

A Morphological Study of Renal Arteries in Atherosclerosis – A Human Autopsy Study

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ABSTRACT

Objective: To assess the different morphological changes in atherosclerotic lesions in renal arteries in relation to age and sex

Study design: Prospective descriptive observational study

Place and Duration of Study: Mortuary of King Edward medical University and mayo hospital, Lahore, Pakistan. Duration of study was one and a half year

Materials and Methods: A total of one hundred and thirty human autopsies were carried out during this study. Ninety were males and forty females. The age range was between 8 and 85 years. The autopsies were done left renal arteries were taken out artery for histological examination. Tissue processing was done. On the average 7-8 slides were prepared from each block by taking ribbons of tissues. The paraffin sections were stained using Haematoxylin and Eosin stain, Curtis's picro-ponceau stain, verhoeff's elastic tissue stain, von kossa's staining technique, periodic acid Schiff (PAS) reaction, Toluidine blue stain and peral's Prussian blue stain.

Results: The fibrolipid plaques were seen in 32 of the 39 cases seen on gross appearance in the right renal artery and 20 of the 24 cases seen on gross appearance in the renal artery. The complicated lesions were present in 15 cases in the right renal artery and 11 cases in the left renal artery. In the right 12 cases showed ulceration, 3 cases showed intimal vascularization and haemorrhage, whereas 2 of these cases also showed thrombus formation. In the left renal artery there were 8 cases showing ulceration, 3 cases showed intimal vascularization and haemorrhage and one of these also showed thrombus formation. The calcified lesions were seen in 9 case in the right renal artery and 7 cases in the left artery. The morphological changes in the media and elastic were in 11 cases in right renal artery and 7 cases in left renal artery.

Conclusion: Incidence of fibro-lipid plaques complicated and calcified lesion are quite high in both renal arteries. The relative high incidence of raised lesions in Right renal arteries may be due to more length, lower position and its position across the inferior vena cava.

Key Words: Morphological, atherosclerosis, renal arteries.

INTRODUCTION

Depolymerisation of acid-mucopolysaccharides involved in the plaque formation results in the loss of metachromasia of the ground substance¹. After that the visible fibers crumble and dissolve completely and it is replaced by lipid droplets and cholesterol². In ulcerated atheroma extensive foam cell are formed that are connected by fibrin-mesh³. Intimal thickening causes hypoxia of mid-zone of media. This provides the stimulus for the ingrowth of capillaries from the adventitial vessels into the thickened intima⁴. Thrombosis may occur on an ulcerating atheroma⁵. In atherosclerosis fine granules of Calcium appear in the ground substance and the necrotic tissues at the marginal layer of ulcers. The relative attenuation of the media is due to the disintegration of the elastic fiber system in the inner layer of the medial coat⁶.

MATERIALS AND METHODS

A total of one hundred and thirty human autopsies were carried out during this study. Ninety were Males and forty females. The age range was between 8 and 85 years. The autopsies were done in the Mortuary of the

King Edward Medical College, Lahore. Right and left renal arteries were taken out and opened lengthwise. One to four sections were taken from each renal artery for histological examination. Tissue processing was done. On the average 7-8 slides were prepared from each block by taking ribbons of tissues. The paraffin sections were stained using Haematoxylin and Eosin stain, Curtis's Picro-ponceau stain, Verhoeff's elastic tissue stain, von kossa's staining technique, periodic acid Schiff (PAS) reaction, Toluidine blue stain and Peral's Prussian blue stain.

RESULTS

Gross Appearances: The fatty streaks were seen in 41 of 130 cases in the right renal artery, and 41 of the 130 cases in the left renal artery. They were present along the long axis of the vessel wall. The fibrolipid plaques were seen in 39 cases in the right renal artery and 24 cases in the left renal artery. The complicated lesions were present in 8 cases in the right renal artery and 7 cases in the left renal artery. Out of these complicated cases in right renal artery the ulceration was seen in 6 cases, intimal vascularization and haemorrhage in one case and thrombus formation in one. In the left renal

artery the ulceration was present in 5 cases, intimal vascularization and haemorrhage in one case and thrombus formation in one case. The calcified lesions were seen in 9 cases in the right renal artery and 7 cases in the left renal artery. The number of the raised lesions in these cases was 2-3. The size of the largest raised lesion in the right renal artery was 3x6 mm and the left renal artery 3 x 5mm. Size of the smallest raised lesion

in both the branches was 3x3 mm. The colour of the fatty streaks was yellow, whereas that of the fibrolipid plaques was yellow to yellowish white. The complicated lesions were yellowish grey and the calcified lesions were yellowish black. All the raised lesions were seen within 0.5 cm of the ostia in these cases (Table No.1).

Table No.1: Atherosclerotic Lesions in Renal Arteries in Relation to Age and Sex (Gross Findings) (130 cases)

| Age in years | Fatty Streaks | | Fibrolipid Plaques | | Complicated Lesions | | Calcified Lesions | |
|--------------|-----------------|-----------------|--------------------|----------------|---------------------|------------|-------------------|------------|
| | R | L | R | L | R | L | R | L |
| | M:F | M:F | M:F | M:F | M:F | M:F | M:F | M:F |
| 6-15 | - | - | - | - | - | - | - | - |
| 16-25 | 5:0 | 5:0 | 1:0 | 1:0 | - | - | - | - |
| 26-35 | 14:9 | 14:9 | 8:1 | 2:0 | - | - | - | - |
| 36-45 | 8:5 | 8:5 | 6:3 | 5:1 | 1:0 | 1:0 | - | - |
| 46-55 | - | - | 6:4 | 5:3 | 2:1 | 2:0 | 2:1 | 2:0 |
| 56-65 | - | - | 8:1 | 5:0 | 2:1 | 2:0 | 4:1 | 3:0 |
| 66-75 | - | - | 0:1 | 1:1 | 0:1 | 1:1 | 0:1 | 1:1 |
| Total | 27:14 | 27:14 | 29:10 | 19:5 | 5:3 | 6:1 | 6:3 | 6:1 |
| %age | 20.76: 10.76 | 20.76: 10.76 | 22.30: 7.69 | 14.61: 3.84 | 3.84: 2.30 | 4.61: 0.77 | 4.61: 2.30 | 4.61: 0.77 |

Table No. 2: Atherosclerotic Lesions in the Renal Arteries in Relation to Age and Sex (microscopic findings) (130 Cases)

| Age in years | Fatty Streaks | | Fibrolipid Plaques | | Complicated lesions | | Calcified Lesions | |
|--------------|-----------------|-----------------|--------------------|----------------|---------------------|---------------|-------------------|---------------|
| | R | L | R | L | R | L | R | L |
| | M:F | M:F | M:F | M:F | M:F | M:F | M:F | M:F |
| 6-15 | - | - | - | - | - | - | - | - |
| 16-25 | 5:0 | 5:0 | 1:0 | 1:0 | - | - | - | - |
| 26-35 | 14:9 | 14:9 | 8:1 | 2:0 | - | - | - | - |
| 36-45 | 8:5 | 8:5 | 5:2 | 4:1 | 2:1 | 2:0 | - | - |
| 46-55 | - | - | 4:3 | 4:2 | 4:2 | 3:1 | 2:1 | 2:0 |
| 56-65 | - | - | 6:1 | 4:0 | 4:1 | 3:0 | 4:1 | 3:0 |
| 66-75 | - | - | 0:1 | 1:1 | 0:1 | 1:1 | 0:1 | 1:1 |
| Total | 27:14 | 27:14 | 24:8 | 16.4 | 10:5 | 9:2 | 6:3 | 6:1 |
| %age | 20.76: 10.76 | 20.76: 10.76 | 18.46: 6.15 | 12.30: 3.07 | 7.69: 3.84 | 6.92: 1.53 | 4.61: 2.30 | 4.61: 0.77 |

R= Right, L = Left

Microscopical changes: The fatty streaks were present in 41 cases in the right renal artery and 41 cases in the left renal artery. The fibrolipid plaques were seen in 32 of the 39 cases seen on gross appearance in the right renal artery and 20 of the 24 cases seen on gross appearance in the left renal artery. The complicated lesions were present in 15 cases in the right renal artery and 11 cases in the left renal artery. In the right renal artery 12 cases showed ulceration, 3 cases showed intimal vascularization and haemorrhage, whereas 2 of these cases also showed thrombus formation. In the left renal artery there were 8 cases showing ulceration, 3 cases showed intimal vascularization and haemorrhage and one of these also showed thrombus formation. The calcified lesions were seen in 9 cases in the right renal artery and 7 cases in left renal artery. The morphological changes in media and elastic were seen

in 11 cases in right renal artery and 7 cases in left renal artery.

On histological examination of the fatty streaks the foam cells alongwith the increase of fluid was present in the intima. Lipid was present both intracellularly and extracellularly alongwith the connective tissue changes. The fibrolipid plaques showed fibrous degeneration and regeneration with mucoid changes. There was a metachromatic change and hyalinization in the atherosclerotic lesion. Number of foam cells was prominent and the number of fibrocytes was also increase. The fat was present in the form of fatty pool and the needle-shaped cholesterol crystal clefts were also demonstrated. Variable number of foam cells was present with the necrotic areas at the base of the lesion. In ulcerated lesions the lipid contents were less in amount. Foam cells with fibrin was present abundantly.

Lymphocytic reaction with fibrin was present abundantly. In cases showing intimal vascularization and haemorrhage, there was neovascularization in the intima. In addition to that the red blood cells and haemosiderin deposits were also present at the junction of media and atherosclerotic lesions. In atherosclerotic lesions showing thrombus formation the fibrin strands were present at the periphery and in between the platelet aggregates. The calcified masses were deposited in the degenerated debris and hyalinized collagen tissue in the intima. Deposits of calcium were particularly present around the necrotic areas, lipid pool and marginal layers of the ulcers in atherosclerotic lesions. The medial coat was relatively attenuated below the sclerotic plaque and was one half or less of the thickness of the media in the adjacent part of the artery. The fibres on the inner third of media were severely degenerated. The fragmented internal elastic lamina was separated apart and was totally deficient over wide areas at the base of large plaques (Table No.2).

DISCUSSION

Gross morphology of Atherosclerotic lesions: The fatty streaks were present along the long axis of the vessel wall. The number of the raised lesions in these cases was 2-3. The size of the largest raised lesion in the right renal artery was 3x6 mm and the left renal artery 3 x 5mm. Size of the smallest raised lesion in both the branches was 3x3 mm. The colour of the fatty streaks was yellow, whereas that of the fibrolipid plaques was yellow to yellowish white. The complicated lesions were yellowish grey and the calcified lesions were yellowish black. All the raised lesions were seen within 0.5 cm of the ostia in these cases (Table No.1)

Microscopic Appearance of Atherosclerotic Lesions

On the light microscopy, the fatty streaks showed the presence of foam cells beneath the endothelial lining. There was increase of fluid in the ground substance. In addition to these changes, the connective tissue was arranged in the form of loose mesh with some fibrin deposition⁷. It seems likely that lipoproteins are transported across intact endothelial cells by micropinocytosis⁸. Lipid was present both intra-cellularly and extra-cellularly. Foam cells are smooth muscle cells containing lipids⁹. Probably local adherence of the platelets at the endothelium releases Mitogenic platelets to the endothelium releases Mitogenic Platelet factors into the arterial wall and causes some intimal smooth muscle cells proliferation¹⁰. In fibro-lipid plaques both connective tissue and lipid changes were prominent. These changes were visible as mucoid swelling due to the presence of protein molecules and acid-mucopolysaccharides. In addition there was a metachromatic change in the ground substance alongwith hyalinization. This change has previously been related to the increased amount of the ground substance². Alteration in intrinsic composition and

molecular size of proteoglycans occurs in atherosclerotic lesion¹¹. The increase in the number of foam cells in fibrolipid plaques was probably due to increase in the smooth muscle cell proliferation and vacuolated forms¹²⁻¹³. In such vacuolated cells the lipid containing inclusions have been associated with the structural elements of smooth muscle cells¹⁴. Foam cells accumulation have been demonstrated in experimentally induced atherosclerosis¹⁵. The number of fibrocytes is increased during plaque formation. It is associated with increased formation of collagen and elastic fibres. These connective tissue components are probably derived from the proliferating smooth muscle cells in the intima. There was high concentration of fibrin in developing atherosclerotic lesion¹¹. It was established that there is an association between accumulation of fibrin and binding of low density lipoproteins (LDL)¹⁶. On the other hand it was proposed that the process of smooth muscle cell proliferation is related to the tumour formation initiated by mutation¹⁷. The lipids were seen in the form of fatty pool and needle-shaped cholesterol Crystal clefts^{18,19}. LDL is important to the initiation and probably the progression of atherosclerotic lesions^{20,21}. In the ulcerated lesions the lipid contents were markedly less in amount. On the other hand foam cells were extensively present at the base and fibrin was seen intervening these cells³. The blood vessels were found in the intima. RBCs and haemosiderin deposits were present at the junction of media and atherosclerotic lesion²². It was also explained that neo-vascularization in the intima may lead to haemorrhage because they run the tissue that does not support them adequately⁶. In thrombus formation Platelet aggregation at the exposed sub endothelial tissue was seen. The fibrin strands were present at the periphery and in between the platelet aggregates. The collagen rich atherosclerotic lesion initiates thrombosis, because it exposes the blood to powerful platelet aggregating (collagen), and coagulation activating (traumatic surface and lipids) factors that are not found in normal vessel wall²³. Fibrinogen leads to the Platelet aggregation associated with release of vasoconstrictor, thromboxane A₂. This hypercoagulability of platelets again is associated with hyperfibrinogenaemia and thrombosis²⁴. Lack of PG12 due to endothelial injury may lead to thrombus formation²³, because PG12 is powerful anti-aggregating vasodilator²². Contrary to above mentioned observations it was described that Fibrous plaque is fibrinoid or organized thrombus^(6,25) This study was supported by the observations that calcified granules were presented around the degenerated debris and hyalinized collagen tissue in the intima^{9,26}. They also observed that deposits of calcium were particularly present at the periphery of necrotic areas, lipid pool and marginal layer of ulcers in atherosclerosis. The fibres on the inner third of media were severely degenerated. Internal elastic lamina was fragmented and was totally deficient over wide areas at the base of large plaques due to rigid pressure^{2,9}.

CONCLUSION

Incidence of fibro-lipid plaques complicated and calcified lesion are quite high in both renal arteries. The relative high incidence of raised lesions in Right renal arteries may be due to more length, lower position and its position across the inferior vena cava.

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