

Original Research Paper

Evaluation of Histopathologic Role in Providing Cause of Death in Sudden Unexpected Natural Death

¹Sree Lakshmi K, ²Ashalatha N, ³S VenkataRaghava, ⁴Raghupathi A R, ⁵Dayananda S Biligi, ⁶Siddique M Ahmed, ⁷Natarajan M

Abstract

Sudden unexpected natural death in an adult is an issue of great concern for medical professionals. Cardiovascular pathology is the most common cause of sudden death. However, no definitive cause of death can be found at post-mortem and subsequent histopathologic examination in a minority of cases. The present study aims to evaluate the role of a histopathologist in providing a conclusive cause of death, to assess the percentage of cases where a conclusive diagnosis could not be offered, age and sex distribution of the cases of sudden death and compare the data with that obtained in other studies. Data from our study showed 89.77% male deaths. Seventy five percent of deaths were seen in < 40 years of age. Maximum number of cases (39.77%) was seen in second decade followed by third decade (26.13%). Cardiac causes of sudden death accounted to 69.13% of the cases. Non cardiac causes contributed 11.36% of cases. In 19.31% cases even after detailed histopathologic examination cause of death could not be concluded.

Key Words: Sudden death; Histopathology; Negative autopsy; Cardiac; Non cardiac

Introduction:

Sudden unexpected natural death cases in adults are steadily increasing world over and is an issue of great concern for medical professionals. [1] Sudden death especially of a young and apparently healthy adult is not only shocking but also has profound impact on the psyche of the society. [2]

The Forensic specialist along with the help of Forensic histopathologist are not limiting themselves to excluding violent causes of death, but are trying to study sudden death cases in depth and unravel the cause behind it. Cardiovascular pathology is the most common cause of sudden death. [3] However, no definitive cause of death can be found at post-mortem and subsequent histopathologic examination in a minority of cases. [4]

The present study aims to evaluate the role of a histopathologist in providing a conclusive cause of death, to assess the percentage of cases where a conclusive diagnosis could not be offered, age and sex distribution of the cases of sudden death and compare the data with other studies.

Methods:

The study is a retrospective study conducted at Department of Pathology of a tertiary care teaching hospital. All the cases of sudden death received over a period of two years between September 2011 and August 2013 were included. These organs are received mostly from Department of Forensic Medicine housed in the same teaching hospital.

Some of the specimens are received as referrals from the health centres located in the surrounding districts. Organs from 554 cases were received during this period for histopathologic examination of which 111 cases were referrals from other health centres. Of the 554 cases received, 88 cases were received with a history of sudden death. Of these 88 cases 5 were referrals and 83 were from our institute. The organs commonly received in a case of sudden death are heart, lung, liver, kidney, spleen and brain.

Sudden unexpected natural death is defined as natural death occurring instantaneously or within 24 hours of onset of

Corresponding Author:

¹Associate Professor,
Department of Pathology,
Bangalore Medical College and Research Institute,
Bangalore, 560008

E-mail: dr_ksl@yahoo.co.in

²Associate Professor

³Assoc. Prof, Dept. of Forensic Medicine

⁴Prof. & HOD, Dept. of Pathology,

^{5, 6, 7}Professor

DOR: 20.02.2014 DOA: 19.03.2014

symptoms in a patient who may or may not have a known pre-existing disease, but in whom the mode and time of death is unexpected. [1]

The autopsies are conducted by Forensic specialists at Department of Forensic Medicine. A total of 7659 cases were autopsied in the two year period. All the autopsies are medico-legal in nature. After a thorough autopsy examination, the Forensic specialist sends organs in 10% formalin to Department of Pathology for histopathologic examination.

In the Department of Pathology, detailed gross examination findings of all the organs received were noted. Tissue sections taken from the organs are formalin fixed, paraffin embedded and slides prepared are stained by routine Haematoxylin and Eosin stain. The slides are viewed under a light microscope and a final diagnosis is given wherever possible.

Results:

Our study showed total 79 (89.77%) male deaths. The youngest case was that of a 16 year old male who died due to rupture of a dissecting aneurysm and the oldest was an 85 year old male who had hypertensive changes in heart and kidney and noncritical narrowing of 2 coronary vessels. Amongst the nine females in this series, the youngest was 20 years who died of myocarditis and the oldest female was 30 years who was a known epileptic of more than 10 years duration. Seventy five percent of deaths were seen in <40 years of age. Maximum number of cases were seen in second decade 35 (39.77%) followed by third decade 23 (26.13%). (Table 1)

Cardiac causes of sudden death accounted to 69.13% of the cases. The non-cardiac causes included cerebral malaria, aspiration of vegetable matter, pneumonia, cerebrovascular accident, SUDEP (sudden unexpected death due to epilepsy) etc. (Table 2)

In this study there were 10 (11.36%) cases of myocardial infarction of which 2 (2.27%) cases showed noncritical narrowing of the coronary arteries. The youngest was 23 years male and the oldest is 65 years male.

There were 3 cases each in 21-30 years age group, 31-40 years and in 61-70 years and 1 in 51-60 years. 30 (34.09%) cases showed evidence of atheromatous plaques in the coronary arteries, of these, 8 cases showed critical narrowing of the coronary arteries with no gross or light microscopic evidence of myocardial infarct and 4 (3.40%) each had features of associated hypertensive changes and evidence of old healed myocardial infarct.

Present study showed 4 (4.54%) cases of hypertrophic cardiomyopathy, 8 (9.09%) cases of myocarditis and 2 (2.27%) cases each of dilated cardiomyopathy, aortic dissection, arrhythmogenic right ventricular dysplasia (ARVD), aspiration and pneumonia. There was 1 (1.13%) case each of rheumatic mitral stenosis with left atrial dilatation, cerebrovascular accident, vasculitis, left ventricular aneurysm, cerebral malaria and acute pyelonephritis with evidence of disseminated intravascular coagulation (DIC). In 17 (19.31%) cases even after detailed histopathologic examination cause of death could not be concluded. (Table 2)

Discussion:

Cardiovascular pathology is the most common cause of sudden death. Coronary artery disease tops the list with 45.45% of cases being attributed to it, followed by myocarditis (9.09%) and cardiomyopathies (9.09%).

Atherosclerosis of coronary arteries and its downstream sequelae are responsible for most of the cardiac morbidity and mortality. [4, 5]

At the early stages of plaque induced stenosis, outward remodeling of the vessel media helps in preserving the luminal diameter. However, as the luminal stenosis progresses, a point is reached at which the demand begins to exceed supply. This is referred to as critical stenosis and it typically occurs at approximately 70% of fixed stenosis. [6]

In the present study 16 cases had critical narrowing of the coronary arteries of which only 8 cases showed light microscopic evidence of myocardial infarction. This could be because of the short interval between the onset and death which precludes the development of characteristic histologic features of myocardial death. 24 cases showed features of noncritical narrowing of coronary arteries.

The atherosclerotic plaque can be seen in one or more of the three major coronary epicardial arteries, i.e. left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA). Significant stenosing lesions can be located anywhere within the vessels but tend to be seen in the first few cms of LAD and LCX and along the entire length of RCA.

In our study, out of 10 cases of myocardial infarction, four cases had triple vessel disease, five cases had 2 vessels affected by atherosclerotic process and 1 case had involvement of only one coronary artery. 8 out of the 10 cases showed evidence of atherosclerotic plaques in left anterior descending artery.

There is one case of left ventricular wall aneurysm. Aneurysms of the ventricular wall are a late complication of large transmural infarcts that experience early expansion. The thin scar tissue in the wall of an aneurysm paradoxically bulges during systole. Death was attributed to contractile dysfunction secondary to the ventricular aneurysm.

Non-atherosclerotic conditions that are associated with sudden death include myocarditis, dilated and hypertrophic cardiomyopathy, rupture of aortic dissection, acquired cardiac arrhythmias, cardiac hypertrophy of any cause including hypertension and miscellaneous causes including drug abuse.

Cardiomyopathies and myocarditis showed equal number of cases in this study (9.09%). Hypertrophic cardiomyopathy (4cases) presents with heart weighing more than 500 gms. Microscopically all the four cases showed haphazard disarray of bundles of myocytes, myocyte hypertrophy with transverse myocyte diameter more than 40µm and evidence of interstitial fibrosis. Rhythm disturbances seen in association of hypertrophic cardiomyopathy can result in sudden death. [7]

Dilated cardiomyopathy presents usually with slowly progressive signs and symptoms of congestive heart failure such as shortness of breath, easy fatigability, and poor exertional capacity. Arrhythmia can occur resulting in sudden death.

ARVC is an uncommon cardiomyopathy accounting for only 2.27% of the sudden death which is much less compared to other studies. [4] It is morphologically characterized by severely thinned out right ventricular wall because of loss of myocytes, with extensive fatty infiltration and fibrosis. [8]

The fibro-fatty replacement leads to ventricular arrhythmias, predisposing the individual to potential sudden death. [4] Eight patients had myocarditis with a macroscopically normal heart. Microscopy showed an interstitial patchy mononuclear, predominantly lymphocytic inflammatory infiltrate associated with focal myocyte necrosis. Most of the cases were seen in <40 years of age (6 out of 8) and 2 of the 8 deceased were females.

Coronary vasculitis is a rare form of coronary artery disease, and even rarer cause of sudden death. [9] In our study there is a case of 22 weeks pregnant woman who was on regular antenatal check-up presenting with vague abdominal complaints. She expired within 6 hours of onset of her complaints. Detailed examination showed evidence of vasculitis involving both LAD and LCX coronary arteries.

There was also evidence of vasculitis involving vessels in liver and kidney.

Rheumatic fever is an acute, immunologically mediated, multisystem inflammatory disease that occurs a few weeks after an episode of group A streptococcal pharyngitis. Acute rheumatic carditis is one of the manifestations of the active phase and it may progress over time to chronic rheumatic heart disease of which valvular abnormalities are key manifestations.

Mitral valve is often involved resulting in mitral stenosis, of which rheumatic heart disease is virtually the only cause. [6] One case in this series was that of a 23 year old male who collapsed and died while at work.

Examination of the heart revealed mitral stenosis with left atrial dilation. Stenotic mitral valve leads to progressive left atrial dilation and may harbour mural thrombi in the appendage or along the wall. Death in this case was attributed to probable embolization of left atrial thrombus.

Aortic dissection occurs when blood splits apart the laminar planes of the media to form a blood-filled channel within the aortic wall.

It begins as an intimal tear through which blood flow under systemic pressure dissects through the media, fostering progression of the medial hematoma. It can be catastrophic if the dissection ruptures through the adventitia and haemorrhages into adjacent spaces. [6, 10] Both the cases in this study presented with a ruptured aortic dissection.

This study showed 19.31% cases having morphologically normal heart in the context of sudden death. It ranges from 1%-23% in various other studies. [2, 4] Various electrical abnormalities of the heart are known to predispose an individual to sudden death.

They include long QT syndrome, Brugada syndrome, short QT syndrome, catecholaminergic polymorphic ventricular tachycardia, Wolff-Parkinson-White syndrome, congenital sick sinus syndrome, and isolated cardiac conduction disease.

The most important of these disorders are the channelopathies, which are caused by mutations in genes that are required for normal ion channel function. The knowledge and awareness on these conditions which are not detected at autopsy has transformed the approach to the negative autopsy. [4, 6, 11, 12]

Non cardiac causes of sudden death in this study include cerebral malaria (1.13%), SUDEP (3.40%), aspiration (2.27%), acute pyelonephritis with features of DIC (1.13%), pneumonia (2.27%) and cerebrovascular accident (1.13%). Cerebral malaria is

characterized by brain vessels plugged with parasitized red cells. It is usually diagnosed ante-mortem. However, occasionally sudden death is known to occur. [13, 14] Epilepsy is a chronic disabling condition of the nervous system. There are 3 cases of diagnosed epilepsy, one of which is of more than 10 years duration. Detailed autopsy examination in these cases did not reveal any definitive cause of death. These 3 cases of sudden death could probably be attributed to sudden unexpected death due to epilepsy (SUDEP).

SUDEP is defined as “sudden, unexpected, witnessed or unwitnessed, non-traumatic and non-drowning deaths in patients with epilepsy, with or without evidence of seizure and excluding documented status epilepticus, in which post-mortem examination does not reveal a toxicological or anatomical cause of death”. SUDEP is essentially a diagnosis of exclusion of other causes of death. [15]

Conclusion:

Cardiovascular pathology is a major contributor for sudden death. In most of the patients the first and only clinical expression of coronary atherosclerotic process is sudden death. The role of the histopathologist is to provide a detailed examination of the organs, especially heart, in order to identify a definitive cause of death. However, sudden death with a morphologically normal heart is a very important negative finding at autopsy.

A substantial number of such negative autopsies have been attributed to conduction system abnormalities, channelopathies, long QT syndrome and catecholaminergic polymorphic ventricular tachycardia (CPVT). Thus, though a histopathologist plays a vital role in providing a definitive cause in sudden death, it is imperative that the heart of all young individuals dying unexpectedly be examined by an expert cardiac pathologist. [4] This will help us reduce the number of negative autopsies in the long run and provide a definitive cause of death.

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Table 1: Age wise Distribution of the Cases

Age	Cases (%)
11-20 years	08 (9.09%)
21-30 years	35 (39.77%)
31-40 years	23 (26.13%)
41-50 years	07 (7.95%)
51-60 years	08 (9.09%)
61-70 years	05 (5.68%)
71-80 years	01 (1.13%)
81-90 years	01 (1.13%)

Table 2: Histopathologic Distribution of Various Cases

Cardiac causes of sudden death	Cases (%)
Coronary artery disease	40 (45.45%)
Myocarditis	8 (9.09%)
Hypertrophic cardiomyopathy	4 (4.54%)
Dilated cardiomyopathy	2 (2.27%)
ARVD	2 (2.27%)
Dissecting aneurysm	2 (2.27%)
Lt ventricular aneurysm	1 (1.13%)
Vasculitis	1 (1.13%)
Rheumatic mitral stenosis	1 (1.13%)
Negative autopsy	
Nothing significant	17 (19.31%)
Non cardiac causes of sudden death	
SUDEP	3 (3.40%)
Pneumonia	2 (2.27%)
Aspiration	2 (2.27%)
Cerebral stroke	1 (1.13%)
Cerebral malaria	1 (1.13%)
Acute pyelonephritis with DIC	1 (1.13%)

ARVD- Arrhythmogenic right ventricular dysplasia, SUDEP- sudden unexpected death in epilepsy, DIC- Disseminated intravascular coagulation