

## Renal Microangiography and Correlated Histopathological Observation of Cows with Nephropathy

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**ABSTRACT.** Seven Holstein-Friesian cows showing chronic nephropathy were studied by renal microangiography and its correlated histopathology. In cases of pyelonephritis associated with severe pathological lesions such as thickening of arterial walls, narrowing of the arterial and arteriolar lumen, and interstitial inflammation and abscess formation, patchy loss of the peritubular capillary plexus from the cortex to the medulla was clearly demonstrated by microangiography. Interlobular arteries were tortuous and attenuated or truncated. Opacification in the vasa rectae and interstitial capillaries was increased. Extensive non-perfused regions could be detected in the cortex. In cases of mild interstitial nephritis and moderate pyelonephritis, microangiography showed focal changes in the renal vasculature. Microangiography is thus shown to clearly demonstrate changes in the renal vasculature corresponding to the severity of the histopathological lesions.—**KEY WORDS:** cow, microangiography, nephropathy.

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Renal disease in cattle has been reported to occur at high incidence [3, 7, 15, 17–19]. Serious disorders may require the slaughter of cattle with consequent economical loss. Thus, clinical diagnosis and therapy should be conducted as soon as possible and basic studies such as renal hemodynamics should help realize these purposes.

For the examination of renal lesions, microangiographic techniques for studying microcirculation in various animal species have been conducted [1, 2, 4–6, 8–14, 16]. Microangiography has been carried out to clarify changes in renal vasculature in the pathogenesis and progression of various renal disorders.

The results of conducting microangiography on bovine species have been previously reported [20]. In the present study, a comparison was made of microangiographical observations and histological changes in bovine cases with nephropathy showing various degrees of severity of renal lesions.

### MATERIALS AND METHODS

**Animals:** Seven 3- to 8-year-old Holstein-Friesian cows were studied. They were clinically diagnosed as nephropathy (4 cases), reproductive disorders (2 cases) or chronic mastitis (1 case).

**Microangiography:** The kidneys taken at autopsy were examined by the method described previously

[20].

**Light Microscopy:** The kidney was sampled and fixed in 10% formalin. Fixed tissues were embedded in paraffin. Sections were stained with hematoxylin and eosin (HE) and periodic acid-schiff (PAS) reaction.

### RESULTS

At autopsy, the kidneys of Cases 1–3 were found to be slightly swollen, and stripping off the capsule was difficult. Multiple small irregular depressions could be seen on the surface of the kidneys. On the cut surface, thick purulent material with calculi of various sizes was present in the calices. Cortical scars with white streaks were found to radiate from the medulla to the cortex. In Cases 4–7, the renal capsule could be easily stripped off. The kidneys showed no significant macroscopic changes except for small depressions and fine white streaks in the cortex of a few lobes.

Microangiography indicated Cases 1–3 to have increased flow of barium sulfate in the vasa rectae and the calices were dilated, causing parenchymal atrophy. Interlobular arteries were tortuous and attenuated or sometimes truncated. Patchy loss of peritubular capillary plexuses was evident in the cortex and medulla. Perfusion was inadequate in most glomeruli. Opacification in the interstitial

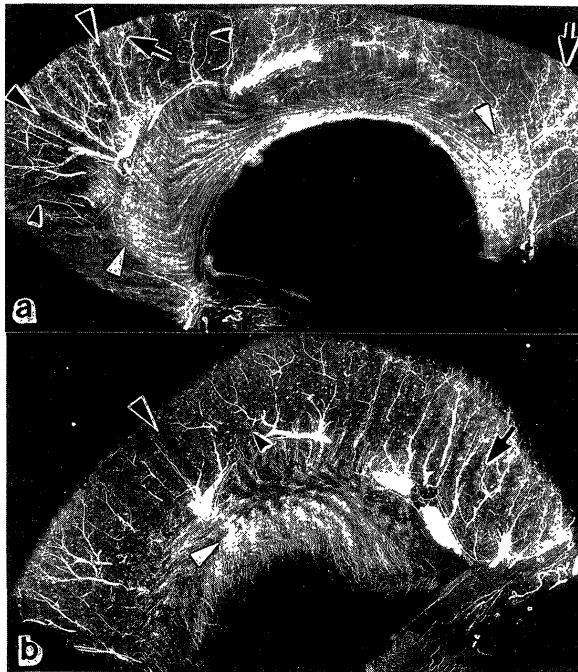


Fig. 1. Microangiograms (1.5-mm section,  $\times 1.8$ ) of renal lobes with severe chronic pyelonephritis and urolithiasis showing dilated calyx and thin parenchyma, negative delineation of postglomerular and peritubular capillaries (arrowheads), decreased number of glomeruli and increased flowing of contrast medium in the vasa rectae (white arrowheads). Focal increase of interstitial capillaries (arrows) and attenuation or truncation of interlobular arteries (small arrowheads) are also shown. Cases 1 (a) and 2 (b).

capillaries had focally increased (Figs. 1 and 2a). These vascular changes were noted in all the lobes of these 3 cases with the degree of severity varying according to the case.

Pathologic findings are summarized in Table 1. All the cases showed various degrees of pyelonephritis or interstitial nephritis accompanied by glomerular lesions. In Cases 1–3, multiple foci of chronic pyelonephritis were seen. The papillary mucosa was heavily infiltrated with mononuclear cells. Occasionally, neutrophils accumulated in the tubules, sometimes with microabscesses in the papilla. Renal tubules were either atrophied or dilated with distended interstitium containing mononuclear cell infiltration, fibrosis and microabscesses (Fig. 3a). Interstitial capillaries were increased in number. Within the inflammatory foci, the walls of small arteries and afferent arterioles had thickened due to concentric fibrosis (Fig. 3b). Such changes were severe in the lobules which macroscopically revealed irregular depressions on the surface (Figs. 4a and



Fig. 2. Microangiogram of Case 2 showing increase of non-glomerular capillaries in the cortex (a). Some glomerular and peritubular capillaries of Case 7 are adequately or unevenly filled (b). 0.5 mm section,  $\times 40$ .

Table 1. Pathological findings

Cow No.	Age (years)	Renal calculi	PN or IN <sup>a)</sup>	GL <sup>b)</sup>	MC <sup>c)</sup>
1	3	+	Severe	Mild	Severe
2	4	+	Severe	Mild	Severe
3	6	+	Severe	Mild	Severe
4	6	–	Moderate	Mild	Moderate
5	7	–	Mild	Mild	Mild
6	7	–	Mild	Mild	Mild
7	8	–	Mild	Mild	Mild

a) Pyelo- or interstitial-nephritis.

b) Glomerular lesion.

c) Microangiographic change.

4b). In most glomeruli, global or segmental proliferation of mesangial cells and matrix could be detected. The capillaries of glomeruli surrounded by inflammatory cells or fibrosis were completely filled or nearly so with barium in all the cases (Fig. 5).

The microangiographic features of Cases 4–7 showed mild or moderate changes. Barium was focally absent in the cortex and glomerular perfusion was either incomplete or lacking. Interstitial capillaries could be focally visualized (Figs. 2b, 6 and 7).

In Case 4, glomerular and interstitial histopathological lesions showed essentially the same features though they were much less severe compared to

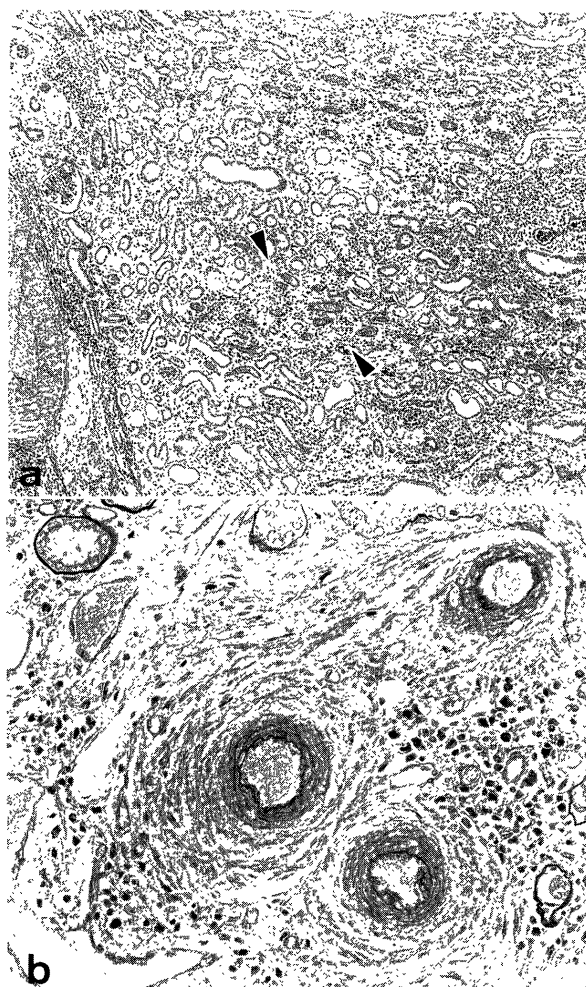


Fig. 3. Vasa rectae with excessive filling of barium sulfate (arrowheads) and chronic pyelonephritic lesion in the medulla (a; HE,  $\times 40$ ), and thickened wall and surrounding fibrosis of interlobular arteries (b; PAS,  $\times 200$ ). Case 1 shown in Fig. 1a.

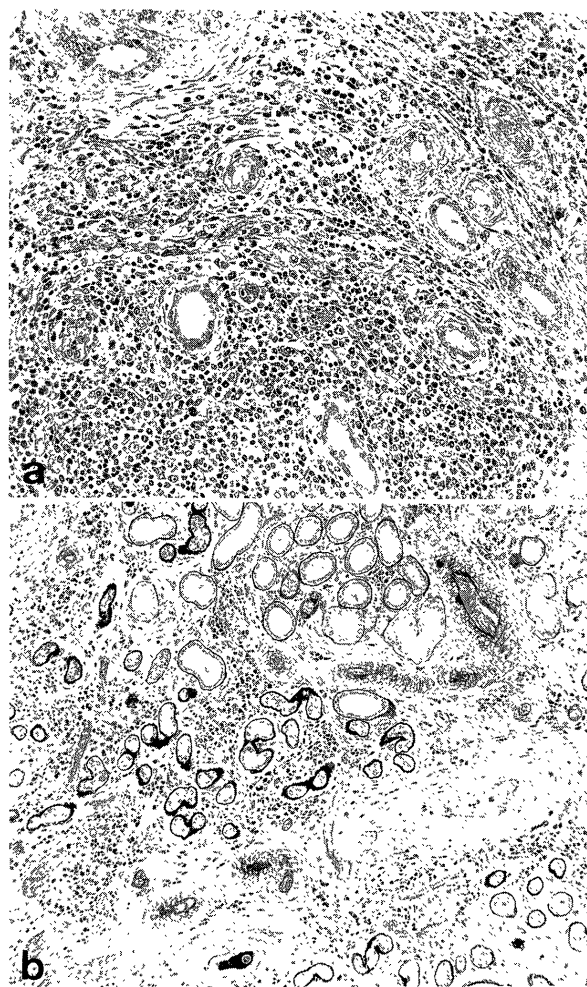


Fig. 4. A chronic pyelonephritic lesion showing atrophied and dilated tubules (a; HE,  $\times 150$ ), and small arteries surrounding with prominent periarterial fibrosis (b; PAS,  $\times 70$ ). Case 2 shown in Fig. 1b.

those noted in Cases 1-3. Glomerular capillaries were segmentally perfused with barium (Fig. 8). Cases 5-7, all exhibiting mild proteinuria without clinical indication of renal disease, showed slightly abnormal features by microangiography. Some interstitial infiltration of mononuclear cells with slight fibrosis was demonstrated histopathologically. Barium was unevenly distributed in the capillaries of glomeruli with segmental lesions (Fig. 9).



Fig. 5. Periglomerular fibrosis and cellular infiltration and thick wall of afferent arterioles with inadequate filling of barium sulfate. PAS,  $\times 150$ . Case 1 shown in Fig. 1a.

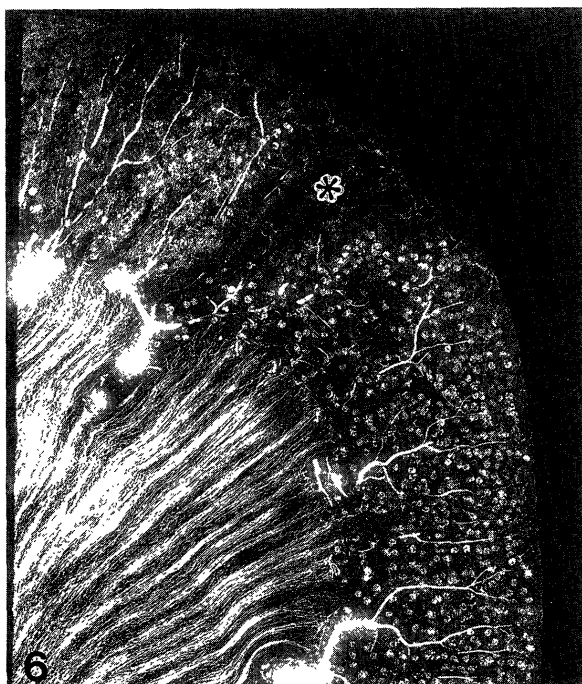


Fig. 6. Microangiogram of a part of the lobe from Case 4 showing attenuated images of interlobular arteries and focally poor cortical perfusion (asterisk) due to cellular infiltration or fibrosis. 1 mm section.  $\times 4$ .

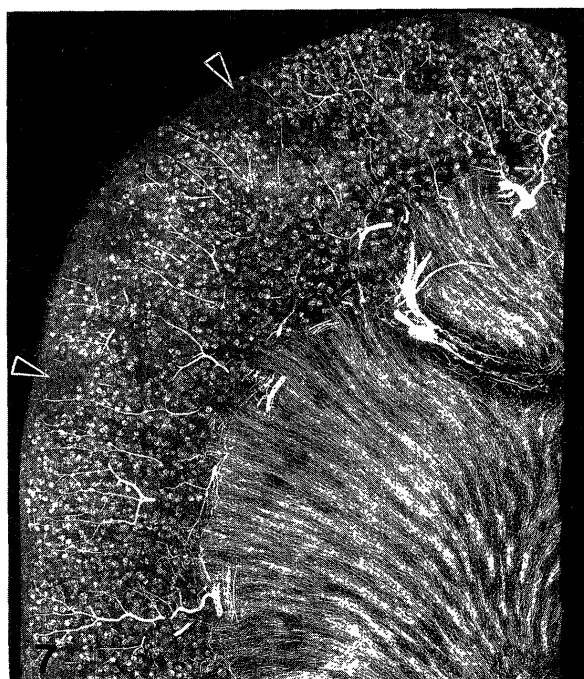


Fig. 7. Microangiogram showing patchy loss of capillary plexus and glomeruli in the outer cortex of Case 6 (arrowheads). 1 mm section.  $\times 4$ .

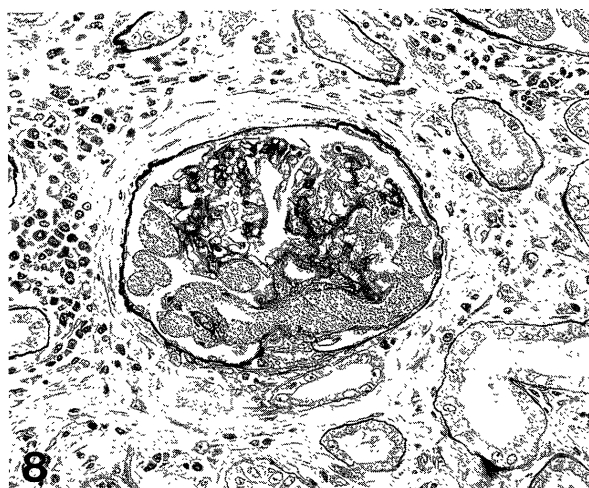


Fig. 8. Glomerulus with incomplete filling of barium sulfate of Case 4. PAS,  $\times 200$ .

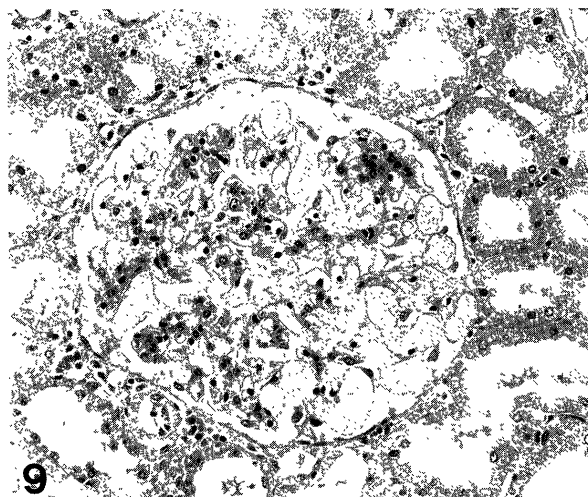


Fig. 9. Segmental increase of cell number and matrix in the mesangium and uneven filling of barium sulfate in a glomerulus. HE,  $\times 200$ . Case 6 shown in Fig. 6.

DISCUSSION

Microangiography has been found to be quite useful in the conduct of basic research on the pathogenesis and pathologic diagnosis of renal disease since it can demonstrate dynamic changes in the microcirculation of various animal species [1, 2, 4-6, 8-14, 16]. However, its application to bovine kidneys has been indicated only in our previous report [20]. Its usefulness for examining 7 cows with mild to severe renal lesions of chronic pyelonephritis or interstitial nephritis was confirmed in this study.

Interstitial nephritis in Cases 5-7 was character-

ized by features such as focal non-perfused regions in the cortex, incomplete perfusion of the glomeruli, and focal increase in interstitial capillaries in the cortex. These changes were histopathologically correlated with the focal interstitial infiltration of inflammatory cells and fibrosis. The glomeruli incompletely filled with barium showed slight increase in cell number and matrix in the mesangium with or without periglomerular fibrosis. But Cases 1–3 with severe pyelonephritis were microangiographically characterized by increased flow of contrast medium in the vasa rectae along with severely abnormal intrarenal arteries including glomeruli as well as extensive non-perfused regions in the cortex. Histopathologically, these changes were shown to be consistent with extensive mononuclear cell infiltration and fibrosis as well as abscess formation in the interstitium. Microangiography and histopathology of the moderate pyelonephritic Case 4 showed changes intermediate between interstitial nephritis and severe pyelonephritis.

The features in the present cases were essentially the same as those of renopathy in other species [1, 5, 6, 9, 10, 13, 14, 16]. In experimental pyelonephritis in rats and rabbits, the numbers of glomeruli and postglomerular and peritubular capillaries have been found to decrease or sometimes disappear showing irregular-shaped interlobular arteries and afferent arterioles. Primary injury in the experimental pyelonephritis was at the postglomerular level and secondary change was marked kinking or spiraling of the intrarenal vessels, due to contraction of fibrous tissue [9, 10]. Chronic pyelonephritis in humans is characterized by tortuosity and attenuation of interlobar, arcuate, and interlobular arteries due to intimal or periarterial fibrosis. The number of perfused glomeruli was patchily reduced, with consequent glomerular sclerosis and periglomerular fibrosis [13].

Microangiographic features in the present cases were more severe than those described in other cases by many authors. In cases of chronic pyelonephritis with calculi, changes such as increased flowing of contrast medium in the interstitial capillaries and vasa rectae were shown to be particularly extensive by microangiography. An increase in the number of capillaries and revascularization around abscesses have been described in experimental pyelonephritis [10]. Increased flow of contrast medium in the vasa rectae and capillaries may have been caused by the higher resistance of

the cortical vasculature due to parenchymal injury.

Microangiography is thus shown by the present study to demonstrate dynamic aspects of intrarenal bloodflow and chronic changes in broader areas as compared to histologic findings.

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