An Autopsy Study of Hypertrophic Cardiomyopathy

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Abstract

Objective: To see the pathological features of this disease in our set up and to emphasise the importance of morphological examination in making the diagnosis of hypertrophic cardiomyopathy (HCM) especially in cases of sudden cardiac death.

Methods: A retrospective, descriptive study of 15 autopsies of this particular disease was carried out at the Armed Forces Institute of Pathology (AFI) Rawalpindi during the period from 1990 to 1995.The hearts along with blood vessels were fixed in 10% formalin and were dissected according to the modified Virchow's method for eliciting the gross appearance of cardiac chambers and valves. Representative sections were taken for histological examination.

Results: All the cases were young adult males. The age range was from 17-34 years (mean, 26-6 years) Ten cases died suddenly and five cases had an evidence of moderate to severe exertion preceding their death. Symmetrical as well as asymmetrical hypertrophy was noted in this study. The thickness of inter ventricular septum (mean 20 mm) and left ventricular wall (mean 22.5 mm) was increased. All the specimens revealed disarray of hypertrophic myocardial fibres and patchy interstitial fibroses.

Conclusion: Sudden death is usually the first manifestation of disease. The hearts showed asymmetric as well as concentric hypertrophy. Myofibre hypertrophy and disarray was an important pathological findings in our cases. While carrying out post-mortem examination of a case of sudden cardiac death one should also keep in mind the possibility of this disease (JPMA 53:459;2003).

Introduction

Hypertrophic cardiomyopathy (HCM) is a primary myocardial disease characterised by hypercontracting, hypertrophic, non-dilated ventricle and this inappropriate myocardial hypertrophy is without any obvious cause such as hypertension or aortic stenosis. It was studied systematically in late 1950s, though first time described nearly a century ago.[1]

Most distinctive morphologic features are disproportionate hypertrophy of ventricular septum, disarray of myofiber in ventricular septum and left ventricular free wall, reduced volume of left ventricular cavity and dilated atria, mitral valve thickening and abnormal intramural coronary arteries.[2]

The purpose of this report was to document the autopsy findings and determine the frequency of this rare disease presenting as sudden cardiac death in Pakistan.

Material and Methods

A retrospective study of 15 autopsies of hypertrophic cardiomyopathy was carried out at the Armed Forces Institute of Pathology (AFIP), Rawalpindi. These cases were diagnosed on postmortem examination during the period 1990 to 1995.

The unopened hearts alongwith blood vessels and other viscera were received at AFIP Rawalpindi for histopathological examination from military medical establishments all over the country. These specimens were of personnel of Defence Forces of Pakistan. The hearts were fixed in 10% formal saline and were dissected according to the modified Virchow's method[3] following the direction of flow of blood for eliciting the gross appearance of cardiac chambers and valves. Thickness of ventricular walls and the interventricular septum was measured. The hearts were weighed in electrical precision balance. From clinical and autopsy records the clinical data were retrieved.

Representative sections for histopathological examination were taken from coronary arteries, right and left ventricular walls, interventricular septum, SA node, AV node and bundle of His. An average of ten sections per heart were taken. Sections were stained with haematoxylin and eosin, elastic von Gieson and Masson's trichrome stain. The histological features studied were myofiber hypertrophy, disarray, interstitial fibrosis and presence of obliterative small vessel disease. The myofiber disarray was classified according to criteria described by Maron and Roberts.[4]

Results

An autopsy of 245 cases of sudden cardiac death was carried out from 1990 to 1995 out of which 15 cases of HCM accounted for 6.1%. All of these cases were males and the age range was from 17 to 34 years (mean age 26.6 years). Ten (71.42%) of 15 cases died suddenly and remained asymptomatic throughout their lives. There was

no previous history of cardiac ailment. Two (13.3%) cases had history of chest pain prior to death, one suffered from loose motions and vomiting and two patients complained of palpitation and shortness of breath (Table). In all cases ischaemic heart disease, hypertension, valvular and congenital heart disease were ruled out.

Five (33%) cases died while doing moderate to severe exertion whereas ten (67%) cases died suddenly and had no relationship to any kind of physical activity.

Electrocardiography could be done in 3 cases only which revealed dysrrhythmias like ventricular premature contractions (VPCs), ventricular fibrillation and tachycardia. Echocardiography was carried out only in 14% patients. In 7% cases no abnormality was detected, whereas in another 7% cases generalised myocardial dysfunctioning was noted.

The weight of the heart ranged from 350 to 620 grams (mean 440 grams). Asymmetric and concentric symmetric hypertrophy was noted in nine and six cases respectively. The interventricular septum and the left ventricular walls were hypertrophic in all and the range of thickness of left ventricular wall was 20 millimeters to 28 millimeters (average 22.5 millimeters). The septal thickness varied from 20 millimeter to 30 millimeters with an average of 23.2 millimeters. Septal endocardial thickening was seen in four cases in the region of left ventricular outflow tract. The coronary arteries of 13 cases were patent and without evidence of atherosclerosis while two had mild to moderate degree of atherosclerosis of left coronary artery (main-stem) and its left anterior descending (L.A.D.) branch. An obliterative small vessel disease with perivascular fibrosis was observed in five cases. Not a single case showed gross and microscopic evidence of myocardial infarction. The conducting system of five hearts showed nonspecific changes like fatty infiltration and fibrosis.

All the fifteen cases showed hypertrophy of myofiber with nuclear enlargement and hyperchromasia. The nuclei were predominantly cigar or typical box shaped. There was disarray of branching myocardial fibers and patchy interstitial fibrosis. All the cases revealed significant myofiber disarray and it was demonstrated in 45 to 50% of an average of 10 sections studied. The disarray was seen in septum and free left ventricular wall both

Discussion

The incidence of HCM in USA is low and accounts 0.02 to 0.2 percent of the population and is found to be in 0.5% of un-selected patients referred for an echocardiographic examination.[5] In Japan the prevalence per 100,000 population is 17.3 which is same as in the Western population.[6] In Pakistan there is hardly any reported data regarding the incidence of this disease.

The exact etiology is unknown, however it has been seen to occur as an autosomal dominant, Mandelian-inherited disease of contractile sarcomeric proteins in certain families.[7] The disease may be seen in children as well as in elderly individuals in seventh to eighth decades of life. The clinical course is extremely variable. Patient may be asymptomatic throughout life or may suffer from attacks of syncope, angina or mild dyspnoea. Sudden death especially in young adults may be the first clinical sign of hypertrophic cardiomyopathy and is the most catastrophic feature of disease's natural history.[8]

Patients at a particular risk of sudden death include young age (<30 years) at diagnosis, a family history of HCM with sudden deaths and genetic abnormalities associated with increased prevalence of sudden death.[9] The mechanisms of sudden death in this disease are not clearly defined and probably complex and it is speculated that arrhythmias especially in the young individuals are related to exercise[10,11] and or ischaemia may play a prominent role.

When a young apparent healthy soldier dies all of a sudden in a unit / battalion, there is a panic and different speculations are made about the incident. Every body wants to know the exact cause of death. For that, in Armed Forces of Pakistan, autopsy is carried out on almost all dying personnel except "Shaheeds". By detailed postmortem examination including histopathological and chemical examination we could ascertain the final cause of death in this small number of cases. So the postmortem examination of natural and unnatural deaths plays a vital role for arriving at a final diagnosis.[12]

The commonest cause of sudden cardiac death is ischaemic heart disease but non-ischaemic sudden cardiac deaths occur in hypertrophic obstructive cardiomyopathy, congenital coronary anomalies, coronary emboli, mitral valve prolapse and myocarditis. When the heart is normal and the coronary arteries are unremarkable, then histological examination of the conducting system may be helpful. In most instances it is normal.[13,14] Our observation was the same when we noted similar nonspecific findings, like fatty infiltration and fibrosis in five cases.

As documented in other series[15,16] sudden death due to HCM occurs in young individuals which is in conformity to our experience where ten patients in the age range 21-30 years died suddenly. However no age is immune for hypertrophic cardiomyopathy and most of the clinical, electrocardiographic and haemodynamic features are same in young and elderly patients.[17] As far as sex distribution is concerned male to female ratio was 2.3:1 in a Japanese study[10] whereas in our study all the cases were male.

Patients with hypertrophic obstructive cardiomyopathy may have diverse clinical manifestations like exertional chest pain, syncopial attacks and sudden death. The chief symptoms in previous studies[17-19] were angina, syncope, dyspnoea and palpitation. These clinical features are also in conformity with our observations. In our study 13% cases felt chest pain and developed syncopial attack before death. Syncopial attacks in this disease may be due to vascular instability which may also result in hypotension during ordinary daily activity or even at rest.[20]

Some individuals may present with sudden death, one of the devastating complications of this disease. In this study 10 of the 15 cases died suddenly, whereas in another Indian study[21], 6 of 14 persons developed sudden death.

Angina, syncope or sudden cardiac death may be due to Haemodynamic abnormalities, or cardiac arrythmia or both. Haemodynamics causes include large intraventricular gradients that may be provoked by exercise. Such relation to exercise / exertion was noted in 33% cases in our set up whereas in a previous study[22] sudden death in hypertrophic cardiomyopathy during exertion occurred in 79.2% cases. They may also be the result of decreased cardiac output related to altered diastolic compliance from the thick noncompliant ventricle.[19]

The mechanisms of sudden death are complex and not clearly understood. Available data[10,29-31] suggests that the arrythmia is the precipitating factor for sudden death. The extent of hypertrophy is associated with occurrence of nonsustained ventricular tachycardia in patients who have hypertrophic cardiomyopathy.[18] In the present study electrocardiography could be done in three cases only which also revealed cardiac arrhythmia.

The condition was known as hypertrophic obstructive cardiomyopathy or asymmetric septal hypertrophy when Teare[23] in 1958 described the disease with asymmetric septal hypertrophy leading to left ventricular out flow obstruction. With the development of M- mode echocardiography and subsequent autopsy studies[24] various types of obstructive and nonobstructive, septal and ventricular free wall involvement and asymmetric and symmetric types of hypertrophy have been found. In a previous study[25] symmetric hypertrophy has been documented in 34% of cases whereas in the present study it was seen in 40% cases.

There is no single histological feature for diagnosis of the disease. Teare in his study noted association of sudden death with asymmetric septal hypertrophy, myofiber disarray and interstitial fibrosis. Later on it was felt that myofiber disarray alone is a nonspecific feature because it has also been seen in normal heart, foetal hearts and in patients with congenital heart disease.[26,27] The myofiber disarray and interstitial fibrosis is patchy. It is highly sensitive and a specific marker when assessed quantitatively alongwith other histologic features, like interstitial fibrosis and enlarged, hyperchromatic nuclei.[28]

Hypertrophic cardiomyopathy is likely to be missed by pathologists at necropsy if the hearts are not opened properly, especially the heart with a small left ventricular cavity and no obvious cause. These hearts show asymmetrical or concentric hypertrophy of left ventricle and septum and histologically marked cellular disorganization, patchy fibrosis and enlarged nuclei.[2] Similar observations were also made in this study.

Conclusion

Hypertrophic cardiomyopathy is an uncommon disorder and mostly affects young individuals. Sudden death is usually the first manifestation of disease. The hearts show asymmetric as well as concentric hypertrophy. Myofibre hypertrophy and disarray was an important pathological findings in our cases. While carrying out postmortem examination of a case of sudden cardiac death one should also keep in mind the possibility of this disease. Individuals with family history of sudden death should not be subjected to physical exertion.

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