Original Article

Histomorphological Spectrum of Various Cardiac Changes in Sudden Death: An Autopsy Study

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ABSTRACT

Background and Objectives: In spite of large number of studies conducted so far, sudden cardiac death remains an enigma and relative importance of acute coronary events as a trigger of sudden death is currently unclear. An autopsy study of heart was therefore planned to observe various histomorphological cardiac changes, and to determine the frequency association of acute coronary events and myocardial infarction with sudden death.

Material and Methods: A prospective randomized study of two hundred autopsied hearts submitted for postmortem analysis was conducted in the Department of Pathology, PGIMS Rohtak over a period of two and a half years from June 2007 to December 2009. The hearts were examined grossly and microscopically to observe various histomorphological changes and findings were correlated clinically.

Results: Out of 200 autopsied hearts, 142 (71%) revealed coronary artery atherosclerosis in one or more vessels. Maximum number of cases (32.5%) revealed three vessel diseases. Significant atherosclerosis (>50% reduction in diameter) was present in 125 (62.5%) cases, while 58 cases (29%) revealed no observable atherosclerotic change. One hundred twenty cases could be categorized under sudden cardiac death, 15.83% revealed changes of acute MI, 40% of healed MI and 44% revealed no change.

Conclusion: The ischemic heart disease was found to be the leading cause of death with coronary atherosclerosis being the most significant pathogenetic mechanism and three vessel disease the most common pattern of involvement. Acute coronary events (occlusive or non-occlusive thrombus/ plaque rupture/ haemorrhage) were observed in only 16% of the cases of sudden coronary death.

Keywords: Autopsy, Sudden Death, Heart, Histology, Morphology

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Introduction

Despite the disparagement of the ignorant and the patronizing smiles of the sophisticated, the necropsy is time honored, which moves with its steady pace maintaining its standard, contributing to knowledge and even on occasion, stimulating the sluggard. The main objective of the autopsy is establishment of final diagnosis and determination whenever possible, of the cause of death. Cardiac autopsy is the main diagnostic tool to study various histomorphological changes in normal and diseased heart (1).

Sudden death is defined as either an unexpected natural death within 1 hour or less from the onset of symptoms; or a non-witnessed death discovered within 24 hours in someone without prior symptoms or any prior condition that would appear fatal. Such a rapid death is often attributed to a cardiac cause. Sudden cardiac death can be prevented if high-risk patients are identified and referred to a cardiologist (2). However, in spite of large number of studies conducted so far, sudden cardiac death shift remains an enigma and relative importance of acute coronary events, as a trigger of sudden death is currently unclear (3-5). The occurrence of sudden death presents a great challenge to the general autopsy pathologist and as cardiac autopsy is the main diagnostic tool to study various histomorphological changes in normal and diseased heart, an autopsy study of heart was undertaken to establish the cause and nature of death, to determine the frequency of acute coronary lesions in sudden cardiac death.

Material and Methods

We conducted a prospective randomized study on two hundred autopsied hearts submitted for postmortem analysis in Department of Pathology, PGIMS, Rohtak over a period of two and a half years from June 2007 to December 2009. Formalin fixed specimens were inspected externally, weighed and then dissected by inflow-outflow method of cardiac dissection. Whenever required, short axis method was followed (6). The heart was weighed after removal of extraneous vessels and residual postmortem blood clot. Sections were taken from right and left ventricular wall, atrioventricular junction, interventricular septum, apex, right and left coronary arteries, valves (tricuspid, mitral, pulmonary, and aortic) and stump of aorta. Both the coronaries were traced as far as possible including two major branches i.e. left anterior descending (LAD) and left circumflex of left coronary arteries. Multiple sections were taken at 4-5 mm interval. Additional sections were taken wherever necessary. Tissues were processed and subjected to paraffin section at 4 μm thickness, and then were stained with routine hematoxylin and eosin staining method (7). Various histomorphological cardiac changes were evaluated and clinically correlated. Wherever required, special staining techniques were applied, i.e. Von kossa for calcification, Von gieson for elastin and Masson's trichome for collagen.

Results

Our study included 184 males and 16 females, with age ranging from newborn to 93 years. Six cases were less than 10 years, nine were between 11-20 years. Maximum number of cases belonged to 41-50 years of age group. The post fixation heart weight ranged from

20 gm to720 gm in males with average being 277 gm and 20 gm to 380 gm in females, average being 260 gm. In males, weight of heart was found to increase until sixth decade and declined thereafter while in females no particular pattern was observed. The alleged cause of death was mentioned in 107 cases only with cardiovascular causes being most common. Ninety three cases were of sudden death with no known cause.

A wide spectrum of histomorphological changes was observed, most common (36%) being Ischemic heart disease (IHD) including features of chronic IHD (25.5%), acute myocardial infarction (MI) (7%) and acute on chronic IHD (3.5%) (Table 1). One hundred and fifteen cases revealed no significant changes in the heart. In IHD group, maximum numbers of cases were in the age group of 61-70 years. Most common pattern was diffuse involvement of heart (47.2%) i.e. involvement of all the areas including portions of left ventricular wall, right ventricular wall and interventricular septum, followed by involvement of left ventricular wall only. Isolated involvement of right ventricular wall was not observed (Table 2). No congenital anomaly was found in autopsy heart of newborn and infants and the microscopic examination of heart and vessels was unremarkable.

Table 1- Spectrum of histopathological changes in autopsied hearts

Sr. No	Findings	No. of cases (%)
1	**a. Ischaemic heart disease (IHD)**	
	*** Chronic IHD**	51 (25.5)
	*** Acute MI (with / without complication)**	14 (7)
	*** Acute on chronic IHD**	7 (3.5)
	b. Cardiac hypertrophy	5 (2.5)
	c. Myocarditis	3 (1.5)
	d. Pericarditis	1 (0.5)
	e. Pancarditis	1 (0.5)
	f. Rheumatic heart disease	2 (1)
	g. Infections – tuberculosis	1 (0.5)
	h. Fibrosis and calcification of valves	5 (2.5)
2.	**Coronary atherosclerosis**	142 (71)
3.	**Aorta**	
	a. Atheromatous plaque	73 (36.5)
	b. Aortitis	1 (0.5)
	c. Aneurysm	1 (0.5)
4.	**Age related changes in myocardium**	
	a. Lipofuscin	119 (59.5)
	b. Fatty infiltration	5 (2.5)

Table 2- Frequency distribution of areas involved in ischemic heart disease

	Chronic IHD	MI	Acute on chronic IHD	Total (%)
Only LVW	10	3	2	15 (20.83)
Only RVW	-	-	-	-
Only IVS	5	1	-	6 (8.33)
LVW+IVS	7	1	-	8 (11.11)
Apex	3	1	-	4 (5.55)
Apex +IVS	2	2	1	5 (6.94)
All	24	6	4	34 (47.22)
Total	**51**	**14**	**7**	**72**

LVW (Left Ventricular Wall) RVW (Right Ventricular Wall)
IVS (Interventricular Septum) IHD (Ischemic Heart Disease)

Out of 200 autopsied hearts, 142 (71%) revealed coronary artery atherosclerosis in one or more vessels. Significant atherosclerosis (>50% reduction in diameter) was present in 125 (62.5%) cases, 58 cases (29%) revealed no observable atherosclerotic change in the sections examined. All cases aged >70 years were having significant atherosclerosis and no case in <10 years age group revealed coronary artery atherosclerosis.

In all the cases examined, Left anterior descending artery (LAD) was the most commonly involved vessels (137 cases), followed by right coronary artery (RCA) (119 cases) and left circumflex (LCx) artery (94 cases). Significant atherosclerosis was present in 119, 75, 71 cases of LAD, RCA and LCx respectively. Complicated plaques revealing atherosclerosis with calcification or acute coronary events (thrombus formation, plaque rupture and intramural hemorrhage) were observed in 53, 27, 9 cases respectively. Seven cases of LAD revealed complete occlusion of the vessel (Table 3). Maximum cases (52%) had involvement of all the three vessels followed by one vessel (26.4%) and two vessel (21.6%) involvements. Cases with complicated atherosclerosis showed calcification, which was confirmed by Von kossa stain, and elastin fibers were found disrupted in few cases of atherosclerosis as demonstrated by Von geison stain.

Many age related changes including Lambl's excrescences (62%), lipofuscin pigment deposition (39.5%), atheromatous plaque in aorta (36.5%) and amyloid deposits (1%) were observed.

Table 3- Frequency involvement of coronary vessels

	Atherosclerosis			Complicated atherosclerosis					Total
	Mild	Mod	Severe	Cal.	T	PR	Both	H'age	
LAD	18	36	30*	36**	11***	3	2	1	137
LCx	23	41	21	9					94
RCA	24	44	24	25	2				119

LAD= Left anterior descending
LCx=Left circumflex
RCA= Right coronary artery
* Complete occlusion in one case
** Complete occlusion in two cases
*** Complete occlusion in four cases
Cal= Calcification
T= Thrombus
PR= Plaque rupture
Both = Thrombus + plaque rupture
H'age = Haemorrhage

Discussion

Keeping in mind the main aim of the autopsy pathologist i.e. to help reach the cause of death and cardiovascular causes being the most common one as mentioned in literature, the cardiac autopsies were performed with the aim to observe histomorphological spectrum that could guide solve the mystery of death, especially sudden death.

In our study, of 200 randomly chosen autopsies, there were 184 (92%) males and 16 (8%) females with maximum number of cases in 41-50 years age group. Various studies on sudden death conducted by Farb A, Thomas A, Chugh SS and others also revealed same proportion indicating that sudden natural death from all causes (cardiac and non cardiac) was more common in men (3-5).

Out of 200 autopsied hearts, almost all the cases of ischemic heart disease had significant coronary artery atherosclerosis. In our study, maximum cases (52%) had involvement of all the three vessels followed by one vessel (26.4%) and two vessel (21.6%) involvement. When compared with other studies there was no particular pattern of involvement of coronaries, but three vessel diseases was more common in all the studies including our study (8-13).

In cases of ischemic heart disease, we tried to find out:

The frequency distribution of various areas involved by examining atleast one section each from LVW, RVW, IVS and apex. Thirty-four of the 72 cases (47.22%) of IHD had involvement of all the areas followed by involvement of only left ventricular wall (20.83%). Isolated involvement of RVW was not seen. Our results were in accordance to those well documented in literature (14).

The frequency of different forms of IHD (acute MI, acute MI with underlined changes of healed MI, healed MI) and compared them with the extent of coronary artery atherosclerosis and observed that changes of healed MI and 3 vessel disease were most common, as in studies of Farb A, Friedman, Liberthson, Davies and others (Table 4) (3,10-12,15-17).

Table 4 - Comparison of frequencies of acute and healed mi and extent of coronary atherosclerosis

Study	MI, %			Coronary atherosclerosis, %			No sign/ mild athero.
	Acute	Healed (Chronic)	Acute plus healed	One vessel	Two vessels	Three or four vessels	
Friedman *et al.*(10)	12	53	NA	15	19	59	-
Liberthson *et al.*(12)	27	44	NA	14	26	60	-
Reichenbach *et al.* (16)	5	74	NA	18	41	41	-
Rissanen *et al.* (11)	77	61	NA	11	31	56	-
Baroldi *et al.* (17)	17	82	NA	25	29	21	-
Warnes and Roberts (8)	-	44	-	16	27	57	-
Davies *et al.* (15)	40	57	NA	26	44	30	-
Farb *et al.* (3)	10	41	11	44	32	23	-
Present study (%)	19.44	70.83	9.72	8.33	27.77	56.94	6.94

As mentioned in literature, sudden coronary death is defined as death within 6 hours of onset of symptoms from a stable medical condition / death of an individual who had been seen in stable condition less than 24 hours antemortem with at least one major coronary vessel having significant atherosclerosis (≥75% reduction in cross sectional area or >50% reduction in diameter), provided no other cardiac or non cardiac cause of death was present (3-5,8-19). In our study, 125 cases had significant atherosclerosis of one or more major coronary vessels, 120 of these cases could be categorized under sudden coronary death while five cases revealed pathologic changes of other cardiac disease including two cases of massive hypertrophy disproportionate to the degree of atherosclerosis and one case each of myocarditis, pancarditis and aortitis. Although coronary atherosclerosis is the major culprit, a wide variety of nonatherosclerotic-related cardiac disease have been associated in sudden cardiac death including cardiomyopathies, inflammatory myocardial disease and ion channel disorders in a few studies (20,21). Examination of myocardium in cases of sudden coronary death revealed changes of acute MI (acute + acute and healed MI) in 19 cases, healed MI in 48 cases and no changes of MI in 53 cases. While observing the various types of acute coronary events, non-occlusive mural thrombus was the commonest event in all the studies, followed by plaque rupture and occlusive thrombus (Table 5) (3, 12, 22). The difference in results of various studies could be mainly due to selection of cases. Cases with history of precordial chest pain revealed active coronary lesions in more number of cases as compared to patients without warning symptoms of pain before death. Probably this was the cause of low incidence of active coronary lesions in our study. Another factor could be handling of tissues, since active coronary lesions are typically. Another factor is focal nature of the lesion, which could easily be missed if sufficient sections at 3 to 5 mm intervals are not taken.

Table 5- Comparison of frequency distribution of acute coronary events in case of sudden cardiac death

	Liberthson *et al.* (12) (1974) n=220	**Davies *et al.*(22) (1992) n=168**	**Farb *et al.* (3) (1995) N=90**	**Present study (2008) n=120**
Mural thrombus (T) (%)	32	43.5	40	7.5
Occlusive thrombus (%)	-	29.8	23	3.3
Plaque rupture (PR)/ (T+PR) (%)	56	7.7	30	4.2
Haemorrhage (%)	2	-	7	1
No acute lesion (%)	-	19	43	84

Many age related changes including lambl's excrescences (62%), lipofuscin pigment deposition (39.5%), atheromatous plaque in aorta (36.5%) and amyloid deposits (1%) were observed in many cases. The incidence of these changes was found to increase with each decade. Few findings such as coronary atherosclerosis (71%), myocardial fibrosis (29%), valvular fibrosis, and calcification (2.5%), although regarded as normal ageing process, have pathological association with chronic ischemic heart disease and distinction between the two is difficult.

In the end, we tried to correlate the pathological changes with alleged cause of death (COD), if mentioned, and to find out the probable cause of death in cases of sudden death with no known cause. The histopathological changes of ischemic heart disease correlated in many cases with the alleged COD mentioned in police papers e.g. heart attack, chest pain or cardiac arrest. There were more chances to get the features of MI if patient presented with heart attack/ chest pain. Features of chronic IHD associated with coronary atherosclerosis were found in many cases with some other alleged COD e.g. cold, accident, drug abuse or some chronic illness like diabetes, indicating that their could just be a precipitating factor over the underlying diseased heart.

Chronic IHD associated with atherosclerosis (24.73%) or only significant atherosclerosis (21.5%) were also seen in significant number of cases without known cause of death, providing the significance of autopsy to determine the cause of death or at least to indicate the probable cause of death.

Conclusion

Ischemic heart disease may be the leading cause of death with coronary atherosclerosis being the most significant pathogenetic mechanism and three-vessel disease the most common pattern of involvement, same fact emphasized by other authors.

We also attempted to evaluate the prevalence of acute coronary events or myocardial infarction and their relation to sudden death. Reported frequency of acute coronary lesions varied from <20% to 80% of cases in previous studies and in cases lacking active lesions, sudden death has been attributed to healed MI/ arrythmia/ vasospasm. In our study, acute coronary events although considered as a trigger for sudden death were found only in some cases, in others probably arrythmias/ vasospasm could be the cause of death. Great variability in incidence of these events could also be attributed to pattern of selection of cases/ sampling of tissue.

Finally, because of heterogeneity in the cause of sudden cardiac death, a detailed and thorough postmortem examination may provide important information regarding the same.

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References

1. Audibert L, Fauchon M, Blanc N, Hauchard D, Gall EA. Phenolic compounds in the brown seaweed Ascophyllum nodosum: distribution and radical-scavenging activities. Phytochem Anal 2010; 21(5):399-405.
2. Kwok KM, Lee KL, Lau CP, Tse HF. Sudden cardiac death: prevention and treatment. Hong Kong Med J 2003; 9(5):357-62.
3. Farb A, Tang AL, Burke AP, Sessums L, Liang Y, Virmani R. Sudden coronary death. Frequency of active coronary lesions, inactive coronary lesions, and myocardial infarction. Circulation 1995;92(7):1701-9.
4. Thomas AC, Knapman PA, Krikler DM, Davies MJ. Community study of the causes of „natural“ sudden death. BMJ 1988 Dec 3;297(6661):1453-6.
5. Chugh SS, Kelly KL, Titus JL. Sudden cardiac death with apparently normal heart. Circulation 2000;102(6):649-54.
6. Ludwig J. Handbook of Autopsy Practice. 3 ed. Towata: New Jersey; 2002.
7. Bancroft J, Gamble M. Theory and Practice of Histological Techniques. 5th ed. Philadelphia: Churchill Livingstone; 2004.
8. Warnes CA, Roberts WC. Sudden coronary death: comparison of patients with to those without coronary thrombus at necropsy. Am J Cardiol 1984;54(10):1206-11.
9. Myerburg RJ, Kessler KM, Castellanos A. Sudden cardiac death. Structure, function, and time-dependence of risk. Circulation 1992;85(1 Suppl):I2-10.
10. Friedman M, Manwaring JH, Rosenman RH, Donlon G, Ortega P, Grube SM. Instantaneous and sudden deaths. Clinical and pathological differentiation in coronary artery disease. JAMA 1973;225(11):1319-28.
11. Rissanen V, Romo M, Siltanen P. Prehospital sudden death from ischaemic heart disease. A postmortem study. Br Heart J 1978;40(9):1025-33.
12. Liberthson RR, Nagel EL, Hirschman JC, Nussenfeld SR, Blackbourne BD, Davis JH. Pathophysiologic observations in prehospital ventricular fibrillation and sudden cardiac death. Circulation 1974;49(5):790-8.
13. Kasthuri AS, Handa A, Niyogi M, Choudhury JC. Sudden death: a clinicopathological study. J Assoc Physicians India 2002;50:551-3.:551-3.
14. Kumar V, Abbas K, Fausto N. Robbins and Cotran Pathologic Basis of Disease. 7 ed. Philadelphia: WB Saunders; 2004.
15. Davies MJ, Thomas A. Thrombosis and acute coronary-artery lesions in sudden cardiac ischemic death. N Engl J Med 1984;310(18):1137-40.
16. Reichenbach DD, Moss NS, Meyer E. Pathology of the heart in sudden cardiac death. Am J Cardiol 1977;39(6):865-72.
17. Baroldi G, Falzi G, Mariani F. Sudden coronary death. A postmortem study in 208 selected cases compared to 97 „control“ subjects. Am Heart J 1979;98(1):20-31.
18. Rahlf G.The heart in the elderly. Pathology: macroscopic and light microscopy findings in the heart. Z Kardiol 1985;74 Suppl 7:9-16.
19. Sekiguchi M, Nishino H, Nishikawa T, Morimoto S, Hiroe M. Age-associated myocardial changes in various heart diseases. A clinicopathologic analysis in biopsied and autopsied myocardium. Jpn Circ J 1986;50(10):1023-32.
20. Ladich E, Virmani R, Burke A. Sudden cardiac death not related to coronary atherosclerosis. Toxicol Pathol 2006;34(1):52-7.
21. Ahmad M, Afzal S, Malik IA, Mushtaq S, Mubarik A. An autopsy study of sudden cardiac death. J Pak Med Assoc 2005;55(4):149-52.
22. Gall E. Autopsy Pathology - a manual and atlas. 2nd ed. Philadelphia: Saunders; 2009.