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Morphometry of Intrarenal Arteries in Progressive Sclerosis

K.J. Henrichs and C.L. Berry

Department of Morbid Anatomy, Institute of Pathology, The London Hospital (Director: Prof. C.L. Berry), London, England and Pathologisches Institut der Universität Heidelberg (Director: Prof. Dr. Dr. h.c. mult. W. Doerr), Heidelberg, Federal Republic of Germany

Summary. Vessels of known position in the vascular tree of the kidneys of two cases with a long history of progressive systemic sclerosis – one normotensive, one hypertensive – were examined morphometrically.

Medial thickness, intimal thickness and the relative content of collagen and elastin in the vascular media were measured. Smooth muscle nuclei were counted in the arterial cross section.

These morphometric data were compared with those obtained from two autopsy cases – one with a history of essential hypertension, one without any hypertensive history. The findings suggest that progressive sclerosis induces intimal thickening in all branches of the renal artery down to a distented diameter of 200 μm.

In the case where progressive sclerosis was complicated by arterial hypertension increased medial thicknesses were found, similar to the findings in the case with a history of essential hypertension.

Key words: Progressive sclerosis – Morphometric investigation of intrarenal arteries – Intimal thickening.

Introduction

It is now well recognised that progressive systemic sclerosis is a multisystem disease. Clinical and morphological observations provide a consistent body of evidence indicating widespread vascular injury during the course of the disease (Sackner, 1966; Treacy, 1963; Norton and Nardo, 1970) in which progressive renal failure may develop at any time – with or without hypertension – and result in death from ureamia.

A primarily vascular lesion may be responsible for the renal deterioration. Histologically the kidney lesion has been described as mucoid swelling of the

Send offprint requests to: Dr. K.J. Henrichs, Pathologisches Institut der Universität, Im Neuenheimer Feld 220/221, D-6900 Heidelberg, Federal Republic of Germany

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intima of intralobular renal arteries (Moore and Sheehan, 1952) fibrinoid necrosis of arterioles and glomerular capillary loops (Kass et al., 1966) with cortical infarcts (Campbell and Le Roy, 1975). Fischer (1963) characterised the changes in progressive sclerosis as initimal thickening of the interlobular arteries together with histological findings of malignant nephrosclerosis (Fahr, 1919). Fennell et al. (1967) have emphasized the morphological similarity between progressive sclerosis and malignant hypertension.

In this paper we present morphometric data on major renal arteries of two autopsy cases with a long history of progressive systemic – one hypertensive and one normotensive. We compare these data with those obtained from an autopsy case with a history of essential hypertension and those obtained from an autopsy case without any hypertensive history.

Material and Methods

The isolated right kidney from each case was inflated with a warm bariumsulphate-gelatine mixture for 2 h via a cannula situated in the renal artery. The average perfusion pressure which was continuously monitored was 150 mm Hg. After cooling radiography was performed and the tissue was fixed in neutral buffered formalin at 4° C. After identification of the arteries by their number of division and grouping them according to their site (interlobar a., arcuate a., interlobular a.) on the radiographs blocks were taken in which arteries were cut at a right angle. In the arteries the internal elastic lamina was perfectly stretched.

If arterial constriction in longitudinal direction is neglected the surface area of the media and the intima in arterial cross sections represents a constant quantity independently of varying degrees of arterial constriction. Sections were stained with haematoxylin, van Gieson's and Miller's stains.

Using a Quantimet 720® (Imanco Cambridge Instruments) the histologic specimens were traced on a screen for morphometry. The line of the internal elastic lamina (I.E.L.) was drawn by a light pen and measured (circumference of IEL). Then the cross sectional areas of the media and intima were separately detected. Using these data the radii of three idealised circles were calculated according to the equations shown in Fig. 1. The average thicknesses of the media and the intima were calculated. Van Gieson's red staining areas and Miller's black staining areas of the media were measured and are subsequently referred as collagen – and elastin – content of the media. Medial smooth muscle nuclei were counted.

Case Histories

Case 1. A 61 year old lady had been suffering from progressive sclerosis which originally presented with Raynaud's disease for approximately 22 years.

In 1968 cervico-thoracic symathectomy was performed for continuing Raynaud's disease which persisted as Raynaud's phenomenon each winter until her death. Soreness, pain and infections of her fingertips occurred repeatedly. Breathlessness developed gradually, swallowing became difficult and dyspnoea at rest was found by 1975. At this time there was impairment of renal function and proteinuria. Severe hypertension developed which was difficult to treat. In 1978 congestive heart failure followed an anteroseptal myocardial infarction. While still in hospital she suddenly collapsed and died. Blood pressure on admission was 205/115 mm Hg although this subsequently settled to 170/110.

Case 2. A 64 year old lady had suffered from progressive systemic sclerosis diagnosed on clinical grounds for at least the last five years of her life. In 1975 fibrosing alveolitis of the lung was evident and was treated with cortico-steroids. The patient experienced progressive dyspnoea and

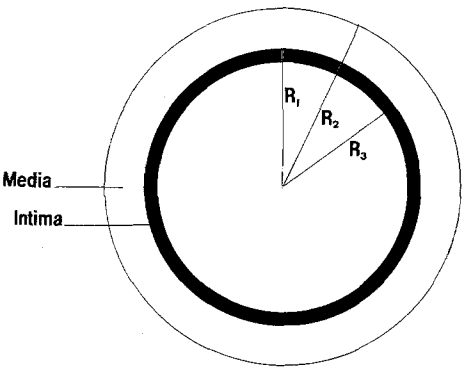

Fig. 1. Principles of the morphometric method. Schematic representation of an arterial cross section. L length of internal elastic lamina (IEL), A_M surface area of media, A_I surface area of intima, $R_2 - R_1$ thickness of media, $R_1 - R_3$ thickness of intima

gastrointestinal symptoms with occasional episodes of dysphagia. She was admitted to hospital with peripheral oedema where she died of congestive heart failure in 1978. There was no evidence of hypertension at any stage of her illness. At autopsy severe fibrosing alveolitis was found.

Case 3. A 59 year old lady was admitted to hospital with intracerebral haemorrhage and died shortly after admission. There was a long history of essential hypertension with blood pressure records at 200/110 mm Hg.

Case 4. A 55 year old lady was admitted to hospital because of neurologic symptoms and died two weeks after admission and was found at autopsy to have a cerebral tumor. There was no history of hypertension. The blood pressures taken at hospital were 120/70 mm Hg.

Results

In both cases of progressive sclerosis severe changes of the renal morphology were found.

Localized thickening of the glomerular capillary walls-often referred as "wire loops" – was seen. Some glomeruli contained fibrin in their lumina, others were necrotic (Fig. 2).

Table 1. Mean number of medial smooth muscle cells

	Progr. Scler. BP normal	Progr. Scler. BP raised	Ess. Hyp.	Normt. control
Interlobar	570	634	696	651
Arcuate	248	308	285	272
Interlobular	78	84	112	79

All smooth muscle cell nuclei or parts of them which could be detected in the arterial cross section were counted.
There is no significant difference in number of smooth muscle cells between the four cases.

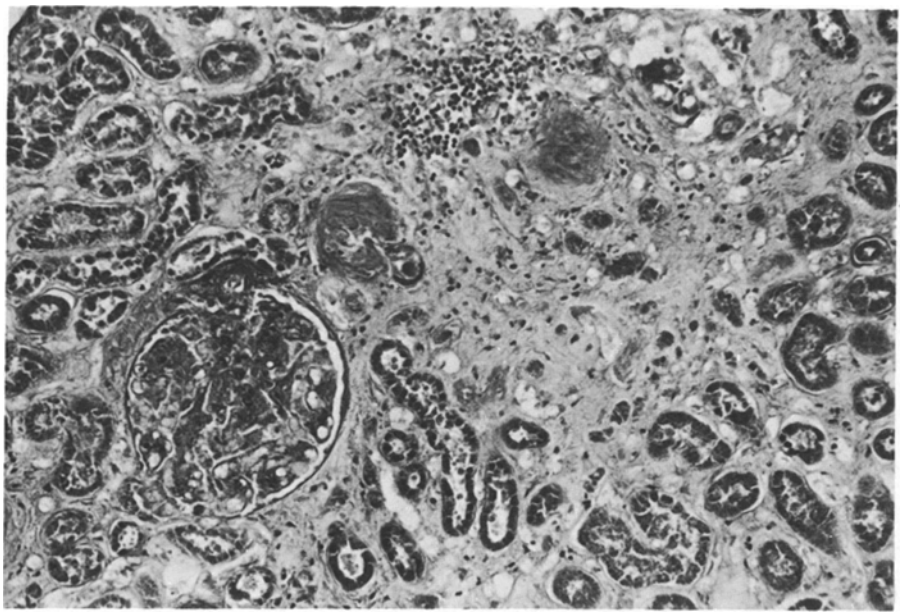

Fig. 2. Thickening of the glomerular capillary wall, sever interstitial fibrosis of the kidney, Case 1. Renal section, H. & E., 1:160

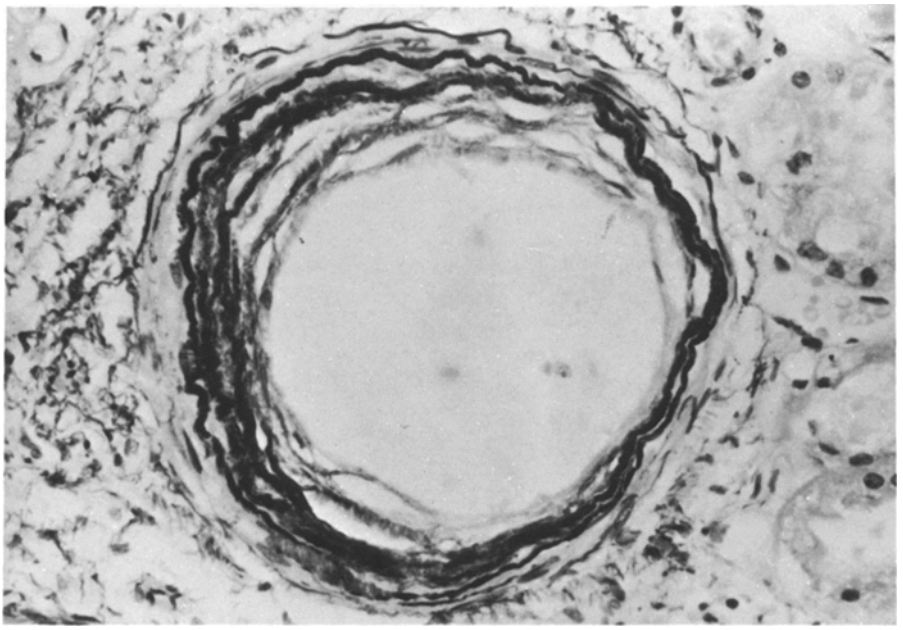

Fig. 3. Typical onion skin appearance of the intima in progressive sclerosis, note the thin media. Case 2, interlobular artery. Renal section, Miller's stains, 1:160

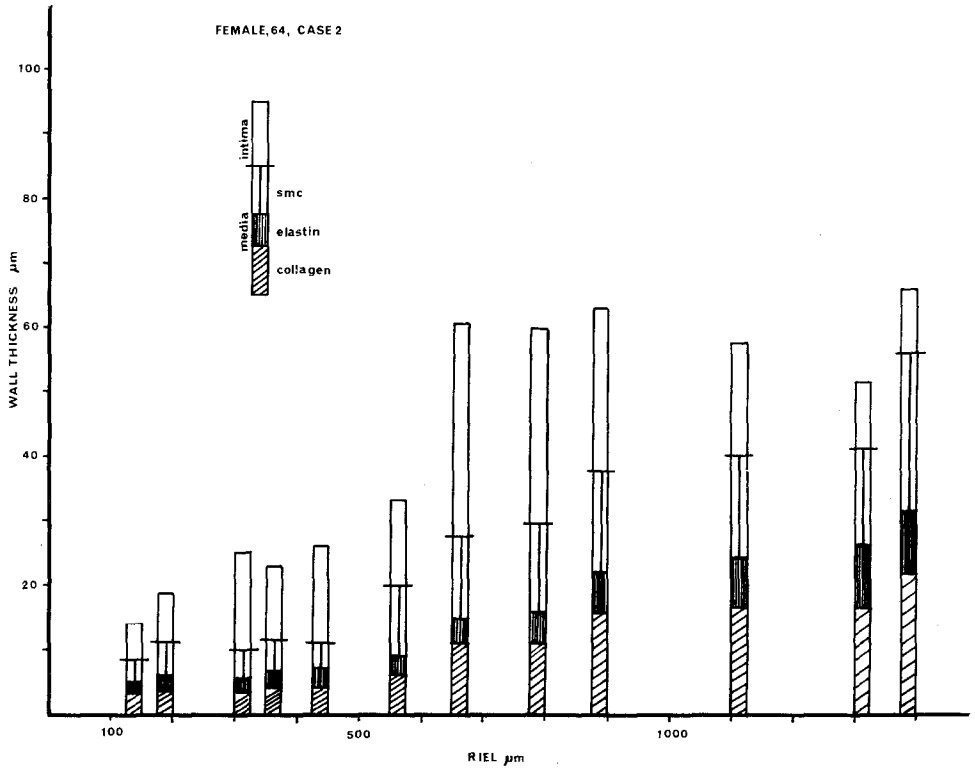

Fig. 4. Morphometric results of intrarenal arteries. Normotensive progressive sclerosis. Each column represents the morphometric results of one artery. The height of the column displays the average thickness of the arterial wall in a cross section, thickness of media and thickness of intima are shown. The relative content of elastin and collagen in the media (surface area in the histologic section) and the surface area of medial smooth muscle cells in arterial cross sections are shown in the medial portion of the column. The arteries with a distended radius of internal elastic lamina (RIEL) up to 400 µm are interlobular arteries, between 400 µm and 900 µm arcuate arteries and between 1,100 µm and 1,400 µm interlobar arteries. Intimal thickening in all intrarenal arteries, greatest thicknesses of the intima were found in the arcuate arteries. Thinning of the media in the interlobular arteries, lower medial content of collagen in comparison with the results in Case 4

The tubules often showed atrophy. In the case with renal failure and the history of malignant hypertension severe interstitial fibrosis was found.

Distinct changes of the renal arterial tree, too, were found in both cases of progressive sclerosis. All groups of arteries examined showed a moderate or severe luminal narrowing, due to intimal thickening. In the hypertensive case obliteration of the afferent arterioles was a common finding, this did not occur in the normotensive progressive sclerosis case. Typical light microscopic findings (onion-skinning, mucinous and fibrous intimal thickening) were found in all intrarenal arteries in both cases (Fig. 3). Morphometry revealed intimal thickening throughout the arterial tree of the kidney in both cases of progressive sclerosis. In the normotensive progressive sclerosis case greatest intimal thicknesses were found in the arcuate arteries (Fig. 4). Intimal thickening

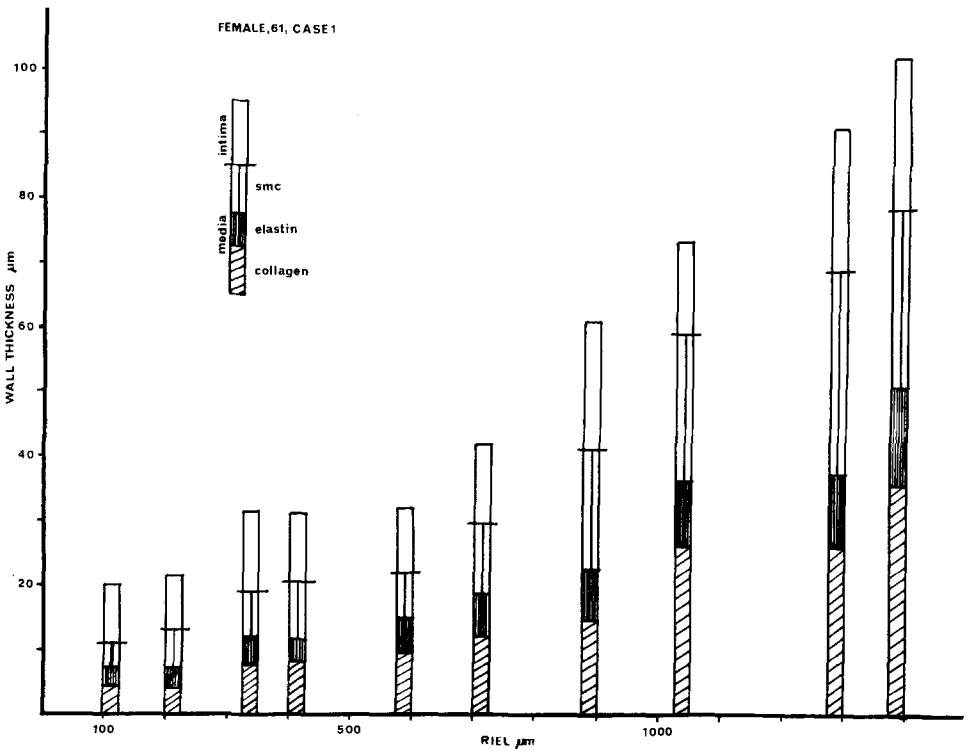

Fig. 5. Morphometric results of intrarenal arteries, hypertensive progressive sclerosis. Compare caption to Fig. 4. Arteries with a RIEL up to 500 µm are interlobular arteries, between 580 µm and 1,050 µm arcuate arteries and between 1,200 µm and 1,500 µm interlobar arteries. Intimal thickening in all intrarenal arteries, increased medial thicknesses in comparison with Case 2

in progressive sclerosis was found to be more pronounced than in essential hypertension.

Thicknesses of the media in the normotensive progressive sclerosis case were not very different to those found in the normotensive control case (Fig. 7); but in the interlobular arteries the media was found to be thinner. In the case where progressive sclerosis was complicated by arterial hypertension all intrarenal arteries showed greater medial thicknesses in comparison with the normotensive progressive sclerosis case (Fig. 5).

Medial thickening was similar to that found in the case suffering from essential hypertension (Fig. 6). Thickening of the media due to hypertension was found in all intrarenal arteries, it was greatest in the interlobular arteries.

Thickening of the media was found to be due to an increased content of collagen and to a greater mass of smooth muscle cells. In the normotensive progressive sclerosis case the number of smooth muscle cells was decreased when compared with the normotensive control case. In the hypertensive cases the numbers of smooth muscle cells were found to be not changed significantly. This indicates that in arterial hypertension hypertrophy of vascular smooth muscle cells occurs.

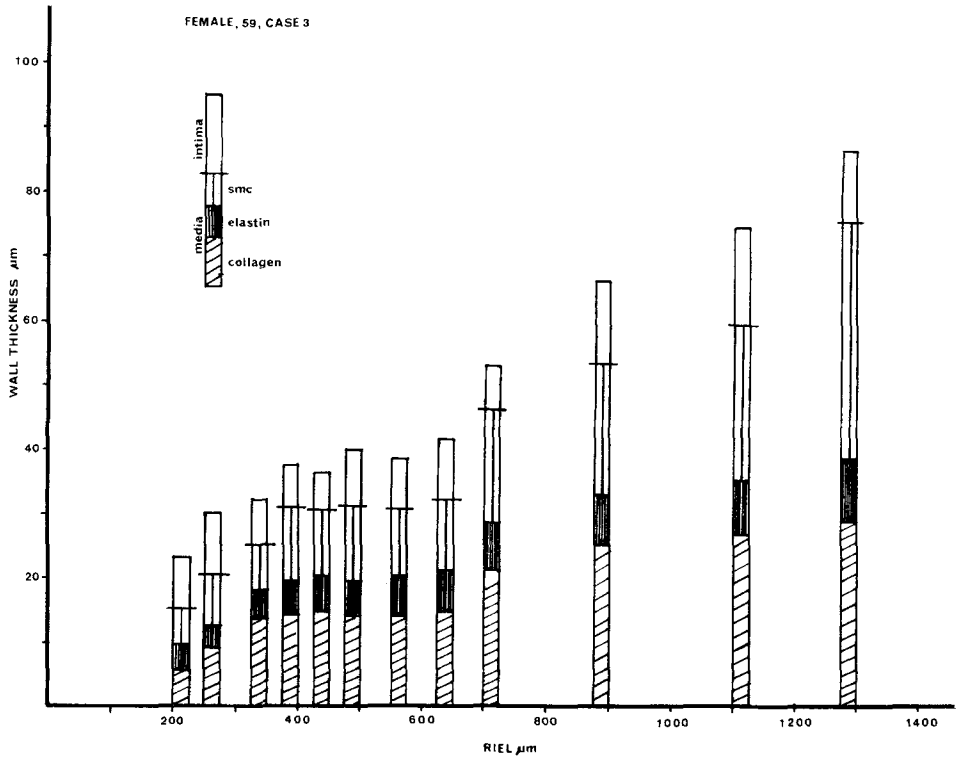

Fig. 6. Morphometric results of intrarenal arteries, essential hypertension. Compare caption to Fig. 4. Arteries with a RIEL up to 500 µm are interlobular arteries, between 550 µm and 900 µm arcuate arteries and between 1,100 µm and 1,400 µm interlobar arteries. Increased medial thickness in all intrarenal arteries in essential hypertension

Discussion

The characteristic vascular lesions of systemic sclerosis have been observed in the interlobular arteries and afferent arterioles (D'Angelo et al., 1969; Cannon et al., 1974; Vidt et al., 1977): mocoid intimal proliferation with a concentric hyperplasia of intimal cells embedded in mucoid ground substance leading to narrowing or obliteration of the vascular lumen.

The ground substance has staining characteristics of glycoprotein and mucopolysaccharide (Fischer and Rodnan, 1958). It has been stated that the vascular changes cannot be distinguished from those observed in malignant nephrosclerosis (Fahr, 1919; Ehrenfeld, 1977; Fischer and Rodnan, 1958). Our data show that the mucoid intimal thickening is not only in the interlobular arteries but also in the arcuate and interlobar arteries in both hypertensive and normotensive progressive sclerosis cases. This is consistent with data obtained by Cannon et al. (1974). The finding of cortical infarction is probably the result of arterial luminal obstruction following intimal thickening. Fibrinoid necroses were not found in the relatively large arteries, but there was a typical fibrous cuff around these vessels.

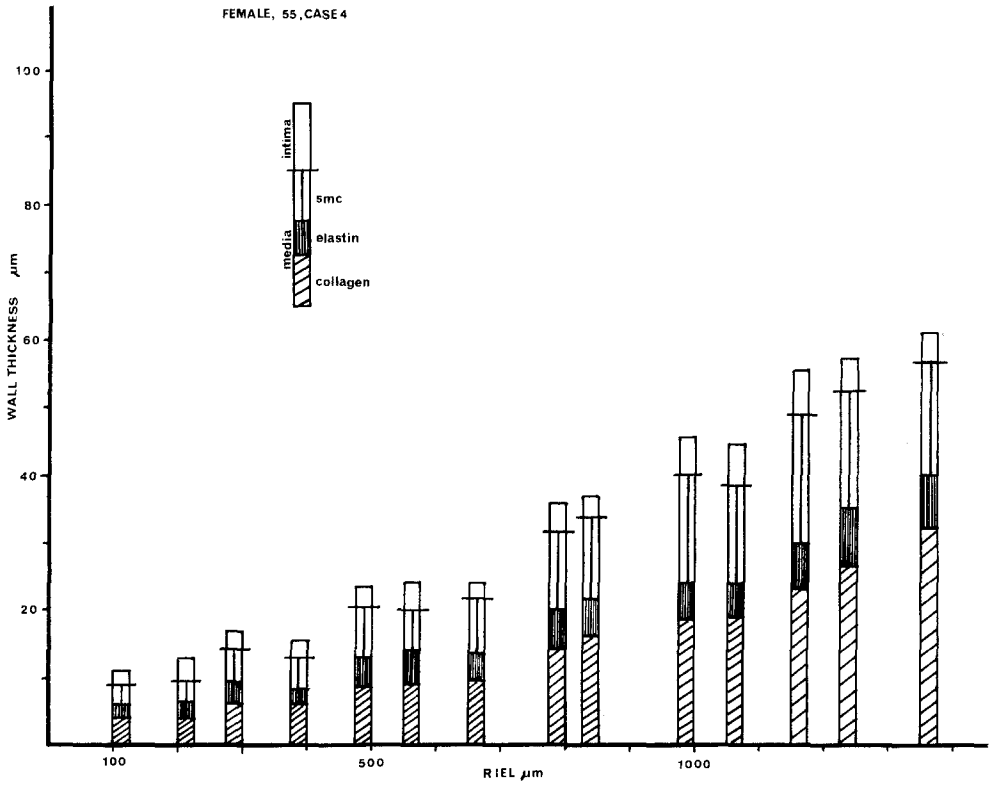

Fig. 7. Morphometric results of intrarenal arteries, normotensive control case. Compare caption to Fig. 4. Arteries with a RIEL up to 400 µm are interlobular arteries, between 400 µm and 900 µm arcuate arteries and between 900 µm and 1,400 µm interlobar arteries. Note the regular increase of wall thickness with increase of RIEL

In normotensive progressive sclerosis the media of the interlobular arteries was found to be thinner than in the hypertensive case, but in this patient the renal arterial media was not as thick as that from the case with essential hypertension.

Thinning of the media in the course of progressive sclerosis was also found by Campbell and Le Roy (1975).

We have shown that long-term hypertension induces medial hypertrophy in the renal arteries with resultant luminal narrowing (Henrichs and Berry, 1979). The luminal narrowing in progressive sclerosis is due to intimal thickening. Although these mechanisms differ the pathophysiological result of both is a lower renocortical blood flow.

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