Pathology of hereditary nephritis

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SYNOPSIS This report describes the renal pathology in three siblings with hereditary nephritis. All three cases showed combined features of chronic glomerulonephritis, pyelonephritis, and interstitial nephritis. Foam cells were seen in only one case. These findings support the contention of Krickstein, Gloor, and Balogh (1966) that the renal changes in hereditary nephritis are those of a mixed nephritis.

In the past few years there have been several reports on hereditary nephritis Krickstein et al, 1966; Mulrow, Aron, Gathman, Yesner, and Lubs, 1963; Perkoff, 1967) and up to 1965 25 families with the disease were reported (Johnson and Hagan, 1965). The clinical aspects of the disease have been well described (Marin and Tyler, 1961; Mulrow et al, 1963; Perkoff, Stephens, Dolowitz, and Tyler, 1951).

Haematuria, proteinuria, hypertension, and episodes of urinary tract infection are usual manifestations of the disease. In the involved families the male members develop progressive renal insufficiency and die in uraemia between the ages of 20 and 30 in most cases. However, the female members of the involved families have much less severe renal disease and few are thought to die of it. Extrarenal abnormalities such as nerve deafness, congenital cataract, or congenital strabismus may be associated with the disease. The mechanism of inheritance is uncertain. Although several authors have described the renal pathology in their reports on hereditary nephritis, there is disagreement as to the significance of the renal changes. Krickstein et al (1966) believe that the renal pathology is that of ‘mixed nephritis’. The purpose of this paper is to describe the renal pathology in three siblings with hereditary nephritis.

CASE REPORTS

The three patients were siblings, two of them twin brothers. Necropsies were performed on two of the three patients. On the third patient a renal biopsy was done. As far as is known other members of the family have not shown obvious evidence of renal disease. However, they are spread over two states and it has not been possible to get a detailed family history.

CASE 1 A 30-year-old Negro male (T.B.) was admitted to the Norfolk General Hospital for the first time three-and-a-half weeks before death; with increasing weakness, fatigue, hypertension, and anaemia. He had been treated for uraemia (blood urea nitrogen between 150 and 170 mg %) in other hospitals during the six months before admission with peritoneal dialysis. Physical examination showed an obese Negro male who was lethargic but not comatose. Blood pressure was 170/115 mm Hg. There was cardiac enlargement with a soft, blowing apical systolic murmur. Clinically, there was no evidence of nerve deafness. Audiometric studies were not done. Urine analysis showed 3+ proteinuria, 3 to 5 white blood cells, and a few epithelial cells per high-power field. The specific gravity was 1-015. Blood urea nitrogen was 220 mg %, and creatinine 16 mg %. During his hospital stay, the patient developed increasing dyspnoea, restlessness, tachycardia, and oliguria. He died after the sudden onset of massive bloody diarrhoea.

At necropsy, there was hypertensive cardiomegaly with left ventricular hypertrophy, fibrinous pericarditis, and uraemic colitis with diffuse mucosal haemorrhage. The renal pathology is described below.

CASE 2 A 24-year-old Negro male (N.B.) was transferred to the Medical College of Virginia Hospitals on 5 June 1967 for treatment of chronic renal disease and hypertension of about two years’ duration. On physical examination he was obese and lethargic. There was cardiac enlargement. Blood pressure was 180/116 mm Hg. Examination of the ocular fundi revealed small exudates, several punctate haemorrhages, and probable optic atrophy. There was no clinical evidence of nerve deafness. Audiometric studies were not done. Urine analysis showed 1+ proteinuria, 10 white blood cells and 20 red blood cells per high-power field, and an occasional granular cast. Blood urea nitrogen was 234 mg % and creatinine 27 mg %. The patient died 10 days after admission.

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At necropsy there was hypertensive cardiomegaly with left ventricular hypertrophy and dilatation, and pulmonary oedema. The renal changes are described below.

CASE 3 A 24-year-old Negro male (K.B.), twin brother of the patient above (case 2), was admitted to the Medical College of Virginia Hospitals for evaluation of his renal and cardiovascular status in view of the family history of hereditary nephritis. On physical examination he was obese, with a blood pressure of 180/120 mm Hg and a grade III hypertensive retinopathy. There was no clinical evidence of nerve deafness. Audiometric studies were not done. Urine analysis revealed proteinuria of 1 to 2+ and a few white blood cells per high-power field. The blood urea nitrogen ranged from 14 to 26 mg % and creatinine was 1-9 mg %. A pyelogram showed bilateral delay in excretion. A kidney biopsy was done.

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Gross examination of the kidneys from the two necropsied patients showed that they were reduced in size, the combined weight being 190 g in the first case and 230 g in the second case. The cortical surfaces were uniformly coarsely granular with a few capsular adhesions. The cortical thicknesses averaged 4 mm with blurring of the cortico-medullary junctions. The calyces and pelves of all four kidneys were normal. Fatty streaks or yellow coloration due to fat were not present. The histological picture of the kidneys in all three cases was fundamentally the same with a few individual variations as described below.

GLOMERULI The glomeruli in all cases showed severe changes. These were involved by a process which ranged from basement membrane thickening in a few to severe fibrosis and hyalinization involving most glomeruli (Fig. 1). Some showed epithelial crescents (Fig. 2). Periglomerular fibrosis was present around a few glomeruli (Fig. 3.). Foam cells were seen in a few glomeruli from case 1 (Fig. 4) but were not present in the glomeruli or in the interstitial tissues in the other cases. Some glomeruli were normal.

![FIG. 1](image1.jpg)

**FIG. 1.** Hyalinization of glomerulus. Interstitial inflammatory infiltrate and tubular atrophy are also seen. Haematoxylin and eosin × 245.

![FIG. 2](image2.jpg)

**FIG. 2.** Glomerulus showing epithelial crescent. Haematoxylin and eosin × 245.
FIG. 3. Periglomerular fibrosis. There is also interstitial inflammatory infiltrate. Haematoxylin and eosin × 245.

FIG. 4. Glomeruli showing foam cells. Atrophic tubules are also seen. Haematoxylin and eosin × 245.

FIG. 5. Interstitial fibrosis and tubular atrophy. A few dilated tubules are also seen. Haematoxylin and eosin × 245.
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TUBULES  The predominant change in the tubules was atrophy and collapse (Figs. 1 and 4), but there were a few areas of tubular dilatation in the superficial portions of the cortex. Tubular epithelium did not appear foamy in any of the cases.

INTERSTITIAL TISSUES  There were varying degrees of interstitial fibrosis (Fig. 5) with chronic inflammatory infiltrate (Figs. 1 and 3). The interstitial fibrosis was more prominent than the inflammatory infiltrate.

BLOOD VESSELS  The blood vessels showed marked fibrous intimal thickening of both small-sized arteries and arterioles in all three cases.

CALYCES AND PELVES  The calyces and pelves were normal histologically.

DISCUSSION

Previous reports of hereditary nephritis have classified the renal lesions as chronic glomerulonephritis (Dubach, Minder, and Antener, 1966; Whalen, Huang, Peschel, and McIntosh, 1961), chronic pyelonephritis (Goldbloom, Fraser, Waugh, Aronvitch, and Wiglesworth, 1957; Perkoff et al., 1951; Whalen et al., 1961) or as interstitial nephritis. Krickstein et al. (1966) in their report state that the renal changes of hereditary nephritis consist of combined features of chronic glomerulonephritis, pyelonephritis, and interstitial nephritis but lack some characteristics of each, so they called it a 'mixed' type of nephritis. Further, they showed that foam cells are frequently present (in 11 of their 18 cases) in the tubules, interstitial tissues, and glomeruli. They believe that this combination of 'mixed' nephritis with the foam cells is the characteristic lesion of hereditary nephritis.

In our cases, also, the renal changes combine the features of chronic glomerulonephritis (severe hyalinization of many glomeruli, crescent formation), chronic pyelonephritis, and interstitial nephritis (periglomerular fibrosis, chronic interstitial inflammatory infiltrate, and fibrosis). Yet some characteristics of each were lacking. For example, in chronic pyelonephritis inflammatory changes in the calyces and pelves are commonly seen, but in our cases they were absent. Unlike classical chronic glomerulonephritis, some glomeruli in our cases were completely normal. Interstitial fibrosis and chronic inflammation were not as severe as usually seen in chronic interstitial nephritis.

In one of the three cases reported here, foam cells were present in the glomeruli. Though other authors (Krickstein et al., 1966) have shown that foam cells are often present in hereditary nephritis, it appears that their importance has been overemphasized. Foam cells are certainly not specific for hereditary nephritis since they are seen in other conditions such as nephrosis and chronic glomerulonephritis (Whalen et al., 1961). Also in the series reported by Krickstein et al. (1966) foam cells were present in only three of the seven young patients in whom renal biopsies were done. Though abnormalities of lipid metabolism based on the presence of foam cells have been suggested as playing a role in the pathogenesis of hereditary nephritis, it appears more likely that the foam cells are a secondary development in the later stages of hereditary nephritis. The prominent vascular changes in the three cases reported here are probably secondary to hypertension.

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