Pyelonephritis and Hypertension

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TSUCHIDA, S., MIURA, K., YAMAGUCHI, O. and ARAI, S. Pyelonephritis and Hypertension. Tohoku J. exp. Med., 1975, 117 (3), 237-243 — Blood pressure changes were followed up for 1-12 years (average; 3.8 years) in 46 cases of confirmed postoperative chronic pyelonephritis which had undergone ureterocutaneostomy, nephrostomy or other urologic operations. Diastolic blood pressure levels averaged 82 mmHg before operation, and 89 mmHg in the chronic stage after the operation. The incidence of hypertension (over 100 mmHg diastolic pressure) was 7% before the operation, but rose to 30% in the chronic stage. Application of an “age- and sex-adjusted score” also served to confirm a mean increase in blood pressure through the development of chronic pyelonephritis. No correlation was found between renal function and blood pressure. Nor was there any definite relationship between family history of hypertension and high blood pressure. In the 14 cases observed for plasma renin activity, values were found to be in the normal range.

The relationship between chronic pyelonephritis and hypertension has been widely studied since it was first pointed out by Longcope (1937). There remains a problem, however, as to the cause-and-effect relationship between the two diseases. This may be because blood pressure has been observed in cases of pyelonephritis only after the onset of the chronic stage, and without reference to pre-disease levels. Further, when observations were made over a long period of time, age-related rises in blood pressure may over-lap. A comparative study of blood pressure levels before and after the development of pyelonephritis should help to clarify the relationship between the two diseases.

We examined 46 patients who had developed chronic non-obstructive pyelonephritis after undergone urologic operation. Controls were provided by blood pressure measurements in other urological cases free from pyelonephritis and renovascular hypertension. For the cases of chronic pyelonephritis the relationships between blood pressure and renal function, and between blood pressure and genetic factor were also assessed. In 14 of these cases plasma renin activity was also studied in related to blood pressure.

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Fourty-six cases of postoperative chronic pyelonephritis, 25 males and 21 females aged between 10 and 77 years, were chosen from patients subjected to ureterocutaneostomy or nephrostomy because of urological diseases. These patients were all free from pyelonephritis before the operations. Diagnostic criteria for chronic pyelonephritis were: frequent attacks of pyrexia within two months after operation, pyelographic evidence of dilatation and blunting of the renal calices and pathogenic bacteria in the urine. Cases of diabetes mellitus were not included in the group. Follow-up observations were made for periods of 1–2 years in 20 cases, 2-5 years in 11 cases, 5-10 years in 11 cases, and 10-12 years in 4 cases. The average was thus 3.8 years.

Diastolic blood pressure was measured after the patients had been in the supine position for 15-20 min. Control readings were taken from 126 subjects, randomly selected from urological cases free of pyelonephritis. Blood pressure readings were corrected by an "age- and sex- adjusted score" (Pickering 1968). This age- and sex- adjusted score is a numerical value for the extent to which arterial pressure exceeds or is less than the expected norm. It represents, in the current technological jargon, the degree of hypertension or hypotension respectively. Plasma renin activity was determined in 14 subjects. This was done by radio-immunoassay of blood sampled from the elbow vein after subjects had maintained upright posture for at least an hour.

**RESULTS**

Fig. 1 shows diastolic pressures for the test subjects before operation or the development of pyelonephritis and after confirmation of chronic pyelonephritis. Diastolic pressures in the chronic stage had risen from pre-operative levels in 30 cases (66%) and had fallen in 9 cases (20%). In the other 7 cases (15%) the levels were unchanged. Diastolic pressure levels before disease were 130 mmHg at maximum and 64 mmHg at minimum (average; 82 mmHg). The corresponding figures in the chronic stage were 126 mmHg and 62 mmHg (average; 89 mmHg).

Among the controls, the incidence of hypertension (over 100 mmHg diastolic pressure) was 6% (8 cases). Among the cases of pyelonephritis, the incidence of hypertension before diseases was 7% (3 cases). This figure was almost compatible with the control figure. In the chronic stage it was as high as 30% (14 cases); some 4.5 times the figure before diseases. In 2 of the 3 pyelonephritics patients who were already hypertensive before disease, diastolic pressure levels were 130 mmHg and 102 mmHg. These dropped in the chronic stage to 116 mmHg and 80 mmHg. In the remaining cases the level was unaltered. Thus the number of cases turning from normotensive to hypertensive in the chronic stage was 12 (28%).

**Age- and sex- adjusted score:** For the 126 control cases, the scores for diastolic blood pressure were distributed almost normally, with a figure of -2.54 as mean and 259.82 as variance (Fig. 2). For the 46 subjects with chronic pyelonephritis, the scores for diastolic pressure before disease gave -1.74 as mean and 156.76 as variance. In the chronic stage the scores gave +4.67 as mean and 268.91 as variance. There was thus a distinct increase in the mean value, and the distribution of scores in the chronic stage shifted to the right (Fig. 3). A comparative
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Fig. 1. Diastolic pressure. Comparison between the levels before disease and in chronic stage of pyelonephritis after operation.

Fig. 2. Frequency distribution of scores in the 126 control cases.

Analysis of mean diastolic pressure between levels before disease and the chronic stage showed a significant difference ($0.01 > p > 0.05$), indicating a general rise in blood pressure for pyelonephritic patients in the chronic stage. A comparative analysis between the pyelonephritic cases in the chronic stage and controls also showed a significant difference ($p < 0.01$), suggesting that blood pressure is generally higher in pyelonephritic patients than in other urological cases.
Fig. 3. Frequency distribution of scores of 46 cases before disease and after confirmation of chronic pyelonephritis.

\( \square \), before disease; \( \blacksquare \), in chronic stage.

Fig. 4. Diastolic blood pressure in chronic pyelonephritic cases with a positive family history of hypertension (Group I), and with a negative family history of hypertension (Group II).

**Blood pressure and renal function:** In 24 cases out of the 46 cases, BUN values were compared with diastolic pressure. No significant correlation was found between the two \((r=0.25)\).

**Blood pressure and family history of hypertension:** Diastolic pressures in the chronic stage were compared between patients with a positive family history of hypertension (14 cases) and those with a negative family history of hypertension (32 cases). The mean diastolic pressure for the 14 cases with a positive family history was 90.3 mmHg, with an incidence of 29% for hypertensives (exceeding 100 mm Hg). The mean level for the rest was 86.1 mmHg, with an incidence of 25% for
TABLE 1. Plasma renin activity and diastolic blood pressure in 14 cases

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>Years of follow-up</th>
<th>P.R.A. (ng/ml/hr)</th>
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<tr>
<td></td>
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<td>Before disease</td>
<td>Chronic stage</td>
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<td>76</td>
<td>F</td>
<td>74</td>
<td>84</td>
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<td>F</td>
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Plasma renin activity: Plasma renin activity was determined in 14 of the 46 cases at the time of blood pressure measurement, and values ranging from 0.13 ng/ml/hr to 2.63 ng/ml/hr were found. The mean was 0.78 ng/ml/hr (Table 1). These values were nearly within the normal range, and no correlation of plasma renin activity level with blood pressure was found.

DISCUSSION

The relationship between chronic pyelonephritis and blood pressure can probably be most profitably pursued through comparative analysis of blood pressure values in pyelonephritic patients before the onset of the disease and in the chronic stage. In the present study, 46 chronic pyelonephritic subjects were followed up for an average of 3.8 years. It was found that the incidence of hypertension, diastolic pressure over 100 mmHg, increased by 4.5 times from 7% before the disease to as high as 30% in the chronic stage. Referring this result to the incidence of hypertension in other urological cases with readings adjusted for age and sex, as well as to the results of comparative analysis of mean diastolic pressures between preoperative and chronic stages, it was evident that blood pressure became significantly elevated in patients with chronic pyelonephritis.

Bengtsson et al. (1968), in a 5.3-year follow-up of confirmed chronic pyelonephritic patients, found that the number of hypertensives, diastolic pressure over 100 mmHg, was finally almost twice as large as observed initially. They emphasized a strikingly rapid shift from initial normotensives to chronic stage hypertensives. In agreement to their findings, our results indicate that normotensives before disease turned to hypertensives in the chronic stage in an appreci-
able percentage. The previous studies revealed that the incidence of hypertension in clinical cases of chronic pyelonephritis ranged from 16.6% to 60% (Longcope 1937; Braasch and Jacobson 1940; Brod 1956; Kleeman et al. 1960; Ueda 1965; Bengtsson et al. 1968). Such a difference may be ascribed primarily to the unestablished criteria for diagnosis of chronic pyelonephritis. As has been pointed out, it is difficult to distinguish between nephrosclerosis and chronic pyelonephritis when bacteria are not detected in the urine. Also, as generally observed the incidence of hypertension is different between non-obstructive and obstructive pyelonephritic cases. It is not surprising that different diagnostic criteria lead to different results for the incidence of hypertension. In the present study, obstructive cases were eliminated, and the subjects were limited to closely defined cases of chronic pyelonephritis. The disease was confirmed on the basis of frequent attacks of pyrexia, turbid urine, pathogenic bacteria in the urine, pyelographic evidence of dilatation and blunting of the renal calices. Our follow-up incidence of 30% for hypertensives among these cases is comparable to the relatively low incidence of 38% found by Bengtsson et al. (1968) for hypertensives in their large series of strictly defined cases. These figures may be considered to indicate a valid range for the incidence of hypertension in chronic pyelonephritis.

With respect to the role of inheritance in hypertension, Brod (1956) provided data showing higher levels in diastolic blood pressure for chronic pyelonephritic cases with a positive family history of hypertension. Bengtsson et al. (1969) also reported that a family history of hypertension was three times as common in hypertensives as in normotensives among pyelonephritic patients ranging in age from 20 to 40 years. They stressed the significance of hereditary hypertension, particularly in young patients. They also suspected that the secondary hypertension due to anomaly of the kidney rather than primary hypertension might play a significant hereditary role. This issue, an extremely complex problem of the hereditary influence on hypertension, could not be pursued convincingly in our limited number of cases.

With regard to the relation of renal function to hypertension, Kleeman et al. (1960) reported that their pyelonephritic cases usually showed no correlation between serum creatinine and systolic pressure, though atrophic kidney cases were related to a high incidence of hypertension. On the other hand, Grieble and Jackson (1960), in a study of autopsy cases of nonspecific pyelonephritis, pointed out a positive correlation between decreased renal parenchyma and clinical hypertension. Bengtsson et al. (1968) divided their pyelonephritic cases into three groups, based on varying levels of serum creatinine, and observed that the depression of renal function was associated with an increase in the incidence of hypertension in each group. They noted, however, that there were some instances showing elevation in blood pressure before depression of renal function. In these circumstances, the question arises as to the stage at which the renal depression is linked with blood pressure changes. The terminal stage of renal failure and advanced atrophic kidney may not be linked in the same way to blood pressure levels. In our series, even the
case with the most depressed renal function gave 74 mg/100 ml in BUN value, suggesting that depressed renal function at that degree bore no relationship to hypertension.

It has been generally agreed that renin activity is not associated with elevation of the blood pressure in pyelonephritic patients, although there is some disagreement on this matter (Andrenko et al. 1971). We previously conducted animal experiments in which non-obstructive pyelonephritis was produced in dogs, and plasma renin activity was observed in relation to blood pressure (Tsuchida et al. 1975). Renin activity, except in the acute stage of the disease, tended to become suppressed despite the general rise in blood pressure. In the present investigation of 14 cases of chronic pyelonephritis, the results were similar to the previous report.

References