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Morphological spectrum of atherosclerotic lesions in a tertiary care Institute in Punjab

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ABSTRACT

Background: The incidence of coronary artery disease (CAD) has risen considerably in developing world due to industrialization, urbanisation and lifestyle changes, especially among Indians and South Asians. The onset of CAD has been seen to occur at an early age and the severity of the disease and mortality associated with CAD has also increased. The pathology of atherosclerosis needs to be re-evaluated to develop targeted therapy which can contain the disease process at the earliest stage. **Aims and Objectives:** Most of the morphological studies on atherosclerosis have been done on autopsy cases. In this study, we have analysed the morphological spectrum of atherosclerotic lesions in live patients. **Materials and Methods:** We retrospectively analysed the histopathology slides of 85 cases whose endarterectomy plaques were received in the Department of Pathology over a period of three and half years (January 2014 to June 2017) and classified the lesions according to Modified American Heart Association classification of atherosclerosis. **Results :** The average age of patients was 60 years and male to female ratio of 4.3:1. Left anterior descending artery was the commonest vessel involved (52.4%). Majority of the cases had fibrocalcific plaques,followed by fibrous cap atheroma and calcified nodules. **Conclusion:** Coronary artery plaques were found even in patients less than 40 years old. Aggressive lipid defense therapy needs to be the cornerstone of management of CAD.

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Key words: Atherosclerosis; Coronary artery; Risk factors; Plaque

INTRODUCTION

Coronary artery disease (CAD) is a type of cardiovascular disease (CVD). The incidence of CAD has risen considerably in developing world due to industrialization, urbanisation, sedentary lifestyle, increased stress and poor dietary habits. CVD accounted for 33.2% of total and 45% of adult deaths in 2015.[1] Atherosclerosis is responsible for CAD and CVD. Keeping these facts in mind, it is the need of the hour to take a comprehensive relook at the pathology of atherosclerosis in order to develop targeted therapy which can contain the disease process at the earliest stage possible.

Most of the studies on morphology of atherosclerotic lesions have been done on autopsy cases. We have analysed the morphological spectrum of atherosclerotic lesions in live patients who underwent endarterectomy during revascularization.

MATERIAL AND METHODS

This was a retrospective analysis of histopathology slides of 85 cases whose endarterectomy plaques were received in the Department of Pathology of our tertiary care institute over a period of three and half years (January 2014 to June 2017). The clinical details of the patients were retrieved from the

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requisition forms. All the patients had undergone coronary artery bypass grafting for stenosis of coronary arteries caused by atherosclerosis. The excised specimens of involved coronary arteries were received in the Department of Pathology. The specimens were routinely processed and stained with Hematoxylin and Eosin (H&E) stain. Special stains like Massons Trichrome were performed wherever required to assess the fibrous component in plaques. The slides of all these cases were reviewed and lesions classified according to Modified American Heart Association classification of atherosclerosis (Table 1).

RESULTS

We studied 85 cases where histopathological examination of coronary artery plaques was done.

The ages of the patients ranged from 37 – 83 years, with average age of 60 years. Most of the cases were in age range 51-70 years. (Table 2) There was stark male predominance with male to female ratio of 4.3:1.

45 cases (52.38%) had lesions in left anterior descending artery, 26 cases (30.95%) had lesions in right coronary artery and 14 cases (16.67%) had lesions in left circumflex artery. (Table 3)

The commonest lesion was fibrocalcific plaque, seen in 58 cases. (Figure 1) The plaque had necrotic core which showed areas of calcificationsurrounded by foamy macrophages and lymphocytes, with surrounding fibrotic areas.

Fibrous cap atheroma was noted in 15 cases (Figure 2). The plaque had foci of necrosis, areas of haemorrhage and fibrin deposits. The plaque was rimmed by a fibrous cap, which was infiltrated by lymphocytes and foamy macrophages.

Four cases had calcified nodules in which fibrocalcific plaque showed large areas of calcification over it. The underlying tunica media had cholesterol clefts and foamy macrophages, surrounded by collagen rich fibrous cap.

Plaque rupture (Figure 3) was seen in two cases. There was infiltration of foamy macrophages and lymphocytes in a ruptured fibrous cap which was communicating with necrotic core of underlying plaque.

Two cases displayed pathological thickening of intima (Figure 4). The arterial wall showed thickening due to proliferation of smooth muscle cells with cholesterol clefts. There was no plaque formation or necrosis.

There were also two cases each of non - atherosclerotic intimal xanthoma and Non - atherosclerotic intimal thickeningwas seen in two cases (Figure 5). The arterial wall showed thickening due to proliferation of smooth muscle cells. There was no lipid accumulation or cholesterol clefts or inflammatory cells.

Table 1: Modified American heart association (AHA) classification of atherosclerosis based on morphological description[12]

	Description	Thrombosis
Non–atherosclerotic lesions		
Intimal thickening	The normal accumulation of Smooth Muscle Cells (SMCs) in the intima in the absence of lipid or macrophage foam cells	Absent
Intimal xanthoma, or “fatty streak”	Luminal accumulation of foam cells without a necrotic core or fibrous cap. Based on animal and human data, such lesions usually regress.	Absent
Progressive atherosclerotic lesions		
Pathological intimal thickening	SMCs in a proteoglycan-rich matrix with areas of extracellular lipid accumulation without necrosis	Absent
Erosion	Luminal thrombosis; plaque same as above	Thrombus mostly mural and infrequently occlusive
Fibrous cap atheroma	Well-formed necrotic core with an overlying fibrous cap	Absent
Erosion	Luminal thrombosis; plaque same as above; no communication of thrombus with necrotic core	Thrombus mostly mural and infrequently occlusive
Thin fibrous cap atheroma	A thin fibrous cap infiltrated by macrophages and lymphocytes with rare SMCs and an underlying necrotic core	Absent; may contain intraplaque hemorrhage/fibrin
Plaque rupture	Fibroatheroma with cap disruption; luminal thrombus communicates with the underlying necrotic core	Thrombus usually occlusive
Calcified nodule	Eruptive nodular calcification with underlying fibrocalcific plaque	Thrombus usually nonocclusive
Fibrocalcific plaque	Collagen-rich plaque with significant stenosis usually contains large areas of calcification with few inflammatory cells; a necrotic core may be present.	Absent

Table 2: Distribution of lesions according to age

Age range (yrs)	Non atherosclerotic intimal thickening	Non atherosclerotic xanthoma	Pathological intimal thickening	Fibrous cap atheroma	Plaque rupture	Calcified nodule	Fibrocalcific plaque	Total
31-40	0	0	0	0	0	0	2	2
41-50	0	2	2	4	0	0	10	18
51-60	0	0	0	3	0	2	22	27
61-70	2	0	0	6	0	2	16	26
71-80	0	0	0	2	0	0	8	10
81-90	0	0	0	0	2	0	0	2
Total	2	2	2	15	2	4	58	85

Table 3: Distribution of lesions according to artery involved

Lesion	Left anterior descending artery	Right coronary artery	Let circumflex artery	Total
Non atherosclerotic intimal thickening	0	2	0	2
Non atherosclerotic intimal xanthoma	2	0	0	2
Pathological intimal thickening	0	0	2	2
Fibrocalcific plaque	30	18	10	58
Fibrous cap atheroma	11	4	0	15
Plaque rupture	2	0	0	2
Calcified nodule	0	2	2	4
Total	45	26	14	85

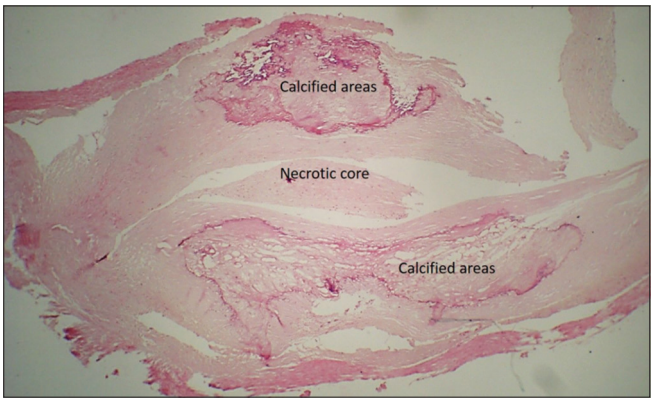

Figure 1 : Progressive atherosclerotic lesion – Fibrocalcific plaque - coronary artery displaying collagen rich plaque with necrotic core & calcified areas; H&E, 40x

DISCUSSION

Most of the atherosclerotic deaths occur in regions with high human development index.[2] Our tertiary care centre also caters to population of Punjab, which is one of better developed states of the country. The patients suffering from CAD have premature onset of modifiable risk factors like dyslipidemia, smoking, hypertension, diabetes, high waist – hip ratio, unhealthy diet, low physical activity, irregular alcohol consumption and psychological stress.[3,4] Recent trends indicate that not only has the age of onset of CVD come down, but the severity of CVD attacks and mortality associated with these events has also increased among Indians and South Asians.[3,5] Gupta et al have demonstrated that the influence of the risk factors increases exponentially with age in Indians of 30-39 years of age and beyond.[6]Moreover, some studies have shown that Indians and South Asians incur more severe and fatal attacks of CVD, resulting in greater morbidity and increased mortality.[5,7]

We found only two cases who were aged less than 40 years and they presented with fibrocalcific plaque. Porwal et al have reported atherosclerotic lesion even in a 15 years old patient. [8]Puri et al found atherosclerotic changes in all cases above 25 years of age in their autopsy study on coronary atherosclerosis. One third of their cases displaying Grade IV atherosclerotic changes were less than 40 years of age.[9] Golshahi et al reported the average age as 31.09 years in their autopsy study.[10]Bhanvadia et al have reported that 37.1% of their cases were less than 40 years old and they had predominantly pathological intimal thickening, which is a precursor of advanced atherosclerosis. Advanced atherosclerotic lesions were common in older age group in their study.[11] Virmani et al also observed that maximum cases were seen between fourth and fifth decades of life and advanced atherosclerotic lesions were predominant in this age group.[12] In our study also, advanced atherosclerotic lesions were more commonly seen in older age groups, viz fifth to seventh decades of life (Table 1).Vyas et al,Dhruva et al and Garg et alhave found progressive increase in atherosclerosis from third decade onwards while Yazdi et al,Wig et aland Singh et al have reported significant increase in number as well as severity of atherosclerosis from second decade of life onwards. [13-18] Marwah et al also found significant atherosclerosis in hearts of all cases more than 70 years of age, in their autopsy study on sudden cardiac deaths.[19]

In our study, male to female ratio was 4.3:1 with 76.5% males and 23.5% of cases being females. These findings

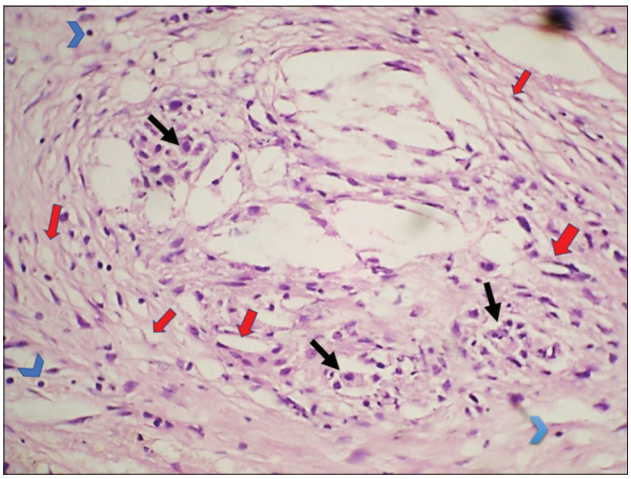

Figure 2 : Progressive atherosclerotic lesion –Fibrous cap atheroma -H&E section showing coronary artery atheromatous plaque with central lipid core and periphery containing cholesterol clefts (red arrows), foam cells (black arrows) surrounded by lymphocytes (Blue arrowheads); 400x

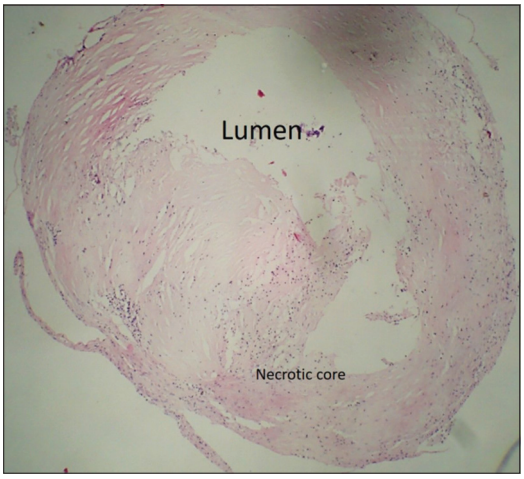

Figure 3 : Progressive atherosclerotic lesion – Plaque rupture - Coronary artery showing plaque rupture with communication between thrombus and underlying necrotic core; H&E, 40x

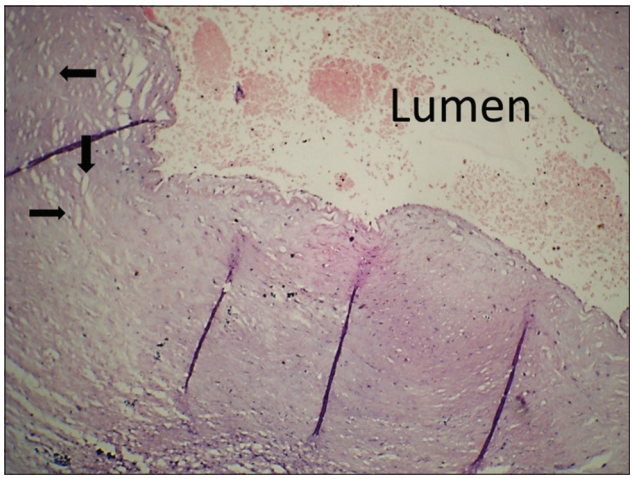

Figure 4 : Progressive atherosclerotic lesion –Pathological intimal thickening - Coronary artery displaying pathological intimal thickening with cholesterol clefts (black arrows), H&E, 40x

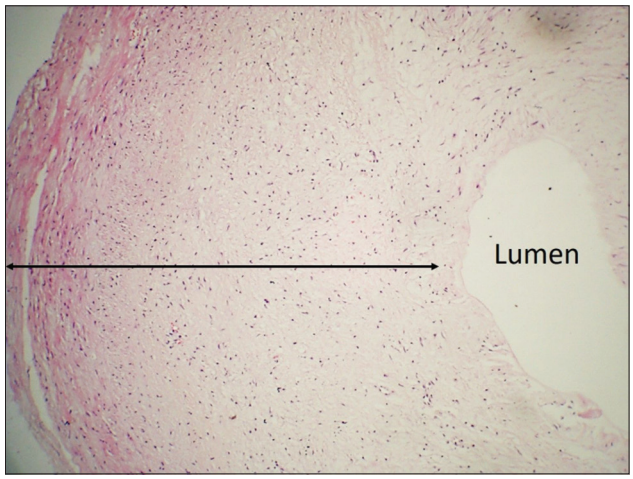

Figure 5: Photomicrograph of coronary artery showing Non atherosclerotic lesion – intimal thickening in absence of lipid or foam cells ; H&E, 100x

are concordant with the findings of other studies on atherosclerotic lesions. Garg et al and Porwal et al found coronary atherosclerotic lesions in 80.9% and 74.75% males respectively, as compared to 19.1% and 25.24% females respectively.[8,15] In study on coronary atherosclerosis by Singh et al, 85% cases were males while only 15% were females while in study by Vyas et al, 82% of the cases were males as compared to 18% females.[13,18]Even Golshahi et al found that 88.5% of their cases were males as compared to 11.5% females.[10] Male preponderance for atherosclerosis can be explained by protective effect of estrogen in females and greater incidence of smoking and alcoholism in males, which may predispose to advanced atherosclerosis.[7,11]

In our study, left anterior descending artery (LAD) was the commonest site of involvement (52.38%) as also reported by Golshahi et al (19.6%), Porwal et al (46.6%), Bhanvadia et al (42%), Vyas et al (40%), Yazdi et al (60%), Garg et al (38.1%) and Sudha et al (47%).[8,10,11,13, 15,16,20] Marwah et al also found LAD as the commonest site for atherosclerotic lesions in their autopsy study of cases having sudden cardiac death.[19] Ivanovic et al also found that two third of their studied plaques were situated in the LAD. LAD plaques were more commonly associated with high risk morphological features.[21]

We have reported findings of one vessel endarterectomy specimen which was found to be blocked by coronary plaque during coronary artery bypass grafting. Other authors have done autopsy based studies and have reported triple vessel and double vessel involvement. Porwal et al, Vyas et al,

Dhruva et al and Garg et al have reported single vessel involvement in 15%, 13%, 31% and 13.3% of their cases respectively.[8, 13-15] All these authors, including Yazdi et al, have reported triple vessel involvement to be commoner than single vessel involvement.[16] Marwah et al also observed that out of 142 cases of coronary artery atherosclerosis in their study, 52% had triple vessel disease followed by single vessel disease in 26.4% and two vessel involvement was present in 21.6%.[19] However, Puri et al and Virmani et al observed predominant single vessel involvement in their study.[9,12]

According to Modified American Heart Association classification of atherosclerosis, we had only two cases each of non - atherosclerotic intimal thickening, non - atherosclerotic intimal xanthoma and pathological intimal thickening. Most of our cases had advanced atherosclerotic lesions in the form of fibrocalcific plaques (69.05%) followed by fibrous cap atheroma (16.67%). Most of the autopsy studies have followed the morphological classification by American Heart Association for atherosclerosis. Porwal et al and Garg et al have reported maximum incidence of pre atheromas while Dhruva et al found more cases of fibroatheroma followed by preatheroma.[8,14,15]

According to Sudha M et al, cases of sudden cardiac deaths were found to have high grade coronary atherosclerotic lesions, majority comprising of vulnerable plaques which have extensive inflammation.[20] Calcification stabilizes plaques and prevents rupture.[22] Most of the disrupted plaques have necrotic lipid rich core, less smooth muscle cells and thin fibrous caps with foamy macrophages at the periphery.[23] Acute coronary syndromes without ST elevation are also associated with plaques having necrotic core which are more unstable and likely to rupture. Patients should receive aggressive lipid defence therapy to stabilise plaques and thus reduce mortality and limit morbidity due to CAD.[21]

CONCLUSION

We have hereby analysed themorphological spectrum of atherosclerotic lesions in live patients in a tertiary care institute of North western region. It is alarming to note that even patients less than 40 years old can harbour features of progressive atherosclerosis in coronary artery plaques at the time of presentation. We are actually sitting on a time bomb. To prevent morbidity and mortality due to CAD, aggressive lipid defence treatment and preventive measures in the form of awareness among the masses, policy changes, adoption of healthy lifestyle practices need to be implemented in the community at war footing.

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Author's contribution:
RKG and RT – Concept and design of the study, reviewed the literature, collected data, analysed data, prepared first draft of manuscript, performed statistical analysis, critically reviewed manuscript, manuscript editing; **VS, SK, GS and SR -** reviewed the literature, collected data, analysed data, critically reviewed manuscript; **PKS and BG -** analysed data, critically reviewed manuscript, manuscript editing.

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