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RESEARCH ARTICLE
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A HISTOPATHOLOGICAL ANALYSIS OF MAST CELLS IN ATHEROMATOUS LESIONS: AN AUTOPSY BASED STUDY

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INTRODUCTION:

Atherosclerosis is a chronic degenerative condition of the arteries that causes major cardiovascular morbidity and mortality around the world. In the Indian subcontinent, it is estimated to be responsible for more than 25% of deaths [(1)]. It starts developing at an earlier age and is found to be in more advanced stages in the Indian population as compared to the patients in western nations. It can induce a variety of problems such as myocardial infarction (MI), stroke, embolization, ulceration, thrombosis, and aneurysm, all of which cause significant morbidity and mortality, impacting the lifespan and quality of life [(2)]. High cholesterol and triglycerides levels have been linked to obesity, increased risk of atherosclerosis, and shorter life span [(3)].

Hyperlipidaemia plays a significant role in developing atherosclerosis, along with development of other conditions like hypertension, diabetes and aging.Mast cells develop from multipotent myeloid stem cells and travel through the peripheral circulation as mast cell precursors before being directed to particular tissues and organs, such as skin and lungs, where they develop into mast cells. Additionally, mast cells are found in the vessel wall, specifically in the heart and perivascular tissue. This may indicate that mast cells play a part in the pathogenesis that impact these tissues, including atherosclerosis, which is primary underlying cause of acute cardiovascular syndromes (e.g., myocardial infarction and stroke) [(4)]. By producing a variety of inflammatory mediators, such as histamine, prostaglandins, cytokines, chemokines, tryptase, and chymase, mast cells aid in the development of atherosclerosis. These mediators cause cellular proliferation, vascular inflammation, and endothelial dysfunction, which results in the formation of macrophage foam cells, seen in the early stages of atherosclerosis [(5)]. The data on role of mast cells in atherosclerosis in Indian population is very meagre. Hence, present study was undertaken to throw more light on role of mast cells in atherosclerosis.

AIM & OBJECTIVES:

To evaluate the distribution of mast cells in atheromatous lesions of various blood vessels (right coronary arteries (RCA), left coronary artery (LCA) and Aorta).

MATERIAL AND METHODS

A cross-sectional study was conducted in our institute on autopsy heart specimens for a period of 6 months from the date of institutional ethical committee approval with convenient sample size. A total of 60 heart specimens were received during the study period were included in the study.

INCLUSION CRITERIA:

Heart specimens which showed atheromatous lesions on histopathological examination were included

EXCLUSION CRITERIA

Autolysed specimens and heart specimens with normal histomorphology were excluded

METHODOLOGY:

The heart was weighed and placed in a 10% buffered formalin solution. Heart was opened by an inflow-outflow approach. Coronary arteries were dissected along the bloodstream. Suspicious lesions such as atherosclerotic plaques, thrombus, lumen constriction and calcification in LCA, RCA, Aorta were examined and submitted for tissues processing (Fig 1). After processing, the stained H&E section were seen microscopically (Fig 23). Microscopic grading of atherosclerosis was done using the modified American Heart Association (AHA) Classification based on morphological features like intimal thickening(grade I) to fibrous cap rupture or thrombus formation (grade VI) [6]. 2% aqueous toluidine blue stain was used as a special stain to demonstrate and quantify mast cells at the site of the atheromatous lesion. Number of mast cells were counted in the intima of artery/mm2. Usually on an average of 1 mast cell /mm^2 of artery was considered as normal, where as in lesions like fatty streaks on an average of 4- 5 mast cells/mm2 was reported [7] (Fig 4)

Fig 1: LCA shows thickened wall and thrombi in the lumen and Aorta shows fatty streaks

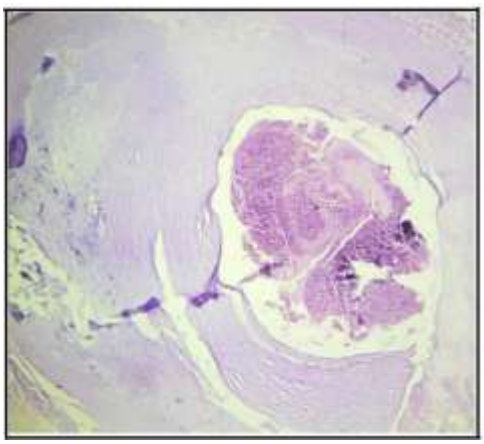

Fig 2: H&E ,400X.

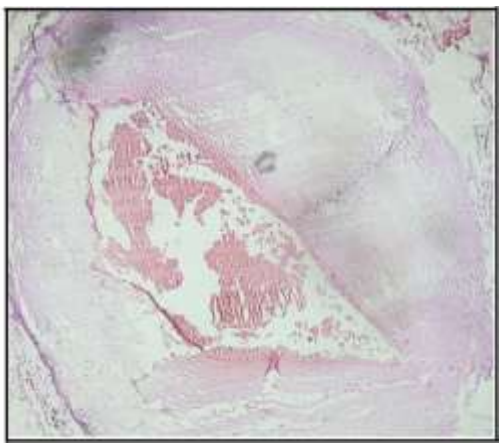

Fig 3: H&E ,100x

Fig 2 & 3: Coronary artery showing atheromatous plaque with foci of calcifications Grade V (H&E, 400x) and with thrombi Grade VI (H&E, 100x)

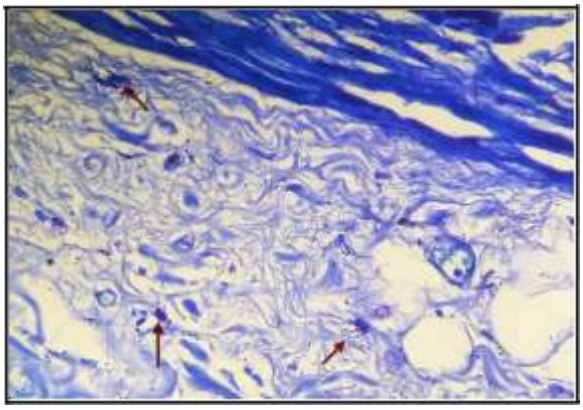

Fig 4: Degranulated mast cells (Toluidine blue stain, 400x)

RESULT AND ANALYSIS

A total number of 60 cases, out of which 32 cases (3x32 = 96 arteries (n) both coronaries and aorta) showed atherosclerosis of various grades.

Table1: Distribution of atherosclerosis based on age

Age	Total no of cases	Percentage (%)
	(32)	
21-30	05	16%
31-40	15	47%
41-50	06	19%
51-60	03	9%
61-70	02	6%
>70	01	3%

The distribution of age was between 21 – 71 years, among which the majority of cases were between 31 – 40 years.

Table 2: Distribution of atherosclerosis in various arteries:

Arteries	**No of arteries (n=96 arteries)**	**Percentage (%)**
LCA	40	42%
RCA	24	25%
Aorta	32	33%

The distribution of atherosclerosis was highest in LCA (42%), followed by Aorta (33%) and RCA (25%)

Table 3: Distribution of various grades of atherosclerosis in the arteries

Grades of atherosclerosis	No of arteries (n=96)	Percentage of cases
I	1	1%
II	5	5%
III	7	7%
IV	25	26%
V	37	39%
VI	21	22%

The incidence of grade V atherosclerosis was highest followed by grade IV and VI

Table 4: Distribution of mean value of mast cells in various grades of atherosclerosis in each of the arteries

	Mean value of mast cells in various grades of atherosclerosis												chi square test and p value
	Grade I		Grade II		Grade III		Grade IV		Grade V		Grade VI		
Arteries	A	B	A	B	A	B	A	B	A	B	A	B	
LCA (n=40)	1	0	2	3.5	3	3.3	12	3.5	15	3.6	8	4.25	2.4 & 0.66
RCA (n=24)	-	-	1	3	2	3.5	7	3.5	9	3.7	4	4	2.48 & 0.6
Aorta (n=32)	-	-	2	3.5	2	3.5	6	3.5	13	3.8	9	4	8.28 & 0.004

LCA – Left coronary artery, RCA – Right coronary artery, A – Number of arteries showing atherosclerosis, B – Mean value of mast cells.

DISCUSSION:

In autopsies, atherosclerosis of the coronary arteries and myocardial infarction are the most prevalent heart conditions. Before developing into coronary heart disease and acute coronary syndromes, atherosclerosis advances asymptomatically over decades. It starts in early age and develops gradually, starting with the accumulation of foamy macrophages and ending with the development of fatty streaks, fibrous plaques, calcium deposits, and complex lesions that range from rupture of the plaque to bleeding and thrombosis [(8), (9)]. Non-invasive imaging as well as the detection of circulating markers of biological processes, can be used to evaluate certain pathological and functional alterations in the arteries. Both rural and urban populations cannot be evaluated for atherosclerosis using these costly and challenging procedures. However, autopsy can be an efficient tool to evaluate atherosclerotic lesions. The present study was carried out on autopsy heart specimens to determine whether, there is significant progression of atherosclerosis with the presence of mast cell in arteries (both coronaries and aorta) [(10)].

In the present study, distribution of age was between from 21- 70 years, among which majority cases were between 31 to 40 years (47%). It is similar to that of study by Garg M et al [11]

Distribution of atherosclerosis based on age

	Age
Current study	31- 40 years (47%)
Garg M et al [11]	31-40 years (46%)

This age distribution might be due to thrombotic factors (smoking, inadequate fruit and vegetable consumption, high fibrinogen, high homocysteine) and atherogenic factors (high fat diet, hypertension, high LDL cholesterol, low HDL cholesterol, and high triglycerides) were found to be relevant in the development of early coronary heart disease [12]. In the present study males (72%) were more affected than females (28%) which was concordant with the Bhargava et al study (74.8% males and 24.2% females) [13]. Yazdi SAT et al., showed 73% males and 61% females [14], Singh H et al., study showed 68% in males and 27% in females [15]. This could be due to lesser sample size, demographic, geographic, racial, lifestyle & dietary variation in population [13,14].

Distribution of atherosclerosis in males and females

	Males	Females
Current study	72%	28%
Bhargava et al [13]	74.8%	24.2%
Yazdi SAT et al [14]	73%	61%
Singh H et al [15]	68%	27%

In the present study the distribution of atherosclerosis was highest in LCA (42%) followed by Aorta (33%) and RCA (25%). These findings are similar to Priya patil et al and Sudha et al studies [10,16]

Distribution of atherosclerosis in coronaries and aorta

	Left coronary artery	Right coronary Artery	Aorta
Current study	42%	25%	33%
Sudha et al [16]	36%	33%	-
Priya patil et al [10]	80%	70%	30%

The incidence of Grade V atherosclerosis was highest in the present study followed by Grade IV and VI (table 3), as compared to that of Sudha et al [16], Virmani et al [6] & Stary et al studies [8,9)] which showed Grade VI to be the most common type followed by Grade V. The differences noted in the incidence rate with other studies might be due to possible factors such as sample size, lifestyle of the sample studied and aggravating factors causing death.

In the present study, the mean value of mast cells is more in Grade VI followed by Grade V, which is same as to the study done by Patil P et al [10]. In our study significant “p” value and chi square value ($P< 0.004$, table 4) is seen in aorta only, where as in the study done by Patil P et al showed significant

"p" value in both coronaries and aorta [10]. These differences could be due to limited sample size and lesser number of arteries examined in the current study. Kovanen PT et al [17]., described a greater number of activated mast cells at the site of erosion or rupture sites. Similarly, Jeziorska M et al., in their study by using immunohistochemical staining for mast cell tryptase and chymase demonstrated increased mast cell activation by diffuse extracellular tryptase staining in advanced atherosclerotic plaques complicated by fissure, hemorrhage and thrombus formation [18]

Limitations:
Sample size
Lesser number of arteries examined
Lack of demonstration of degranulated mast cells by immunohistochemistry

CONCLUSION:

Autopsy is the most effective approach to examine atherosclerotic lesions. This study emphasizes the necessity of screening for cardiovascular risk factors at an early age. It contributes significant data to the literature on the morphology of atherosclerotic lesions. Despite the fact that the current study only included a limited number of specimens, the majority of the findings were consistent with previous research. To summarize, the current study indicated that mast cells are abundant in atherosclerotic lesions of coronary arteries, and that the number of mast cells increased as atherosclerosis progressed. Identifying the cellular and molecular mediators of inflammation during atherogenesis might be extremely beneficial in the treatment of coronary heart disease.

REFERENCES

1. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart. 2008; 94:16-26.
2. Vyas P, Gonsai RN, Meenakshi C, Nanavati MG. Coronary atherosclerosis in noncardiac deaths: An autopsy study. J Midlife Health.2015 Jan -Mar;6(1):5-9.
3. Palatine P, Julius S. Elevated heart rate: a major risk factor for cardiovascular disease. Clin Exp Hypertens 2004; 26(7-8):637-44.
4. Bot I, Bison EAL. Mast cells in atherosclerosis. Thromb Haemost 2011;106(5):820-6.
5. Kelley JL, Chi DS, Abou-Auda W, Smith JK, Krishnaswamy G. The molecular role of mast cells in atherosclerotic cardiovascular disease. Mol Med Today. 2000;6(8):304-08.
6. Virmani R, Kolodgie FD, Burke AP, Finn AV, Gold HK, Tulenko TN, et al. Lessons from sudden coronary death: A comprehensive morphological classification scheme for atherosclerotic lesions. Arterioscler Thromb Vasc Biol. 2000;20: 1262-75.
7. Kaartinen M, Penttila A, Kovanen PT. Accumulation of activated mast cells in the shoulder region of human coronary atheroma, the predilection site of atheromatous rupture. Circulation. 1994;90: 1669-78.
8. Stary HC, Chandler AB, Glagov S, Guyton JR, Insull Jr W, Rosenfeld ME, et al. A definition of initial, fatty streak, and intermediate lesions of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation. 1994;89: 2462-78.
9. Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull Jr W, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis: a report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. Circulation. 1995; 92:1355-74.
10. Patil P, Muthuveilu N, Ahmed S, Chaudhary AS. A histopathological study of mast cells in atheromatous lesions on autopsy specimens. Natl J Lab Med.2021 Apr;10(2): PO29-PO33.
11. Garg M, Aggarwal AD, Kataria SP. Coronary atherosclerosis and myocardial infarction an autopsy study. J Indian Acad Forensic Med. 2011; 33:39-42.

12. Gupta R, Gupta JK, Basal R, Vashisha J, Mahout M, Kala A, Parmar RB. Atherothrombotic risk factors and premature coronary heart disease in India: a case control study. Indian J Med Res. 2011 jul; 134(1):26-32.
13. Bhargava MK, Bhargava SK. Coronary atherosclerosis in North Karnataka. Indian J Pathol Microbiol. 1975; 18:65–77.
14. Yazdi SAT, Rezaei A, Azari JB, Hejazi A, Shakeri MT, Shahri MK. Prevalence of Atherosclerotic Plaques in Autopsy Cases with Noncardiac Death. Iranian J Pathol. 2009; 4(3):101–104.
15. Singh H, Oberoi SS, Gorea RK, Bal MS. Atherosclerosis in coronaries in Malwa region of Punjab. JIAFM. 2005; 27:236–9.
16. Sudha ML, Sundaram S, Purushothaman kumar PS, Prathiba D. Coronary atherosclerosis in sudden cardiac death: An autopsy study. Indian J Pathol Microbiol 2009; 52(4):486-9.
17. kovanen PT, Kaartinen M, Paavonen T. Infiltrates of activated mast cells at the site of Coronary atheromatous erosion or rupture in myocardial infarction. Circulation.1995; 92:1084-88.
18. Jeziorska M, McCollum C, Woolley D. Mast cell distribution, activation and phenotype in atherosclerotic lesions of human carotid arteries. J Pathol.1997; 182:115-22.