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ORIGINAL ARTICLE

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Asymmetrical atrophy of the renal medulla: a previously unreported abnormality

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Abstract Investigation of the smaller of a pair of unequal kidneys showed a band of atrophy in the inner medulla, sparing the papillary tip, which was viable and contained collecting ducts. The kidney had extensive cortical atrophy with glomerulocystic disease and multiple tiny renal cell neoplasms. These changes were considered secondary to the medullary lesion. Study of 85 other kidneys taken at autopsy and surgery showed 8 other cases with similar band-like atrophy in the medulla to various degrees. All 9 cases had severe vascular disease. This asymmetrical or band-like atrophy of the renal medulla seemed to be fairly common but previously unreported, could be differentiated from renal papillary necrosis, and was most likely due to an episode of severe ischaemia, possibly in kidneys with pre-existing vascular narrowing.

Key words Renal medulla · Atrophy
Renal vascular disease · Glomerulocystic disease

Introduction

When we examined the smaller of a pair of unequal kidneys taken at autopsy, we discovered an abnormality not previously reported. The main feature was a band of atrophy in the middle part of the medulla, with relative sparing of the tip of the papilla. We then looked at a series of kidneys taken at surgery and autopsy to see if the lesion could be found in other cases.

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Materials and methods

Sections 5 μm thick of formalin-fixed, paraffin-embedded material were stained by haematoxylin and eosin. Some sections were also stained by Weigert's elastic-haematoxylin-van Gieson, and others were stained by an immunoperoxidase method. For this, dewaxed sections were covered with hydrogen peroxide in methanol to block endogenous peroxidase. After a wash, sections were covered with either sheep antiserum to Tamm-Horsfall protein (The Binding Site, Birmingham, UK) at a dilution of 1:600, or mouse monoclonal antibody C3D-1 to antigen CD15 (Dako, High Wycombe, UK) at 1:10, or mouse monoclonal antibody QBend 10 to antigen CD34 (Oxoid, Basingstoke, UK) at 1:25, or rabbit antiserum to von Willebrand factor (Dako) at 1:200. Tamm-Horsfall protein is a marker of thick limbs of the loop of Henle and of casts [5]. CD15 is found in thin limbs of the loop of Henle [6]. CD34 and von Willebrand factor are markers of endothelial cells [10, 11]. The streptavidin-biotin-peroxidase system (Dako) was used to detect sites of antibody binding, with hydrogen peroxide-diaminobenzidine as substrate. Controls were normal human kidney sections stained in the same way.

The initial case and the features of the lesion are described in Results. To investigate the prevalence of the lesion, consecutive series of three types of kidney were examined: (1) shrunken kidneys taken at autopsy between 1985 and 1993 (n=45); (2) kidneys removed surgically between 1982 and 1993, excluding those removed for renal neoplasms, hydronephrosis and reflux nephropathy (n=28); and (3) renal transplants removed surgically in 1992 and 1993 and shown to have chronic vascular rejection (n=12).

Results

Initial case

A man 61-years-old was shown at autopsy to have died of a myocardial infarct. He had had six cerebral infarcts over the previous 20 years and was on treatment for hypertension. There was severe atherosclerosis. The right kidney was large, 185 g, and finely scarred, but showed only mild subcapsular chronic ischaemic damage on microscopy. The left kidney was small, 50 g, contained many small cysts, and had fine nodules on the capsular surface. On microscopy, the left ureter was present and not dilated. The left kidney showed various changes seen throughout the kidney. The cortex had almost complete

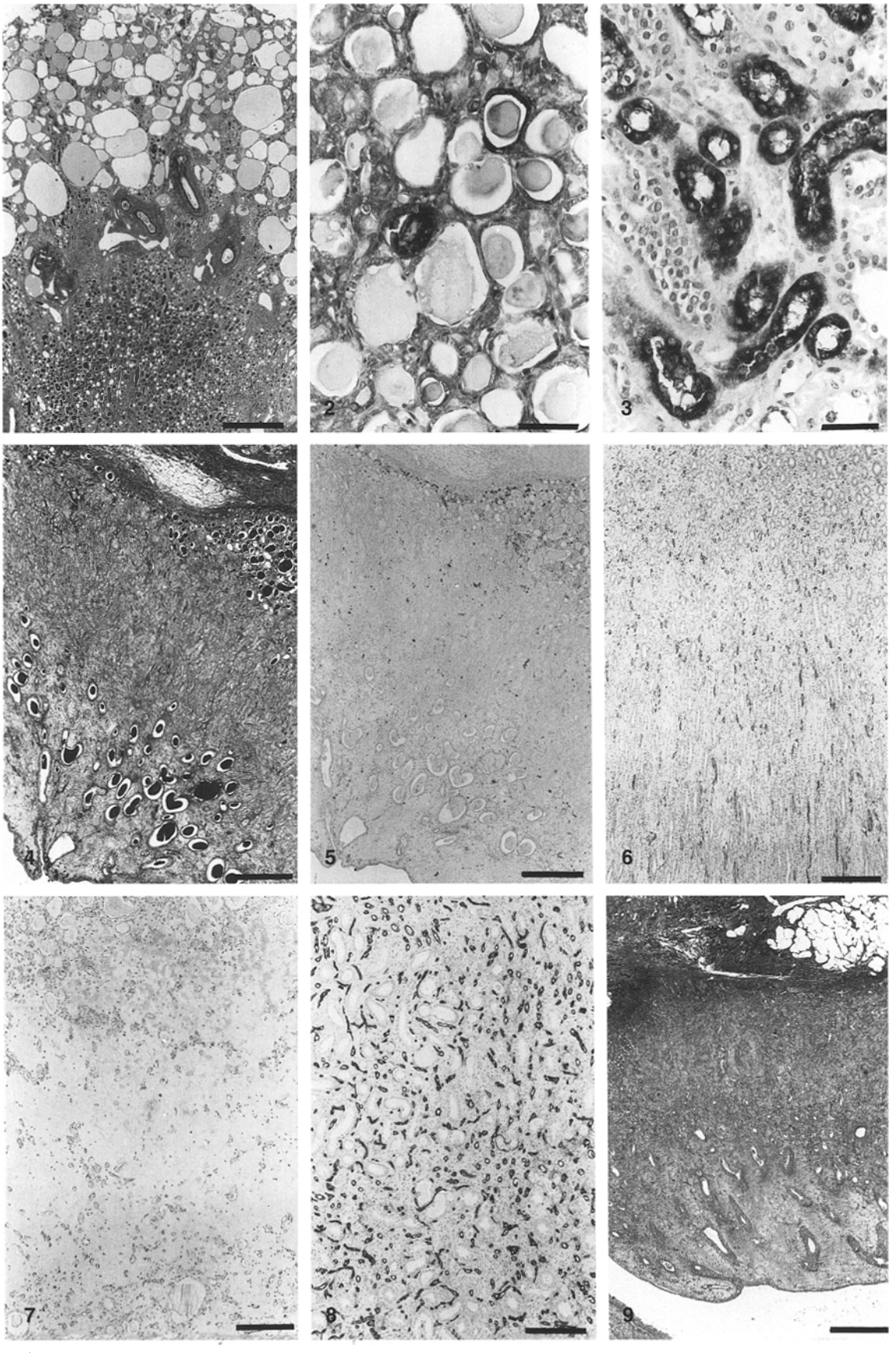
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Table 1 Clinical and pathological features of nine cases with asymmetrical atrophy of renal medulla

Number	Sex	Age	Source of kidney	Weight of affected kidney	Other findings
1 (initial case)	M	61	Autopsy	50 g	Cerebral infarcts; myocardial infarct; severe generalised atherosclerosis; hypertension; other kidney 185 g
2	M	25	Transplant nephrectomy	135 g	Transplanted 15 years ago; now on dialysis; chronic vascular rejection; acquired cystic disease
3	F	42	Nephrectomy	50 g	Renal artery stenosis; non functioning kidney; hypertension
4	F	45	Nephrectomy	35 g and 40 g	On dialysis; bilateral nephrectomy for poorly controlled hypertension; IgA nephropathy
5	M	64	Autopsy	50 g	Peripheral vascular disease; abdominal aortic atherosclerosis and thrombosis; hypertension; other kidney 150 g
6	F	68	Autopsy	50 g	Ruptured thoraco-abdominal aortic aneurysm; hypertension; other kidney 125 g
7	M	72	Autopsy	50 g and 50 g	On dialysis; myocardial infarct; hypertension; apparently hypertensive nephropathy
8	M	75	Autopsy	70 g	Cerebral infarct; abdominal aortic aneurysm; carcinoma of bronchus; other kidney 150 g
9	M	79	Autopsy	30 g	Cerebral infarcts; myocardial infarct; abdominal aortic aneurysm; other kidney 120 g

loss of tubules. Glomeruli were cystic and there were a few larger cysts (Fig. 1). There were many tiny neoplasms, mostly clear cell and papillary. There were a few collections of lymphoid cells mostly at the medullary aspect of the cortex. The outer medulla had dilated tubules with casts. A few tubules and casts were shown to contain Tamm-Horsfall protein on immunoperoxidase study (Fig. 2), with many fewer tubules stained than normal (Fig. 3). The inner medulla showed two zones. There was a band of fibrosis with virtually no tubules passing through it, outside the tip of the papilla, which was viable, contained collecting ducts, and was covered by viable transitional epithelium (Fig. 4). Immunoperoxidase study showed hardly any thin limbs of the loop of Henle (Fig. 5), compared with the many thin limbs in the normal kidney (Fig. 6). There were small blood vessels in the papillary tip and a few crossing the band of fibrosis (Fig. 7), compared with the rich vascular pattern of the normal medulla (Fig. 8). There was no evidence of dysplastic areas of renal tissue. The arcuate and interlobar blood vessels were patent but had intimal fibrosis.

Fig. 1 Cortex and outer medulla in left kidney of initial case. The cortex is atrophic, with many glomerular cysts. Tubules in the outer medulla are dilated. Weigert's elastic-haematoxylin-van Gieson. ×10, *bar*=1 mm

Fig. 2 Outer medulla of kidney in Fig. 1, stained by immunoperoxidase method for Tamm-Horsfall protein. A cast and a few tubular cells stain, showing that at least some tubules are thick limbs of the loop of Henle. Compare Fig. 3. ×200, *bar*=50 μm

Fig. 3 Outer medulla of normal kidney, stained by immunoperoxidase method for Tamm-Horsfall protein. Thick limbs of the loop of Henle are stained. Compare Fig. 2. ×200, *bar*=50 μm

Fig. 4 Medulla of kidney in Fig. 1. The renal medulla has a band of fibrosis without tubules. The tip of the papilla has dilated collecting ducts. EHVG. ×20, *bar*=0.5 mm

Fig. 5 Medulla of kidney in Fig. 1, stained by immunoperoxidase method for CD15. Hardly any thin limbs of the loop of Henle are seen. Compare Fig. 6. ×20, *bar*=0.5 mm

Fig. 6 Medulla of normal kidney, stained by immunoperoxidase method for CD15. Thin limbs of the loop of Henle are stained. Compare Fig. 5. ×20, *bar*=0.5 mm

Fig. 7 Medulla of kidney in Fig. 1, stained by immunoperoxidase method for endothelial marker CD34. Small blood vessels are seen in the medulla, but many fewer than normal. Von Willebrand factor had identical distribution. Compare Fig. 8. ×50, *bar*=200 μm

Fig. 8 Medulla of normal kidney, stained by immunoperoxidase method for CD34. Many small blood vessels are seen. Compare Fig. 7. ×50, *bar*=200 μm

Fig. 9 Medulla of kidney of case 4 in Table 1. This resembles the initial case (Fig. 4). EHVG. ×20, *bar*=0.5 mm

Autopsy and surgical series

Similar changes to those seen in the initial case were found in five autopsy cases, two non-transplant surgical cases, and one renal transplant (Fig. 9). Variations from the initial case were: (a) two cases were bilateral; (b) all cases were incomplete compared with the initial case in that a few tubules crossed the fibrosed band in the medulla; (c) glomerular cysts were prominent in six cases, and did not affect every glomerulus in these cases; (d) not every papilla was affected on the sections available; and (e) no other case had renal neoplasms. Details of the eight additional cases, and the initial case, are given in Table 1. All patients had severe vascular disease.

The autopsy and surgical series contained seven examples of renal papillary necrosis, both recent and old. This was easily differentiated from the lesion described here since in papillary necrosis the papillae were either recently necrotic or had lost their tip. There were also many atrophic kidneys in which there was uniform atro-

phy of the medulla, without the band of fibrosis sparing the tip of the papilla typical of the lesion described here.

Discussion

The affected kidney in the initial case had striking abnormalities. We interpreted the asymmetrical atrophy in a band across the mid medulla as the primary structural change in the kidney, associated with loss of collecting ducts and thin limbs of the loop of Henle at this site. The loss of these structures caused obstruction of tubules in the outer medulla and cortex, with atrophy of many tubules including thick limbs of the loop of Henle, which are sensitive to damage [7]. There was also development of glomerular cysts, presumably due to intrarenal obstruction. The lesion seems to be another association of glomerulocystic disorders, which in the condition we describe can be unilateral [9]. The multiple cortical neoplasms, which were a feature of the initial case only, were probably analogous to the neoplasms arising in acquired multicystic renal disease [3].

There were indications that the affected kidney in the initial case had developed normally, without evidence of dysplasia. There was also no evidence of a disorder of urinary drainage from this kidney, as the ureter appeared normal and the pelvis was not dilated. The uniformity of the change throughout the kidney was against reflux damage [4].

The relative sparing of the innermost medulla clearly differentiated the lesion we describe from renal papillary necrosis, several examples of which were found in the series. Papillary necrosis is often bilateral and is usually due to analgesic damage, ascending infection or sickle cell disease [2], none of which were features of this series. There was also no evidence in the nine cases of renal cortical necrosis. Indeed, medullary lesions were not mentioned in a standard work on cortical necrosis [12]. The lesion we describe therefore seems to be unrelated to either papillary necrosis or cortical necrosis.

The most likely cause of the band-like atrophy of the medulla is an episode of ischaemia, possibly in a kidney with pre-existing arterial narrowing. There was evidence of severe vascular disease, mostly atherosclerotic, in all nine cases. The band did not seem to be an area of infarction, since a few blood vessels could be seen within it and some cases still had a few tubules crossing it. The variability between kidneys and between papillae in the same kidney may be explained by local variations in blood supply. There is controversy about the blood supply of the renal papilla. Baker [1] suggested that there is a dual supply, one from juxtamedullary glomeruli and the vasa recta arising from them, and the other from branches of arteries in the wall of the renal calyx, that supply the tip of the papilla. Ljungqvist and Lagergren disagreed and said that there was only one blood supply to the papillae, from juxtamedullary arterioles. We did not investigate the arrangement of medullary blood vessels but showed a few small vessels crossing the band of atrophy. Relative resistance of the medulla to ischaemia would explain the observation that necrosis of the papilla is not a feature of acute ischaemia causing either tubular necrosis [1] or renal cortical necrosis [12], but does not explain the apparently different sensitivity of the layers of the medulla seen in our study. Possibly the collecting ducts in the innermost medulla are more resistant to ischaemia than collecting ducts and thin limbs in the mid medulla, and survive an ischaemic episode better, especially if there has been slow development of the ischaemia.

The importance of our observation is that it shows a previously undescribed lesion apparently causing intrarenal obstructive damage. The lesion appears to be fairly common. The innermost medulla, that is, the tip of the papilla, seems able to survive an insult that damages other parts of the medulla, which is the opposite of the position in renal papillary necrosis.

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