GLOMERULONEPHRITIS
MORPHOLOGY, NATURAL HISTORY, AND TREATMENT

PART II OF TWO VOLUMES

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Contents

PART II

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Renal Failure, Glomerulonephritis and Glomerular Epithelial Cell Hyperplasia

SUMMARY

Sixty-three patients with acute renal failure, glomerulonephritis, and glomerular epithelial cell hyperplasia as a major histological finding were studied. There was no clear-cut predilection for age or sex. Presenting signs and symptoms in order of frequency were azotemia, oliguria, and edema. Fifty-two patients never regained adequate renal function, 7 have chronic renal failure and 4 are normal. Thirty-three had a history of a prior acute illness and 15 had a past history of renal disease that was thought to have resolved.

Four of 6 patients who had little interstitial disease initially and who received intensive drug therapy have stable renal failure compatible with normal work and pleasure activities. An additional 7 patients have stable but reduced RF. These, too, had much less severe interstitial changes at onset than the general group. It thus appears that attempts at therapy should be made in those patients with less severe interstitial disease even if the glomerular changes are severe.

That oliguria in patients with glomerulonephritis signified a poor prognosis

for subsequent adequate renal function is well established (1–4). The exceptions to this rule are those patients with historical or laboratory data suggestive of an antecedent streptococcal infection as the cause of the nephritis (5). Typically, the latter patients have had hypercellularity involving cells within the glomerular tuft, whereas those who never recover renal function demonstrate hypercellularity of the epithelial cells.

The etiology of this form of glomerulonephritis is not known. The onset is insidious and the morphologic changes and decline in renal function are often advanced before the patient seeks medical advice. The observation that IgG may be seen deposited in a linear fashion on the glomerular basement membrane has led to the speculation that this is an auto-immune disease. A recent report of glomerulonephritis with linear deposits of IgG or the GBM following a viral infection with subsequent complete resolution raises the hope of reversal of even the most florid renal lesions if the etiologic agent can be eradicated or the renal response abrogated (6). In light of this observation and the emergence of excellent renal-dialysis support and more potent chemotherapeutic agents, the need to revaluate this syndrome comes more clearly into focus.

This is a report of 63 patients with anuria and glomerulonephritis that was characterized histologically by epithelial cell hyperplasia. Four patients recovered normal renal function and 18 subsequently had reduced renal function. Of the remainder, 20 are maintained by chronic dialysis without evidence of life-threatening disease in other organs.

MATERIALS AND METHODS

Patients

Sixty-three patients admitted over the last 12 years to the University Hospital with the sudden onset of glomerulonephritis and renal failure were selected. Those with other diagnoses such as lupus erythematosus, periarteritis, intravascular infection, Wegener's granulomatosis or clear-cut streptococcal infections were excluded. Renal failure was defined as oliguria ($<$600 ml/day), azotemia, and declining renal function.

Renal biopsies were obtained shortly after admission (within 2 weeks) to the hospital in all but 1 patient. The tissue was bisected longitudinally and one-half was fixed in 6.25% glutaraldehyde in 0.1 *M* cacodylate, pH 7.4. After fixation the specimen was again bisected. One fragment was embedded in paraffin, sectioned at 1 to 3 microns, and stained. The second fragment was postfixed in OsO_4 and embedded in Epon. Then sections were examined in an AEI-300 electron microscope. More recently the second half of the original tissue has been frozen in liquid nitrogen,

sectioned in a cryostat, and stained with various, monospecific fluoresceinated antiglobulins.

RESULTS

Clinical and Renal Function Data

The age distribution (Table 1) spans a wide range without clear evidence of clustering at any point. Thirty-six patients were men and 27 were women. Seven of 20 patients under the age of 21 were boys and 13 were girls. Over the age of 60 the ratio was reversed with 12 of 14 being men.

Nearly all patients were virtually anuric on admission or shortly thereafter (Table 2). Azotemia was documented in all cases; in fact, signs and symptoms of uremia precipitated admission in many instances.

Hypertension was an uncommon finding in this group of patients. The exceptions were those between the ages of 21 and 30 years. In no case, however, was there severe elevation of the blood pressure.

In slightly more than one-half of the patients there was a history of an acute febrile illness within one month of the onset of renal failure. The illness was characterized by many as "flulike" and frequently abated spontaneously. In most cases this was followed by changes in the urine flow-rate or color that were apparent to the patient.

Fifteen patients had been noted to have an episode of "nephritis" in the past or urinary abnormalities (protein, cells, or casts) had been recorded. In all instances these had cleared and none had residual impairment of renal function.

Peripheral edema was present in nearly half of the patients on admission.

Table 1

Year	Number of Patients	Sex	
		Male	Female
0–10	6	2	4
11–20	14	5	9
21–30	7	5	2
31–40	3	2	1
41–50	9	5	4
51–60	10	5	5
61–70	10	8	2
71–>	4	4	0

Table 2 Summary of Clinical Features

Age	Number of Patients	Anuria	Hypertension	Edema	Prior Acute Illness	Prior Renal Disease
0–10	6	4	1	3	1	—
11–20	14	13	3	8	8	5
21–30	7	4	6	6	3	3
31–40	3	2	—	—	1	—
41–50	9	7	1	5	4	3
51–60	10	6	3	2	6	2
61–70	10	10	—	3	8	2
71 and >	4	4	—	2	2	—

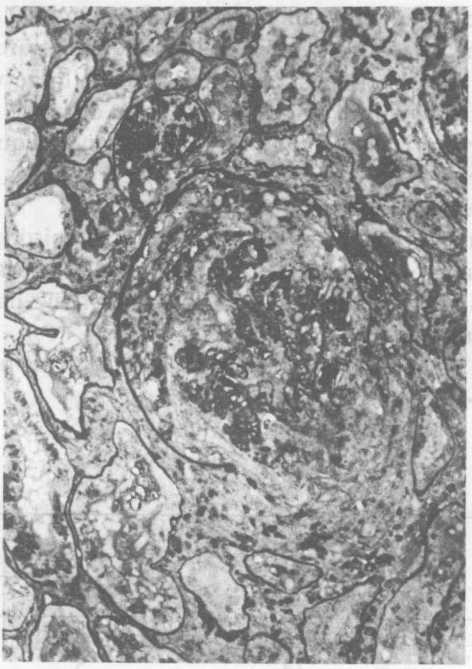

Figure 1. Glomerulus with marked hyperplasia of epithelial cells. The glomerular capillary loops are compressed (PAS x180. From Striker et al. (1970), *Human Pathology* 1,615 with permission).

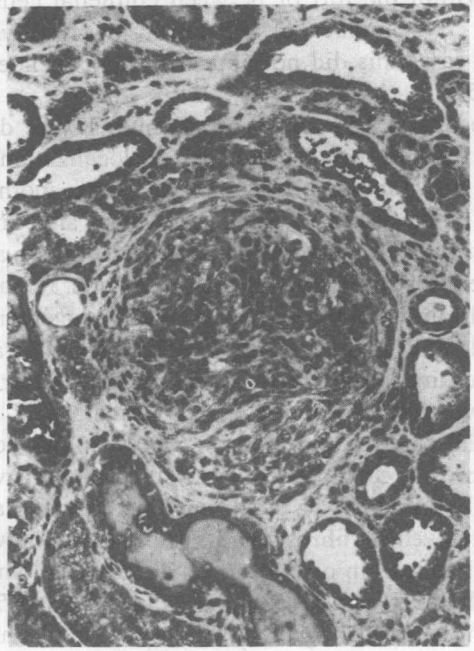

Figure 2. Epithelial cells fill Bowman's space. The cells are assuming an elongate shape and basal lamellae could be demonstrated by electron microscopy. H and E x180.

Histology: General

Diffuse epithelial cell hyperplasia affecting more than 50% of the glomeruli was present in 43 patients, whereas proliferation of cells within the tuft was seen in a similar distribution in 19. The typical picture was marked proliferation of epithelial cells forming a mass that filled Bowman's space surrounded by a flattened mass of glomerular tufts (Figure 1). Mitotic figures were often seen in these cells and they were noted to extend into the neck regions of the proximal tubule. Neutrophils, in large numbers, were often present between epithelial cells and occasionally within the tuft. In such renal corpuscles Bowman's membrane was commonly indistinct or appeared disrupted, with an increase in the number of interstitial connective tissue and inflammatory cells. In 11 instances a substantial amount of basal lamella was seen between the epithelial cells that had now assumed a more elongate configuration (Figure 2).

Fibrin, detected by trichrome or phosphotungstic acid stains, was