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Original Research Article

Spectrum of Histopathological Changes in Ischemic Heart Disease: An Autopsy Study

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Abstract

Background: cardiovascular disease comprising of mostly ischemic heart disease and stroke are leading cause of death worldwide. WHO estimates that India accounts for just over a fifth of these deaths. A thorough autopsy under expert supervision and histomorphological examination of heart plays an essential part to confirm the cause of death.

Aims and objectives: This study was conducted to study the spectrum of histopathological changes in ischemic heart disease.

Material and methods: A retrospective study of 252 cases of formalin fixed heart specimen was undertaken in the Department of Pathology, Chhattisgarh Institute of Medical Sciences, Bilaspur, Chhattisgarh. Out of 252 specimen, 32 specimen of heart showed autolytic changes and hence their histomorphological findings were not included in the study. A detailed gross and microscopic examination was performed, and findings were correlated with available clinical data to establish the cause of death.

Result: Atherosclerosis was the most common lesion found in 124 cases (64%) followed by medial hypertrophy in 56 cases (28%) and intimal hyperplasia in 46 cases (23%). Other frequent findings were disruption of myocardial architecture 44 cases (22%) and patchy interstitial fibrosis 47 cases (23.5%). Also seen was presence of collateral formation in 39 cases (19.5%) and recanalization in 22 cases (11%). Microthrombi in circulation was seen in 27 cases (13.5%). These cases could have been the undiagnosed covid patients. Fibromuscular dysplasia was seen in 12 cases (6%) and thickening of pericardial fat in 10 cases (5%). Fibrous cap formation was seen in 7 cases (3.5%) and transmural inflammation in 12 cases (6%). Other less common findings were presence of Lines of Zhan in 7 cases (3.5%), Giant cell arteritis in 2 cases (1%) and dissection of aorta in 2 cases (1%).

Conclusion: Atherosclerosis was found out to be the most common lesion responsible for causing mortality.

Keywords: Ischemic heart disease, Autopsy, Histopathology.

Introduction

The term autopsy is derived from ancient Greek word autopsia, means “to see for oneself”, autos (“oneself”) and opsis (“eye”) [1]

Cardiovascular diseases (CVD) are the leading cause of death worldwide with an incidence of 60-70% [2] and now have become the leading cause of morbidity in India.[3] cardiovascular disease, comprising mostly ischaemic heart disease and stroke, is the leading cause of death worldwide, accounting for 17·7 million deaths annually. Of these deaths, 6·2 million (35%) occur in middle age (30–69 years). [4]

WHO estimates that India accounts for just over a fifth of these deaths [4]and therefore reduction of global cardiovascular mortality greatly depends on India, where cardiovascular disease develops a decade earlier in life compared with high-income countries. [5]

Aim

To evaluate the spectrum of histomorphological changes in ischemic heart disease in autopsy samples and confirming the cause of death.

Material and Methods

A retrospective study of 252 cases of formalin fixed heart specimen was undertaken in the Department of Pathology, CIMS Bilaspur, Chhattisgarh. These autopsies were performed under the supervision of forensic experts. In this study whole heart specimen or tissue bits from heart were included. Out of 252 specimen, 32 specimens of heart showed autolytic changes and hence their histomorphological findings were not included in the study. The samples were received in formalin fixative (10%). Clinical details and proper history were collected for the respective case. After fixing the specimen for 24 hours grossing was performed. During grossing firstly the samples were weighed and then measured, followed by examining the external surface for any gross abnormality like any congenital anomaly, change in color, presence of infarct, tear, rupture etcetera. The vessels were analysed for wall thickness, change in texture, presence of any occlusion or plaque. The mitral valve and tricuspid valve were examined for presence of any vegetation, hardening and presence or absence of any thrombi. After thorough examination with naked eye and measuring the thickness of ventricular walls, 4-5mm thick section were taken from representative site such as Aorta, right ventricular wall, left ventricular wall, interventricular septum, right coronary artery, left coronary artery. The sections were stained in Hematoxylin and Eosin and examined under microscope. The histopathological findings were kept in record and were correlated with gross findings and were further extrapolated to draw light upon the cause of death.

Results

Out of 252 cases 32 cases showed autolytic changes and 20 cases of heart were received in pieces, hence their histopathological findings could not be included in our study. We performed our study on 200 formalin fixed specimens of heart. All the cases were divided into various strata depending upon age, sex, mode of death, and spectrum of histopathological changes in the heart. The youngest case was a set of 2 day female twins and oldest being 86 year old male forming a age group range of 0-86 years and mean age of 41.54. The incidence of IHD was found to be higher in male population. Out of 200 cases only 56 were female and rest of the cases were male with M:F ratio being nearly 3:1. The mean age of ischemic heart disease in male population was 43.8 and in females 25.2.

The weight of heart after fixing overnight in formalin solution ranged from 20- 340 gms in males and 20- 270 gms in females. The weight of heart was found to be in upper range in male population in deaths

related to chronic alcoholism due to thick layer of pericardial fat associated with it. The weight of heart was found out to be 290 gms in male subjects and 240 gms in female subjects.

The mode of death was found to be variable. The most common clinical history was being some sort of cardiovascular event (45%) like heaviness and pain in chest, difficulty in breathing, shoulder pain and dizziness. Second most common cause was chronic underlying illness (33%) most common being Diabetes in adults followed by chronic alcoholism (5%). In children most common etiology was being congenital heart disease. Rest of the patients were brought dead without much significant clinical details available to access the cause of death.

A wide array of histopathological changes was noted in various specimens. The most common finding was presence of atherosclerosis in coronaries, left coronary artery being the most commonly involved.

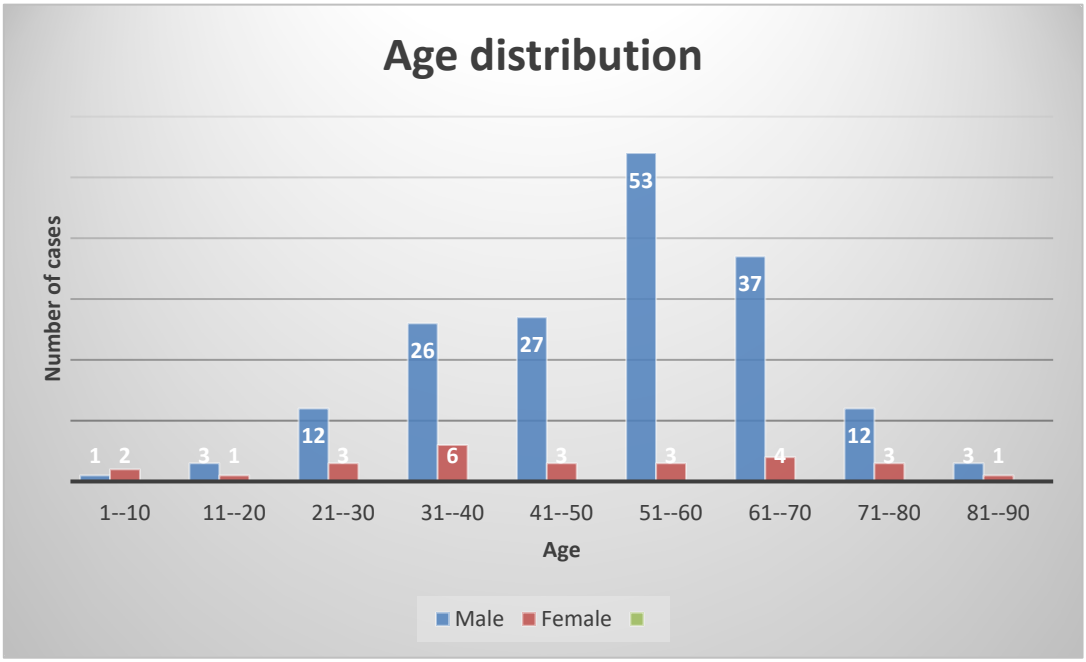

Figure 1: Age Distribution

Table 1: Histopathological Changes in Ischemic Heart Disease

S. NO	HISTOPATHOLOGICAL CHANGES	NUMBER OF CASES
1.	Atherosclerosis	124(64%)
2.	Fibrous cap	7(3.5%)
3.	Interstitial fibrosis	47(23.5%)
4.	Fibromuscular dysplasia	12(6%)
5.	Medial hypertrophy	56(28%)
6.	Intimal hyperplasia	46(23%)
7.	Microthrombi	27(13.5%)
8.	Collateral formation	39(19.5%)
9.	Recanalization	22(11%)
10.	Dissection of aorta	2(1%)
11.	Thickening of pericardial fat	10(5%)
12.	Transmural inflammation	12(6%)
13.	Giant cell arteritis	2(1%)

14.	Disruption of myocardial architecture	44(22%)
15.	Lines of Zhan	7(3.5%)

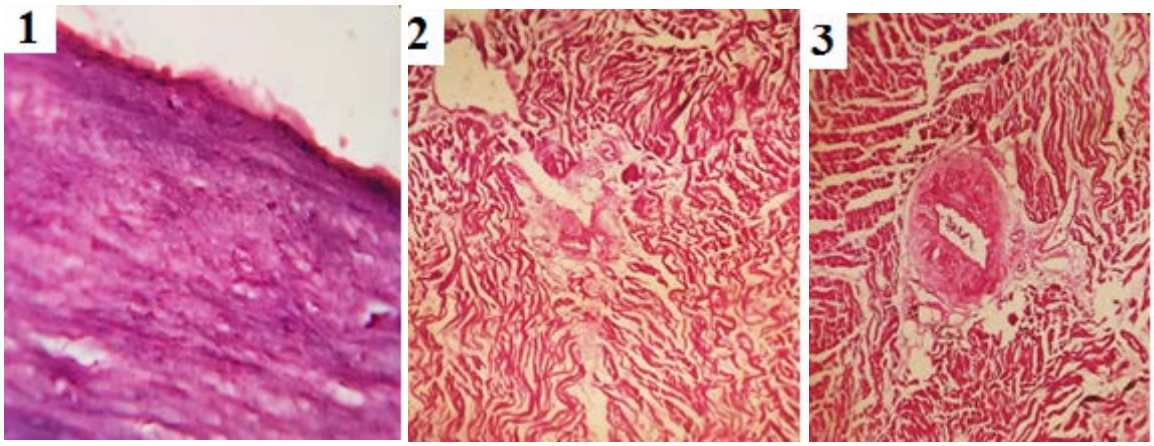

Figure (1): Fibrous cap; (2): Patchy interstitial fibrosis; (3): Fibromuscular dysplasia

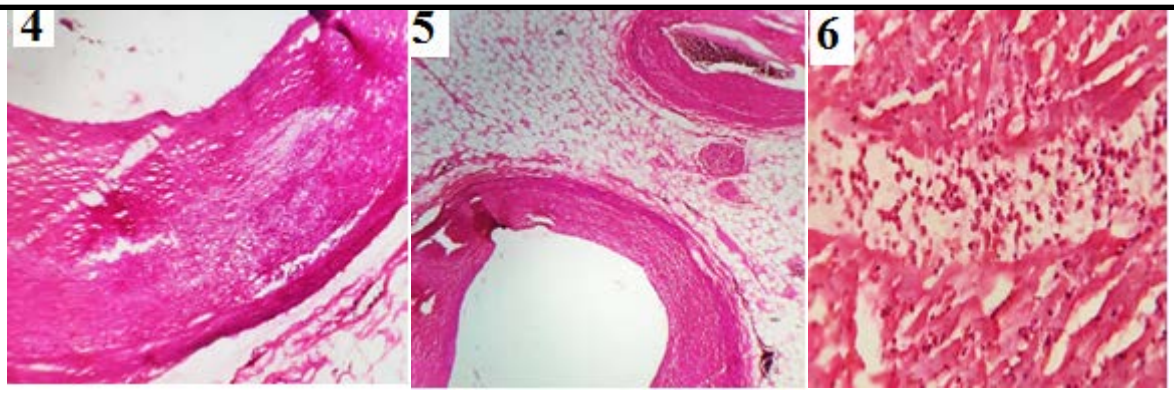

Figure (4): Atheroma; (5) Collateral formation; (6) Dense Inflammation

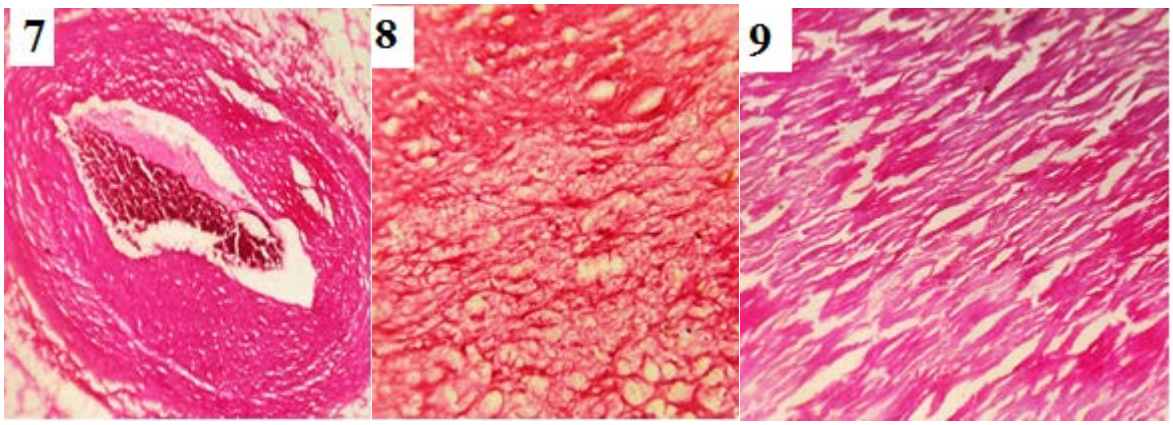

Figure (7): Medial hypertrophy, intimal hyperplasia, clot; (8): Foam cells deposition; (9): Disruption of myocardial architecture

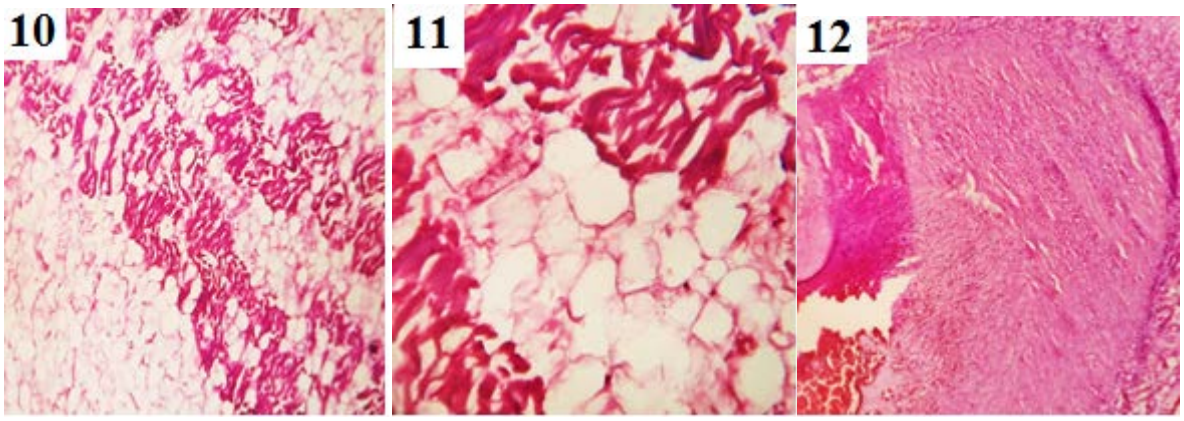

Figure (10) and (11): Thicking of pericardial fat; (12): Transmural inflammation

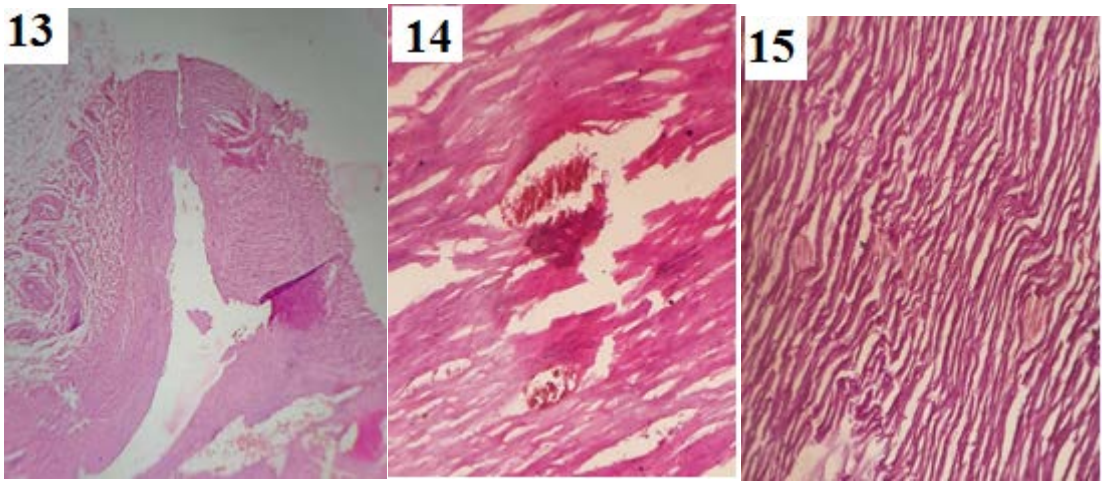

Figure (13): Dissection of aorta; (14) and (15): Microthrombi

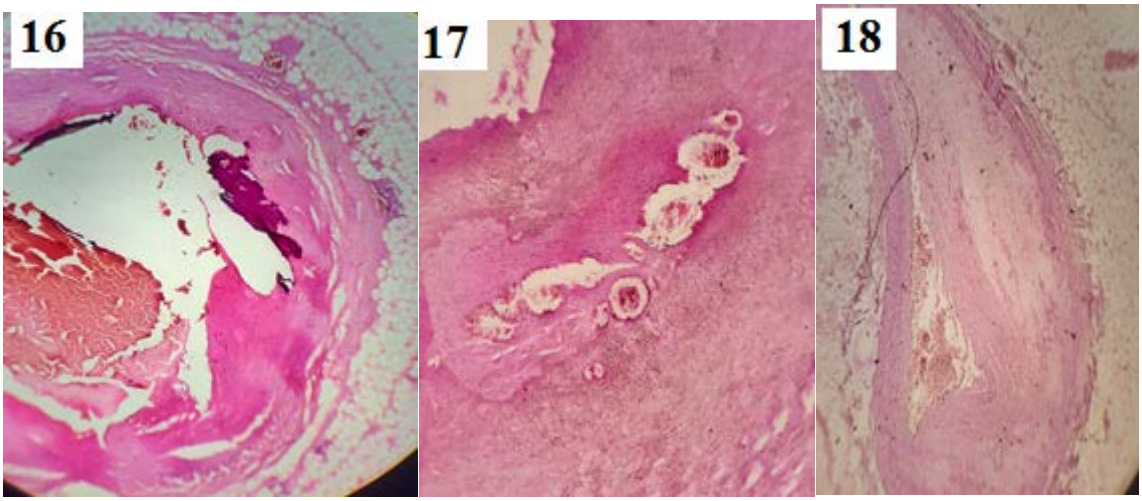

Figure (16): Fibroatheroma; (17): Recanalization; (18): Fatty streak

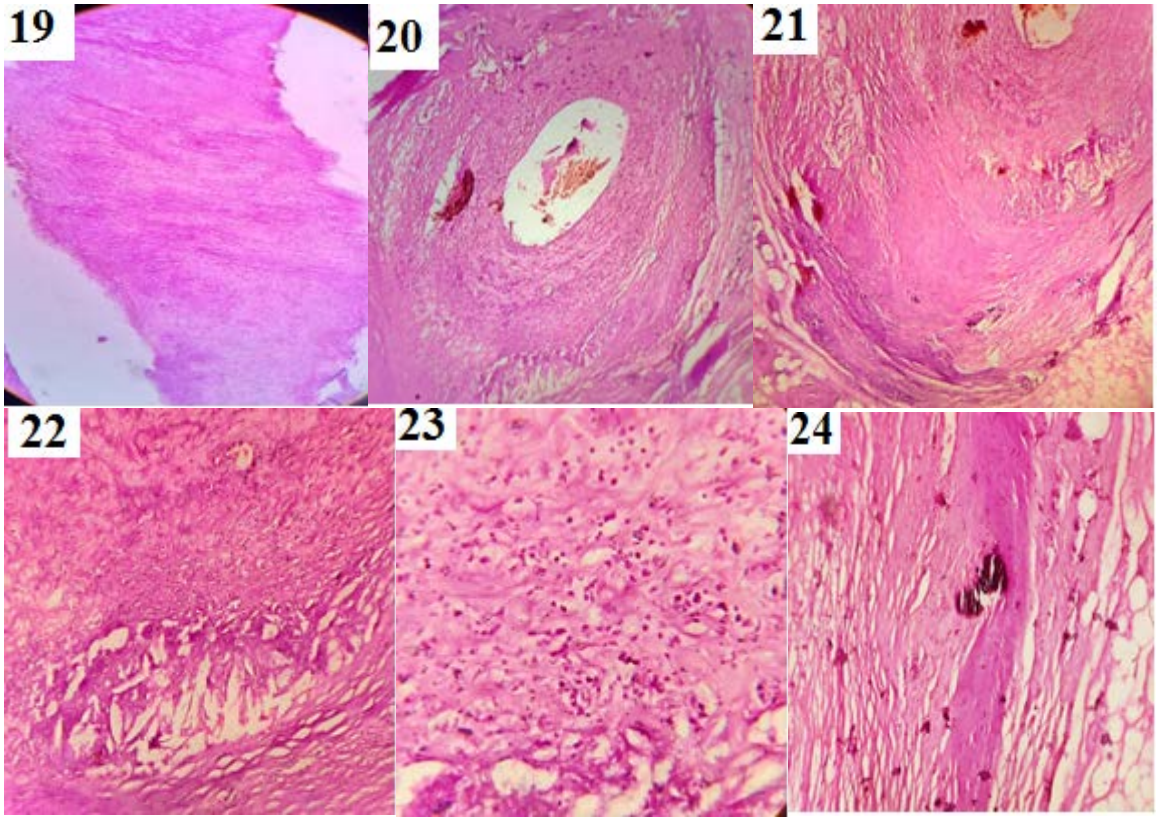

Figure (19): Lines of Zhan; (20-24): Giant cell arteritis-Narrowing of lumen, granuloma like lymphocytic collection, histiocytes with calcification

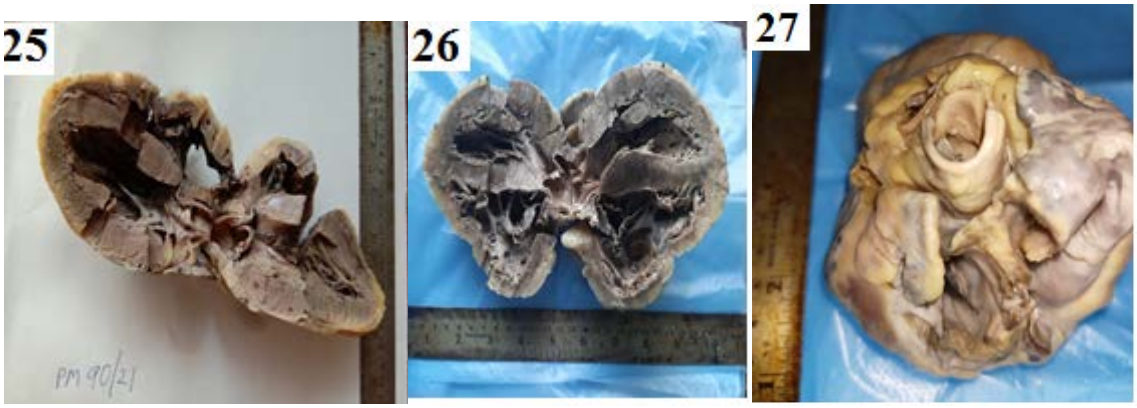

Figure (25): Giant cell arteritis causing dilatation and obliteration of RCA; (26): Thickening of pericardial fat; (27): Fatty steak formation in Aorta

Discussion

A thorough study of the cause of death including detailed sampling during postmortem examination and correlating it with microscopic features can establish whether the death occurred due to cardiovascular event or not. Postmortem examination is the only means to establish the cause of death. In our study we included microscopic features of 200 cases. Ischemic heart disease and changes induced by it were found to be more common in male population, M:F ratio being nearly 3:1. The incidence of cardiovascular events were most prevalent in 5-6th decade irrespective of gender. In a

study conducted on 200 cases for a period of two and a half years by Marwah et al [6] also showed that histopathological changes in heart were more common in males (92%) than in females (8%) with maximum number of cases being in 41-50 years age group. Garg et al [7] in their study of 141 cases over two years period also had most of the cases (48.9%) with cardiovascular deaths in the age group 41-60 years.

In our study atherosclerosis was the most common finding present in most of the cases who have had history of cardiovascular event (64%). Similar findings have been reported by Garg et al (55.3%)7, Chandrakala Joshi [8] (64%) and Ekta Rani et al [9] (77.3%) have shown atherosclerosis to be the commonest finding in their studies.

Patchy areas of interstitial fibrosis was seen in 47(23.5%) cases along with disruption of myocardial architecture 46 cases(23%) which indicates some sort of remote ischemic injury. Medial hypertrophy in 56(28%) cases and irregular intimal hyperplasia in 46(23%) cases were seen concordant with each other. Medial hypertrophy is most often noted as a secondary response to hypertension and can occur in both large and small muscular arteries. Intimal hyperplasia is the universal response of a vessel to injury, and it is an important reason of late bypass graft failure, particularly in vein and synthetic vascular grafts. Also seen was presence of collateral circulation in 39(19.5%) cases and recanalization in 22(11%) cases. Anastomotic channels, known as collateral vessels, can develop in the heart as an adaptation to ischemia. [10,11]

Lines of Zhan were noted in 7(3.5%) of cases. Lines of Zahn are a characteristic of thrombi. [12] They have visible and microscopic alternating layers (laminations).[13,14] Platelets mixed with fibrin form lighter layers. [13] Red blood cells form darker layers. [13] Lines of Zahn can be used to confirm diagnosis of a thrombus. [12] Their presence implies thrombosis at a site of rapid blood flow that happened before death. They are more common in thrombi formed in the heart or aorta. [15] In veins or smaller arteries, where flow is not as constant, they occur less frequently. [16]

Two cases (1%) showed dissection of aorta. The rupture was most likely due to myocardial infarction as there was associated ischemic necrosis, inflammation and hemorrhage at the site of rupture.

Transmural inflammation was seen 12(6%) cases. This can be a possible cause of sudden cardiac death as transmural inflammation can instigate rupture of unstable plaque. Maresi E et al [17] describe a case of sudden cardiac death caused by the simultaneous multivessel rupture of unstable atherosclerotic plaques, triggered by a transmural inflammatory process (coronaritis).

We found presence of microthrombi in 27(13.5%) cases. These patients could have been the undiagnosed covid patients who suffered stroke due to presence of microthrombi in the circulation. In a retrospective study of 214 hospitalized COVID-19 patients from Wuhan, China, 5.7% of the severe patients suffered a stroke. [18] One of the emerging hallmarks of severe COVID-19 is a coagulopathy that has been termed “sepsis-induced coagulopathy” (SIC) with high D-dimer levels and elevated fibrinogen. [19,20] SIC is a precursor state to DIC and associated with elevated prothrombin time (PT), elevated D-dimer, and thrombocytopenia, but without hypofibrinogenemia. It is related to an infection-induced systemic inflammatory response with endothelial dysfunction and microthrombosis with organ failure and usually no bleeding. [20]

Fibrous cap formation was seen in 7(3.5%) cases and fibromuscular dysplasia in 12(6%) cases out of which 8(4%) were

female. In study by Begelman et al [21] it was found Fibromuscular dysplasia is an uncommon angiopathy that occurs in young to middle-aged, predominately female individuals. The disease consists of a heterogeneous group of histologic changes, which ultimately lead to arterial narrowing. Clinical manifestations reflect the Giant cell arteritis was present in 2(1%) of the cases. One of the cases was a 24-year-old male and other was a 63-year-old male. There was presence of wall thickening with significant narrowing of vessel lumen. Adventitia showed granuloma like collection of lymphocytes and histiocytes with broadening of vasa vasorum. Medial layer showed hypertrophy, calcification and focal areas of degeneration.

A study by SamsonM et al [22] demonstrated that GCA-related stroke essentially affects the vertebrobasilar territory and mainly occurs in old men with associated vascular risk factors. Although rare, GCA symptoms must be searched for in elderly patients with stroke. Our study shows GCA can affect younger population as well.

We had received whole heart specimen of a 28 year old male who had history of ingestion of some tablets which were presumed to be poisonous. Two hours after taking the tablets he started having pain in chest, weakness over left side of face, difficulty in speech and swallowing, altered sensorium. On microscopy features were suggestive of Myocardial infarction, right ventricle characterized by myocardial ischemia, occlusive thrombi and intense congestion of blood vessels. Later on it turned out that the patient had consumed Sildenafil citrate without achieving an erection or participating in sexual activity. A case report by Habek et al [23] emphasize that stroke is, although rare, real side effect of sildenafil. Potential users should be warned before taking it, especially if they have other stroke risk factors, as recommended by the manufacturer.

A common finding which was present in 10(5%) cases was thickening of pericardial fat pad. This also resulted in difficulty in localizing coronaries while performing the grossing of the specimens. On microscopy of such specimens there was presence of features of myocardial ischemia. A study by Mohamed Al-Rawahi et al [24] demonstrated growing evidence that pericardial fat has direct effect on atrial fibrillation prevalence, severity and recurrence after ablation. Pericardial fat is also highly metabolically active and is an important source of several adipokines and cytokines. [25] Although obesity may impact AF incidence via several mechanisms, a relation between local pericardial fat depots surrounding the heart and AF has been recently described which may have important pathophysiological implications.

Conclusion

This study has taken consideration into histopathological findings of ischemic heart disease and correlating it with the cause of death. In our study atherosclerosis is the leading cause of morbidity in ischemic heart disease. There was presence of microthrombi in considerable number of cases which are most likely to be covid induced. This proves the importance of getting tested for covid symptoms so as to intervene into the ongoing pathophysiology responsible for covid induced stroke. The autopsy is a vital tool to establish the cause of death.

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