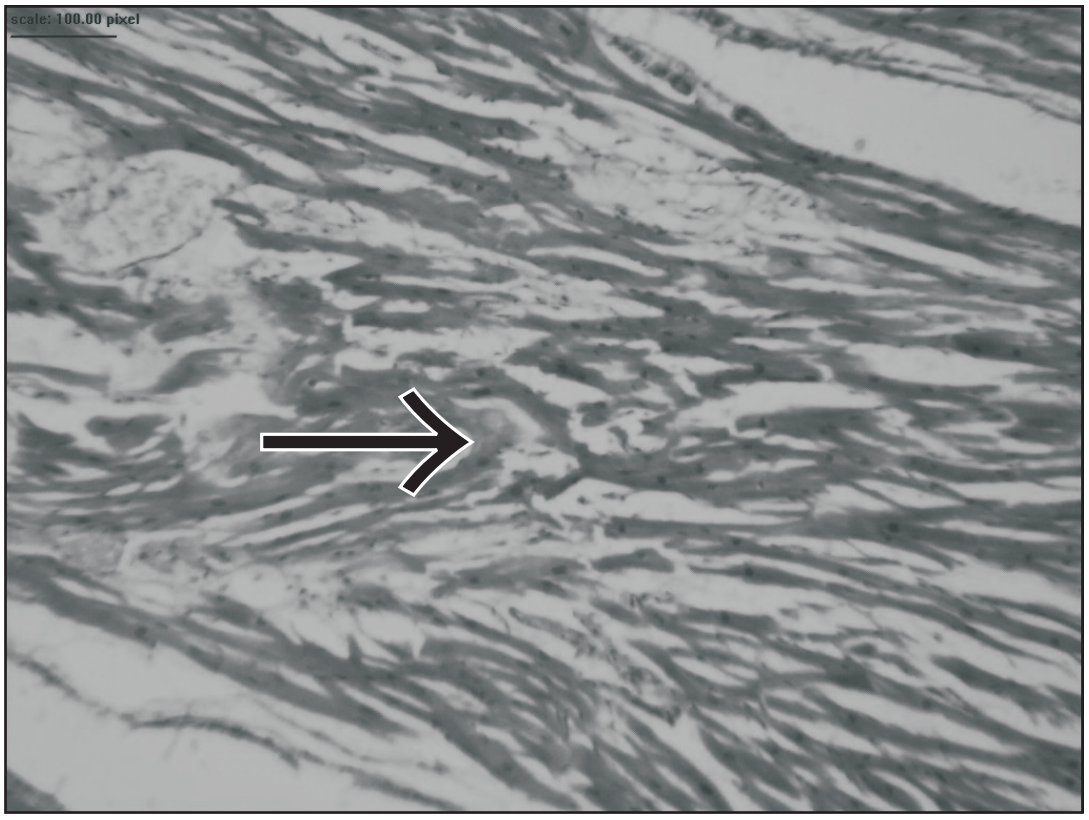

Fig (1): Low power view of left ventricle myocardium showing fibre disarray