Renal Histopathology in Hypertensive Diabetic Patients

GERHARD DITSCHERLEIN

SUMMARY A total of 250 renal biopsy specimens from diabetic patients and from the kidneys of 400 autopsy cases were examined histologically and compared to kidneys from 160 autopsied nondiabetics. The morphological findings were assessed in relation to hypertension. There was a high prevalence of arteriolosclerosis, glomerulosclerosis, and pyelonephritis; in addition, early diabetic glomerulopathy and glomerulonephritis, particularly of the membranous type, were noted in a remarkably high percentage of diabetic patients. Ninety-three percent of patients with hypertension had arteriolosclerosis, and a good correlation existed between the extent of this lesion and the level of blood pressure. Even in 66% of normotensive patients, however, arteriolosclerosis was found. This fact and the involvement of the vas efferens argue against the notion of arteriolosclerosis being exclusively a sequela of hypertension. More than 70% of patients with glomerulosclerosis suffered from hypertension, compared to less than 50% of patients without either that condition or early diabetic lesions. The majority of diabetic patients with pyelonephritis and glomerulonephritis were hypertensive. We conclude that hypertension in diabetic patients with renal involvement may result from different renal lesions that can be differentiated only by histological examination. (Hypertension 7 [Suppl II]: II-29-II-32, 1985)

KEY WORDS • biopsy specimens • autopsy • arteriolosclerosis • glomerulosclerosis • glomerulonephritis

During recent years, some reviews have dealt with hypertension in diabetic patients, particularly in relation to diabetic nephropathy.1-3 There is little information, however, on the relationship of hypertension to morphological lesions in the kidney. Renal lesions are usually summarily diagnosed as "diabetic nephropathy." This term may be useful for physicians who have to rely on clinical information, such as persistent proteinuria and decline in glomerular filtration rate, to assess renal involvement, but pathohistological examination may more precisely specify the renal lesion or detect superimposed pathology. Consequently, histological studies are important not only for evaluating renal prognosis but for clarifying the pathogenesis of hypertension.

Material and Methods

Biopsy specimens taken from 250 diabetic patients and kidney tissue obtained from 400 autopsy cases were examined histologically. In 131 biopsy cases semithin sections (cut with Ultramicrotome OmU2 of C. Reichert AG, Vienna, Austria) were investigated with Movat's silver impregnation method,8 which permits one to recognize lesions in fine detail, such as moderate basement membrane thickening, slight mesangial expansions (i.e., the early stage of diabetic glomerulosclerosis), as well as spike formation along the basement membrane (e.g., in membranous glomerulonephritis). The autopsy and biopsy series differed in some important respects (Table 1). In the biopsy series, 88 patients had type I diabetes, 108 patients type II diabetes, and the rest could not be classified with certainty. This was also true for a large percentage in the postmortem series. Hypertension was diagnosed according to WHO criteria (> 160 mm Hg systolic, > 95 mm Hg diastolic). Statistical evaluation was performed using the t test and the chi-square test respectively. Only statistically significant differences are discussed.

Results

Diabetic glomerulosclerosis (GS) was found in the autopsy series in 45.3% and in the biopsy material in 37.2% of patients. Information on hypertension in patients with GS is given in Table 2. The numbers with hypertension were similar in the autopsy and biopsy
The relationship between AS and hypertension in dia-
microscopic examination was difficult because of the frequent
betics in our material is presented in Table 3.
We found chronic pyelonephritis (PN) in 90
series. More than 70% of the patients with GS had
hypertension, compared with 40 to 50% of other
diabetics. In contrast, in patients with early diabetic
glomerular lesions, the prevalence of hypertension
was lower than in those with manifest GS, but not
significantly different from the prevalence in patients
without glomerular lesions. We also noted that in pa-
tients below 40 years of age, 67% with GS had hyper-
tension. This was certainly more than the expected
prevalence of essential hypertension in this age group.
A frequent finding in kidneys of diabetics is arterio-
We observed this in 79.5% of the
autopsied diabetics compared with 48% in 160 nondia-
etics of the same age distribution. In 68% of the
biopsy series, arteriolosclerosis (AS) was observed.
The relationship between AS and hypertension in dia-
etics in our material is presented in Table 3.
An important finding was the involvement of the
postglomerular vas efferens, which was noted in 60%
of our autopsy cases with GS and in 18% of the other
diabetics. In postmortem examination of supposed
nondiabetics, this lesion was very rarely found. Hyper-
tension was documented in 74% of diabetics with AS
of the vas efferens.
We found chronic pyelonephritis (PN) in 90
(22.5%) autopsy cases; in 43 patients, acute inflammatory
lesions were present. Sixty-nine percent of the
90 autopsy cases had a history of hypertension, but fur-
ter evaluation was difficult because of the frequent
combination of PN with GS and/or AS respectively
(Table 4).

<table>
<thead>
<tr>
<th>Table 1. Comparison of Biopsy and Autopsy Series</th>
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<tbody>
<tr>
<td>Series</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td>Female/Male ratio (%)</td>
</tr>
<tr>
<td>Age at examination (yr)</td>
</tr>
<tr>
<td>&gt; 60</td>
</tr>
<tr>
<td>Age at manifestation (yr)</td>
</tr>
<tr>
<td>&lt; 30</td>
</tr>
<tr>
<td>&gt; 50</td>
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<tr>
<td>Duration of diabetes (yr)</td>
</tr>
<tr>
<td>&lt; 6</td>
</tr>
<tr>
<td>&gt; 15</td>
</tr>
</tbody>
</table>

The proportion of cases of GS in our postmortem
series corresponded to what was reported in the total of
8141 diabetic autopsy cases described in the litera-
ture.1 Our findings on hypertension in diabetic patients
with and without GS (see Table 2) were also in agree-
ment with postmortem data in the literature; no investi-
gator found hypertension in all patients who had GS,
but its prevalence in diabetics with GS was always
higher than in diabetics without GS (for survey, see
ref. 7). Furthermore, in our series, hypertension was
more frequent in the nodular than in the diffuse type of
GS. This supports the notion that nodular GS is a more
advanced type of lesion. Moreover, in patients with
eye diabetic glomerular lesions, the prevalence of

<table>
<thead>
<tr>
<th>Table 2. Hypertension in Diabetic Patients with and without Glomerulosclerosis</th>
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<tbody>
<tr>
<td>Series</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Without GS</td>
</tr>
<tr>
<td>With GS</td>
</tr>
<tr>
<td>Early glomerular lesions</td>
</tr>
</tbody>
</table>

In a biopsy series, glomerulonephritis (GN) was
found in a remarkable percentage (15.3%) of speci-
mens that could be examined in semithin sections.
Noteworthy was the relatively high prevalence of
membranous GN (Table 5); however, various other
GN types were also observed. Most of the patients
with GN were hypertensive. Combination with GS
was apparent in eight specimens with membranous
GN; six of these patients were hypertensive.
Finally, three patients with slight to moderate amy-
loidosis were not hypertensive.

Discussion
The demographic composition of our autopsy series
corresponded to available information on the diabetes
population of East Berlin and was therefore representa-
tive of the population of diabetics in general. In con-
trast, the biopsy series had a preponderance of male
patients, younger patients, and patients with earlier
stages of diabetes. This reflects patient selection for
renal biopsy. In a way, however, the two series com-
plemented each other. In assessing the relationship of
hypertension and renal lesions, the high percentage of
younger patients in the biopsy series was useful.
Our results demonstrate that the morphological fea-
tures of diabetic nephropathy are quite heterogeneous.
Moreover, the combination of several lesions, particu-
larly GS, AS, and/or PN, was relatively frequent. This
point was emphasized decades ago.7,9 Finally, glomer-
ular lesions other than glomerulosclerosis or arterio-
losclerosis must be taken into consideration — indeed,
glomerulonephritis was unexpectedly frequent in our
series. The occurrence of such combinations makes it
difficult to assess the relationship between hyperten-
sion and specific renal lesions.

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more frequent in the nodular than in the diffuse type of
GS. This supports the notion that nodular GS is a more
advanced type of lesion. Moreover, in patients with
eye diabetic glomerular lesions, the prevalence of
This finding suggests that at least in many patients, hypertension does not play a role in the genesis of this vascular lesion. Certainly in hypertensive diabetics the probability for AS to occur is very high.

In a previous study we described a positive correlation between the level of blood pressure and the severity of AS; however, this must not be interpreted to indicate a cause-effect relationship. It cannot be excluded that AS is the first lesion that triggers the rise of blood pressure, although it certainly may also be the result of hypertension. An important clue in this respect may be AS of the vasa afferentia, which is said to be specific for diabetes.11-12 This finding was remarkably common in middle-aged patients and those with diabetes of long duration. It is difficult to conceive, but not altogether impossible, that hypertension in the arterial tree could be transmitted into the postglomerular vessel. Besides, even in malignant hypertension, we never observed involvement of the vasa efferentia.

From all these facts we conclude that hypertension is not the primary disturbance leading to AS in diabetic patients. It seems more likely that diabetes initiates vascular lesions, which in turn initiate or aggravate hypertension, thus creating a vicious circle.

For several reasons we cannot assess whether pyelonephritis contributes to hypertension in diabetics:

1. Biopsy specimens are not representative, because PN as a focal lesion can never be excluded in small biopsy samples.
2. In the autopsy material, PN was frequently combined with other lesions, for instance about 40% of patients with nodular GS and AS also had chronic PN. This was a higher percentage than in patients with PN who had neither GS or AS (12%).
3. The group with pure chronic PN in the absence of GS or AS was so small that no general conclusions could be drawn.

We share the view of Heptinstall,14 who questioned the relationship of chronic PN to hypertension because of controversial findings.

There are few reports on GN in diabetics, and its occurrence in these patients is generally considered coincidental. Our biopsy results, however (see Table 5), clearly indicated that GN is by no means infrequent in diabetics, if adequate morphological techniques are applied. We found mostly GN of the membranous type, which agreed with recent anecdotal observations.15,16 Until now, we had observed a total of 12 diabetics with membranous GN; in 8 patients this was combined with GS mostly of modest intensity. Other types of GN are more rare. At any rate, the differential diagnosis of glomerulopathy in diabetic patients must take into consideration the presence of GN. Hypertension in diabetic patients with membranous GN and GS is presumably due principally to the concomitant presence of GS.

**References**


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**Table 3. Occurrence of Arteriolosclerosis in Autopsied Kidneys of Diabetic Patients with and without Hypertension**

<table>
<thead>
<tr>
<th>Series</th>
<th>Hypertension</th>
<th>No hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>f</td>
<td>%</td>
</tr>
<tr>
<td>Without AS</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>With AS</td>
<td>265</td>
<td>171</td>
</tr>
<tr>
<td>Totals</td>
<td>325</td>
<td>183</td>
</tr>
</tbody>
</table>

**Table 4. Hypertension in Autopsy Material of Diabetic Patients with Chronic Pyelonephritis**

<table>
<thead>
<tr>
<th>Renal lesion</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>f</td>
</tr>
<tr>
<td>PN combined with GS (+ AS)</td>
<td>50</td>
</tr>
<tr>
<td>PN combined with AS</td>
<td>29</td>
</tr>
<tr>
<td>PN without GS or AS</td>
<td>11</td>
</tr>
<tr>
<td>Totals</td>
<td>90</td>
</tr>
</tbody>
</table>

**Table 5. Glomerulonephritis in Biopsy Material of Diabetic Patients with Hypertension**

<table>
<thead>
<tr>
<th>GN type</th>
<th>n</th>
<th>Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membranous GN (combined with GS)</td>
<td>12</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Mesangiproliferative GN</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Membranoproliferative GN</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Crescentic GN</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Proliferative sclerosing GN</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Focal proliferative GN</td>
<td>1</td>
<td>—</td>
</tr>
<tr>
<td>Totals</td>
<td>22</td>
<td>15</td>
</tr>
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</table>
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