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Arteries and veins formed within renal vessels: a previously neglected observation

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Summary. An abnormality of blood vessels was noted in a biopsy of a renal transplant. This took the form of apparent development of a new artery inside and concentric with the old, with elastic laminae and a muscular media, separated from the old internal elastic lamina by poorly cellular tissue. In a systematic study of material from another 119 renal transplants, 13 nephrectomy specimens for chronic pyelonephritis and hydronephrosis, 28 renal biopsies showing interstitial nephritis, and 18 renal biopsies showing small vessel vasculopathy of accelerated hypertensive type, similar arterial changes were seen in another 10 renal transplants that showed chronic vascular rejection, 1 case of chronic interstitial nephritis, and 3 cases of vasculopathy, 2 with accelerated hypertension and 1 with systemic sclerosis. One renal transplant also showed apparent development of new muscular veins inside old veins. Immunohistological study for smooth muscle actin confirmed that the apparently new arterial and venous structures contained smooth muscle cells. The arterial abnormality may be called arterialisation of intrarenal arteries. This change appears to be not rare, is distinctive, and has scarcely been previously recognised or reported as a response of intrarenal blood vessels to damage.

Key words: Kidney – Blood vessels – Arterialisation

Introduction

Blood vessels in the kidney have a variety of reactions to disease. During study of a biopsy of a renal transplant, we noted a vascular abnormality that was not mentioned in standard texts. This took the form of apparent development of an arterial media inside the old artery and concentric with it.

In order to study this further, we examined consecutive series of material from renal transplants and of material from three groups of non-transplant renal conditions. One group had acute arterial changes, one had chronic arterial changes, and one, a group with interstitial nephritis, was selected because it would include a range of acute and chronic stages of a disorder that was not primarily vascular (Colvin and Fang 1989). We also used immunohistology to investigate the abnormality.

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Materials and methods

Percutaneous needle biopsies of kidney were fixed in formol saline, embedded in paraffin wax, and serially sectioned to give about six sections on each of ten numbered slides. Two slides towards the ends of the series were stained with haematoxylin and eosin (H&E), two adjacent slides were stained with periodic acid-methenamine silver (PA-silver), and other slides were stained as appropriate, for instance with Miller's elastic stain – haematoxylin – van Gieson (EHVG). Nephrectomy specimens were fixed and embedded in the same way and sections were stained with H&E, EHVG and other stains as appropriate.

The abnormality to be described in the Results was first noted in a routine biopsy of a renal transplant. Consecutive samples of renal transplants taken over a period of 18 months were then reviewed retrospectively. These samples comprised 157 needle biopsies and 27 transplant nephrectomy specimens, from 119 kidneys. Three groups of non-transplant renal material were also reviewed: 13 nephrectomy specimens for chronic pyelonephritis and hydronephrosis, 28 needle biopsies showing interstitial nephritis, and 18 needle biopsies showing the small vessel vasculopathy seen in accelerated hypertension, systemic sclerosis and the haemolytic-uraemic syndrome, with fibrinoid necrosis of arterioles and intimal mucoid thickening in small arteries (Churg et al. 1987a). Clinical notes were reviewed on those patients whose histological material contained the abnormality. Renal vessels are named using recommended nomenclature (Kriz and Bankir 1988).

Several biopsies and nephrectomy specimens were stained by an immunohistological method. Further sections were cut and dewaxed. Endogenous peroxidase was blocked with 0.3% hydrogen peroxide in methanol for 10 min. After washing, sections were covered with mouse monoclonal anti-smooth muscle actin (BioGenex, Upton-upon-Severn, UK), at 1:800, incubated at room temperature for 1 h, washed, covered with biotinylated anti-mouse immunoglobulin for 45 min, washed, and covered with peroxidase conjugated streptavidin for 45 min. Both the anti-mouse immunoglobu-

lin and the streptavidin were in a StrAviGen Super Sensitive kit (BioGenex). After washing, peroxidase activity was revealed with 0.05% diaminobenzidine with 0.03% hydrogen peroxide. Sections were counterstained with Mayer's haemalum and mounted in Piccolyte.

Results

The abnormality has a distinctive appearance which once seen is easily recognised again. Inside the original internal elastic lamina of an artery is a band of loose, poorly cellular tissue, and inside that is a concentric cellular band that resembles the media of a muscular artery (Fig. 1). Delicate rings of elastic tissue are seen, sometimes forming a new internal elastic lamina (Fig. 2). Arcuate and cortical radial (interlobular) arteries are mostly affected. On immunohistology, the original arterial media and the new structure stain for smooth muscle actin (Fig. 3). This change is called apparent arterialisation in the Results.

Renal transplants

The arterial change was seen in material from 11 renal transplants out of 120, including the 1 in which the lesion was first noted. The change was in 6 transplant nephrectomy specimens and 6 biopsies from 5 transplants (Figs. 1, 2).

All 11 transplants had evidence of chronic ischaemic damage with global sclerosis of a variable proportion of glomeruli, tubular atrophy and interstitial fibrosis. Not all arteries showed apparent arterialisation, and some had roughly concentric intimal thickening by loose fibrous or fibrocellular tissue sometimes apparently in waves of different ages, without the differentiation of innermost layers to resemble an artery (Fig. 4). In 1 case an artery had muscular tissue throughout the thickened intima. Six grafts were studied by immunohistology for smooth muscle actin. All had reactivity for actin in the apparently arterialised arteries (Fig. 3). One transplant, in place for 7 years, also had apparent reformation of muscular veins within interlobar and arcuate veins (Fig. 5). On immunohistology there was reactivity for actin in these apparently reformed veins. Generally, veins in renal transplants had much less intimal thickening than arteries, although a few had loose intimal fibrosis, some of which could be a result of organisation of thrombus (Fig. 6).

The grafts with apparent arterialisation had been transplanted between 2 months and 7 years, median 4 years. All clinically had chronic failure of renal function and the graft sampled at 2 months had failed to function after an episode of acute vascular rejection 10 days after transplantation. All patients had received cyclosporin A and at least one other immunosuppressant drug. Nine of the 11 patients also received anti-hypertensive drugs.

Chronic pyelonephritis and hydronephrosis

No example of apparent arterialisation was seen in the 13 nephrectomy specimens. All showed severe intimal thickening of arteries by roughly concentric fibroelastic tissue (Fig. 7).

Interstitial nephritis

The 28 renal biopsies showed a range of changes from acute eosinophilic interstitial nephritis to chronic interstitial nephritis with late damage to the kidney. Apparent arterialisation was seen in a cortical radial (interlobular) artery in one case, a biopsy from a man of 30 years with chronic active hepatitis, renal impairment for at least 5 years before the biopsy, and histological features of chronic interstitial nephritis. He had never been hypertensive and had not received immunosuppressant drugs before the biopsy.

Small vessel vasculopathy

Of the 18 renal biopsies showing small vessel vasculopathy, 10 were from patients with accelerated hypertension, 6 with systemic sclerosis, and 2 with haemolytic-uraemic syndrome. Apparent arterialisation was seen in 3 biopsies, 2 with accelerated hypertension and 1 with systemic sclerosis (Fig. 8). This was only evident in cortical radial (interlobular) arteries since there were no larger vessels in the biopsies. The 3 patients were biopsied between 6 days and 1 month after clinical presentation.

Discussion

The change we describe in arteries is a genuine and intimate part of the arterial structure and is not to be confused with the artefact in which an artery appears pushed inside another (Wallington 1979). The change we describe is distinctive and appears to be the development of a new artery with elastic laminae and muscular media inside the old artery. This change could be described as arterialisation of intrarenal arteries. In one case there was also the appearance of reformed muscular veins inside the old veins. The new vessels inside the old do not appear to be the result of recanalisation of thromboses. These new vessels are large and concentric, unlike the small, eccentric, and often multiple vessels usually seen following thrombosis (Duguid 1946; Dible 1958). Also, no thrombus was seen in affected vessels in our series.

The arterial change was found in chronic vascular rejection, acute small vessel vasculopathy and chronic interstitial nephritis. Standard accounts of chronic vascular rejection describe intimal thickening of arteries by proliferation of smooth muscle cells and formation of collagen in a mucopolysaccharide matrix, sometimes with foam cells (Porter 1983; Churg et al. 1987b; Croker

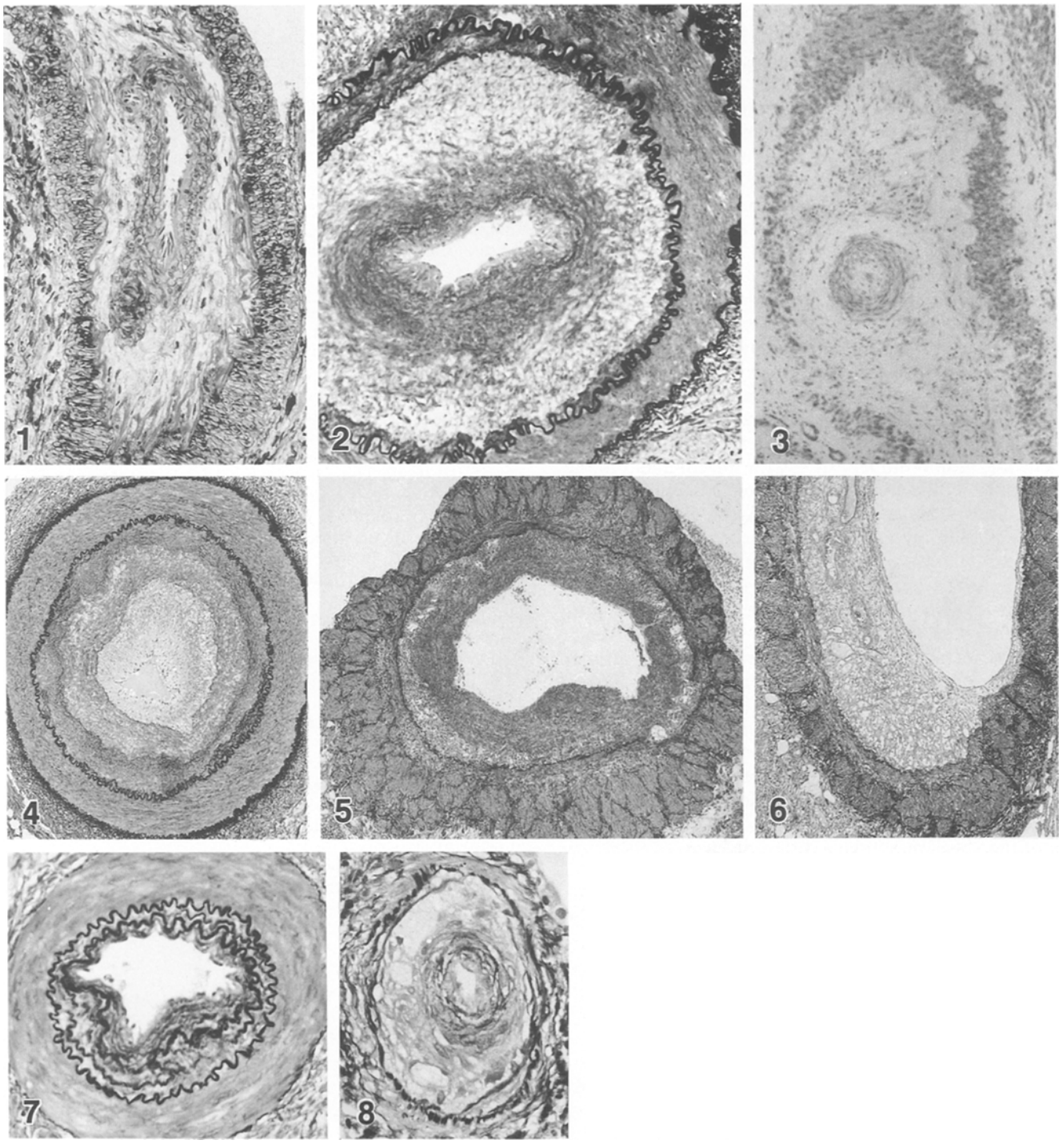

Fig. 1. Arcuate artery in a biopsy of a renal transplant, taken 1 year after transplantation. The innermost part of the thickened arterial intima appears differentiated into a structure resembling a small artery. PA-silver, ×150

Fig. 2. Arcuate artery in a nephrectomy specimen of a renal transplant, taken 5 years after transplantation. Within the apparent arterial structure in the thickened intima are delicate elastic fibres, forming a new internal elastic lamina. EHVG, ×75

Fig. 3. Arcuate artery in a nephrectomy specimen of a renal transplant, taken 3 years after transplantation. Smooth muscle actin is detected in the original media and in the central circular structure that resembles a new arterial media. Immunoperoxidase stain for smooth muscle actin, ×75

Fig. 4. Interlobar artery in a nephrectomy specimen of a renal transplant, taken 7 years after transplantation. There appear to be three rings or waves of intimal thickening by loose fibrous tissue containing a little elastin, without the formation of an artery as seen in Figs. 1 and 2. EHVG, ×30

Fig. 5. Interlobar vein in the same nephrectomy specimen as in Fig. 4. The innermost part of the thickened venous intima appears differentiated into a structure resembling a vein. EHVG, ×30

Fig. 6. Interlobar vein in a nephrectomy specimen of a renal transplant, taken 14 years after transplantation. There is eccentric intimal thickening by loose fibrous tissue containing small blood vessels, without formation of a new venous structure. EHVG, ×30

Fig. 7. Arcuate artery in a nephrectomy specimen showing hydronephrosis and a staghorn calculus. There is roughly concentric intimal thickening by well-developed rings of elastic tissue. EHVG, ×150

Fig. 8. Cortical radial (interlobular) artery in a renal biopsy of a case of accelerated hypertension. The innermost intima appears differentiated into a small artery. PA-silver, ×300

and Salomon 1989). Venous changes in chronic vascular rejection are rarely mentioned but can be found, and we found one example of venous changes analogous to arterialisation. The changes in acute small vessel vasculopathy of accelerated hypertension, systemic sclerosis and haemolytic-uraemic syndrome are described as mucinous thickening of the intima of cortical radial (interlobular) arteries with cellular proliferation, giving a concentric, onion skin appearance (Churg et al. 1987a; Goldblatt et al. 1989).

We are aware of two previous illustrations of the change we report, although these are without detailed descriptions. Zollinger (1966) does not mention it in the text but indicates in Fig. 398 a newly formed media in an artery in chronic pyelonephritis. Meadows (1978) again does not mention the change in the text but in Fig. 12. 28 illustrates an arcuate artery in a nephrectomy for chronic glomerulonephritis, with the comment in the legend that 'in this arcuate artery there is a condensation of the intimal tissue giving rise to the appearance of a "vessel within a vessel"'.

The explanation of arterialisation of intrarenal arteries can only be speculative. One possibility is that it represents a response of a blood vessel to sudden narrowing followed by a steady phase in which the vessel adjusts to its new conditions. Slow, insidious intimal thickening of vessels as seen in the multilayered fibroelastic thickening of benign nephrosclerosis (Fig. 7; Heptinstall 1983; Churg et al. 1987c; Goldblatt et al. 1989) or in the more usual changes of chronic vascular rejection (Figs. 4, 6; Porter 1983; Churg et al. 1987b; Croker and Salomon 1989) may not be accompanied by the same acute stresses in the vascular wall and the adaptation of the vessel may take a different form.

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