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Histopathological Analysis of Coronary Atherosclerosis: An Autopsy Study

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Abstract

Introduction: Atherosclerosis of coronary artery accounts for a large proportion of cardiac morbidity and mortality. We studied the possible association between the histo pathological changes of the coronary atherosclerotic lesions.

Methods: We performed a retrospective and prospective autopsy analysis on 200 cases age range 19–90 years including both male and female during March 2015 to march 2019. The following variables were considered: sex, age, medical history, autopsy findings to macroscopic and histological evaluation of the heart. The autopsies were performed according to standard techniques. In all autopsy cases the heart was dissected following standard autopsy protocol by using inflow and outflow method and a section of the right coronary artery (RCA), a 5 cm segment of the left anterior descending artery (LADA) distal to the origin of the circumflex artery, but including the region of origin of the circumflex branch and left coronary artery (LCA) from its origin. fixed in 10 % formalin, marked for identification and sent for histopathological analysis.

Results: Atherosclerotic plaques were identified in 162 male (77.1%) and 48 female (22.8%) of female. Atherosclerotic plaques were typically concentric and eccentric and was also associated with necrosis, calcification, as well as had a higher inflammatory cell count. Furthermore, intima and media thickness of coronary arteries were significantly higher the degree of microscopic lesion of atherosclerosis

increased proportionally with the increase in the intensity of lipid deposition.

Conclusion: In this study we found that increasing age is an risk factor for coronary artery disease. an enhanced understanding of the patho biologic processes responsible

for atherosclerotic changes might allow for early identification of a high-risk coronary plaque and thereby provide accurate knowledge of coronary artery disease load in population

Keywords: Atherosclerosis, Coronary artery, Autopsy, Plaque

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of death of women and men worldwide and this number is increasing worldwide Aging is associate with structural and functional changes of the vessel wall, which result in decreased vascular distensibility and elevated arterial stiffness^{1,2}. As a result of increasing arterial stiffness, systolic blood pressure increases, causing a rise in left ventricular workload and as a result of it hypertrophy, and diastolic blood pressure

decreases, leading to an impaired coronary perfusion ³. Chronic systemic inflammation also plays an important role in atherogenesis, and may play a role in formation of vulnerable coronary plaques, thereby precipitating acute thrombosis and clinical coronary vessel events ⁴. Atherosclerosis is a pathologically diverse disease with heterogeneous mechanisms of progression. Beginning of Irreversible atherosclerotic plaques occur with smooth muscle cell-rich lipid pool

lesions called as pathologic intimal thickening and it is a lipid-driven, chronic inflammatory disease of the vessel wall in which both innate and adaptive immune responses play a role. Atherosclerosis is a complex process involving inflammation and cellular proliferation in the arterial wall. This proliferation is mediated by a variety of thrombotic factors, and vasoactive molecular growth factors, cytokines, Mature lesions exhibit calcification⁵, which is mediated by cells similar to osteoblasts ^{6,7}. Infection may cause formation of atherosclerotic lesions⁸. Role of hemostatic factors ^{9,10}], insulin resistance ¹¹, homocysteine, immune factors ¹², inflammation markers ¹³, specific fatty acids ^{14,15} also has been proved in atherosclerotic lesion

Coronary artery calcification (CAC) is a linearly of the total burden of coronary atherosclerosis.

Aim and objective-The objective of the study was to determine the possible association between the histopathological changes of the coronary atherosclerotic lesions.

Materials And Methods:our study is an Retrospective and Prospective 5 yrs study performed in the Department of Pathology ,M.G.M medical college and M.Y Hospital, Indore on 200 cases based histopathological analysis of autopsy specimen(Heart) received in our department and their association of smoking history as per record. For Retrospective study: Case sheet and reports used and for Prospective study we receive specimen containing submitted to the department of pathology, M.G.M.

Medical college, Indore. We included sealed container and well preserved in formalin- with labeling of specimen, seal namuna of police station, panchnama report and hospital documents, if H/O of hospitalization present and we excluded autolytic sample. gross examination done inflow and outflow method is used for Grossing of heart and for microscopic examination H&E staining method was used. The heart was dissected following standard autopsy protocol at autopsy. we used inflow and outflow method for dissection of heart. First of all, sections of coronary arteries was taken after tracing in corresponding groove. After gross a 5 cm section of the right coronary artery (RCA) in the atrio-ventricular groove from its origin, a 5 cm segment of the left anterior

descending artery (LADA) distal to the origin of the circumflex artery and a 5 cm section of left circumflex artery was also taken.

All the sections of coronary arteries from each case were fixed in 10 % formalin, marked for identification and sent for histopathological analysis. Paraffin sections were made and the sections stained using Hematoxylin and Eosin (H & E) dyes. Histopathological examination. In all subjects, the heart was fixed with 10 % formalin. All specimens of coronary arteries were taken from each heart for histo pathological examination. Twenty-six blocks from the right and left coronary artery were cut into 5-µm-thick serial sections and each section was stained with hematoxylin and eosin stains.

Observation And Result-

| | NO OF CASES | Percent |
|---------------------|-------------|---------|
| 10-39 yrs age group | 59 | 29.5% |
| 40-90 yrs age group | 141 | 70.5% |
| Total | 200 | 100% |



In our study cases below 40yrs of age having atherosclerotic lesion are 59(29.5%) and above 40 yrs of age 141(70.5%) cases have atherosclerotic lesion.

| | No. of cases (In LAD) | No. of case(In LCxA) | No. of case(In RCA) |
|-----------------------------------|-----------------------|----------------------|---------------------|
| Stenosis of less than grade IV | 80 | 110 | 90 |
| Stenosis of grade IV | 120 | 90 | 110 |
| Total | 200 | 200 | 200 |

Table 2.-Grading of Stenosis in coronary vessels

In our study out of 200 cases of myocardial infarction 120 cases(60.0%) in LAD,103 cases(45.0%) in LCA,(55.0%) cases in RCA show coronary stenosis of grade IV.

| % Of Stenosis | Grade | No. of case In LAD | No. of case in LCxA | No. of cases in RCA |
|------------------|-------|--------------------|---------------------|---------------------|
| <25% | Ι | 11 | 25 | 20 |
| 26-50% | II | 12 | 36 | 30 |
| 51-75% | III | 57 | 49 | 40 |
| 76-100 | IV | 120 | 90 | 110 |
| | | 200 | 200 | 200 |

Table.14.- Degree of Coronary artery stenosis

In both LAD and RCA out of 200 cases maximum 120(60%) and 110(55%) cases show grade IV stenosis. In LxCA 90 cases (45%) have grade IV stenosis.

Histopathological, moderate to severe atheromatous lesions were observed in the coronary arteries. In some cases, a numerous number of macrophages and lymphoplasmacytic-rich infiltrates were detected. In most cases, severe atheromatous lesions containing abundant chronic inflammatory cells infiltration predominantly comprises of Lymphocytes and neutrophils. Calcium deposits were frequently observed in the tunica media and adventitia of coronary arteries. These histologic changes were consistent with atherosclerotic deposits, Numerous macrophages with foamy cytoplasm infiltrated the tunica intima and media. In severe lesions, the tunica media contained enlarged macrophages. with foamy cytoplasm, hyaline material, fibrofatty plaque. and mineralized material. In some cases, lesions were characterized by dense intimal fibrosis with necrotic debris and foam cells typical of atherosclerosis.in proximal lesion proximal lesions were more commonly atheromatous plaques as compared with distal narrowing's. Inflammatory cells were more abundant within segments with luminal atherosclerotic plaques. Calcium deposits were more commonly seen in segments containing luminal atherosclerotic plaques Whereas the presence of calcium



Figure1.severe narrowing of LAD due to Atherosclerotic changes Figure2. Atheroma formation



Figure3.Calcification in RCA



Figure 4 Atheromatous changes with narrowing of LxCA

deposits had an excellent specificity of luminal atherosclerotic plaques, the majority of atherosclerotic plaques were not calcified, and hence, sensitivity was much lower. Although we had not stained the internal elastic lamina because of extreme superficiality of the calcified areas, we supposed that most of them were intimal in location. In the present study, calcium in the coronary plaque is often fragmented and may be located deep in the plaque or close to the surface However the frequency of calcified nodules (with surface thrombus), a form of calcification that results in irregular nodules of calcium is higher in coronary disease.

Discussion-

Atherosclerosis is a disorder of large- and mediummuscular arteries. characterized sized by inflammatory changes of smooth muscle cells and formation of atherosclerotic plaques of necrotic cores; calcium deposition and collection of modified lipids, endothelial cells, leukocytes, and foam cells16. Buildup of material and infiltrates leads to vascular remodeling, acute and chronic obstruction of coronary lumen occur abnormalities of blood flow, and reduced oxygen supply to systemic target organs 17,18 Atherosclerosis is the most common pathologic process responsible for cardiovascular disease 19,20. The autopsy study provides a means of understanding the basic process which sets a stage for clinically significant atherosclerotic cardiovascular disease. There is no valid method of sampling and study of coronary artery in living population. It was, therefore, considered that death suspected due to cardiovascular pathology, probably provide the best sample of the living population for studying atherosclerosis. In this study, the histological examination of the serially sectioned coronary arteries from 200 cases who died of suspected myocardial infarction and un revealed the frequent presence of atherosclerotic lesions and their grading from grade I to grade IV. The lesions are characterized by infiltration in the intima and media of coronary artery, monocytes foam cells, richlymphocytes and deposits of mineral material, mainly composed of cellular matrix network, as well as fragmentation of the elastic fiber system. Age is a powerful risk factor for coronary heart disease. The development of atherosclerosis increases markedly with age, sex, smoking, alcohol and life style. The coronary atherosclerosis is also increasing with rapid pace in all age group also.

Autopsies performed on casualties of the Korean War revealed coronary artery involvement in 77.3 % of the hearts studied,

Data after the Vietnam War noted the presence of atherosclerosis in 45 % of casualties with severe disease in 5 %. One hundred eleven victims of noncardiac trauma underwent pathologic examination of their coronary arteries to estimate the presence and severity of coronary atherosclerosis. Sudden coronary death (SCD) in older individuals is generally associated with extensive coronary atherosclerosis, although it may be the first manifestation of ischemic heart disease. Low-density lipoprotein remains the most important risk factor for development of atherosclerosis in humans

and has been also associated with atherosclerosis in

animals17,19,21,22. immune and inflammatory mechanisms of atherosclerosis have gained tremendous interest in the past 20 years23,24

Data suggest an important role for chemokines and chemokine receptors in atherosclerosis and highlight a network of cytokines that modulate the immune

response and inflammation of the arterial wall 25,26. it has been shown in humans that all phases of atherosclerosis are regulated by inflammatory mechanisms,

the possible impact of chronic inflammation in the development of atherosclerosis in animals and the importance of preventive diagnosis should be considered 26,27

In our study, an increased number of inflammatory cells, atheromatous changes and areas of necrosis and calcification seen in segments containing atherosclerotic plaques, consistent with findings from studies on atherosclerosis of coronary arteries 29,30

Moreover, lymphocytes were more abundant in sections containing atherosclerotic plaques, in our study, lymphocytes were the predominant inflammatory cells in the majority of atherosclerotic plaques The findings of a study by van der Wal et al.31also suggested a predominance of lymphocytes in venous compared with arterial plaques. Although the reasons for a predominance of lymphocytes in vessel atherosclerotic lesions need further investigation

In the present study, it was observed that 162 cases

(81.0%) were males and 38 (19.0 %) were females showing atherosclerotic changes

which are concordant with other researchers' findings that showed 74.8 % males and 24.2 % females.32,33 IThej et al., showed 62 % were males & 50 % were females in Indian population 34. Study reported by

Yazdi SAT et al., showed 73 % males and 61 % females had atherosclerosis in a population of Iran.This difference is again explained by the demographic, geographic, racial, lifestyle & dietary

variation in population 35 Singh H et al., have reported the incidence of atherosclerosis in the coronaries to be 68 % in males and 27 % in females 36.

In our study we found that Coronary artery calcium (CAC) has been demonstrated to be associated with the risk of coronary heart disease.

Rumberger et al. have made additional recommendations for specific cut points for mild, moderate, and severe coronary artery calcium Thus, coronary calcium is not a marker for neither unstable nor stable plaques.

Atherosclerosis and coronary artery disease are huge health concerns but It is well known that lifestyle modification and drug therapy in selected individuals can reduce the risk of hard cardiac events.

Conclusions

Our study suggested that atherosclerotic changes vary according to age and sex. calcification is found more frequently in advanced lesions; Histopathological investigation has shown that plaques with microscopic evidence of mineralization are larger and associated with larger coronary arteries than plaques or arteries without calcification. Finally, histopathological studies provide the most accurateclues to a better understanding of human coronary artery disease. With better insight into disease pathophysiology, novel interventions could be introduced to improve care and future outcomes for patients undergoing coronary artery disease

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