Seven Cases of Hypertension Due to Segmental Renal Ischemia

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SUMMARY

During the last 10 years, 7 hypertensive patients due to segmental renal ischemia or infarction among total 48 cases of renovascular hypertension have been observed in our clinic.

These 7 cases of renal arterial branch stenosis consist of 5 men and 2 women. The youngest case was aged 12 and the oldest 31. Their blood pressures were ranged from 160-225 mmHg in systolic and from 84 to 150 in diastolic. Abnormal intravenous pyelogram was found in 4 out of 7 cases. So far as our experience was concerned, clinical features, urinalysis, radioisotope renography, renoscintigraphy and split renal function study were of little value for screening of the patients with renal arterial branch stenosis. However, angiography and provocation test of renin secretion are the best tools for making diagnosis of this type of hypertension. Surgical treatment including nephrectomy and revascularization relieved the hypertension in 5 patients. Antihypertensive drugs were given in one of 5 operated cases and in 2 non-operated cases. Six out of 7 patients remained normotensive.

Additional Indexing Words:
Renovascular hypertension Segmental renal infarction Renal arterial branch stenosis Renal aneurysm Angiography Renin Surgical treatment

It has been well known that systemic hypertension can be developed by renal ischemia after constriction of the main renal artery, and be relieved by surgical treatment.1) 2) However, hypertension due to segmental ischemia or infarction in major branches of the renal artery is seldom reported in the previous papers.3) Our purposes in this paper are to present hypertensive patients with branch stenosis of renal artery observed in our clinic and to discuss both etiologic and diagnostic problems from the practical point of view.

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CLINICAL MATERIALS

Since 1961, we have treated 48 cases of renovascular hypertension in whom diagnosis was verified by the physical findings, intravenous pyelography, split renal function test, estimation of plasma renin activity and angiography. In this series, branch stenosis of renal artery was found in 7 cases. There were 5 men and 2 women. The ages ranged from 12 to 31 years. Four out of these 7 patients were younger than 20 years of age.

RESULTS

(1) Clinical Histories

Histories and clinical data are summarized in Table I. Case 1, a high school boy, had a history of trauma on his abdomen during a play of rugby game. Soon thereafter, he complained of his right flank pain with nausea and vomiting for several hours. Two months after this episode, he was noted to have an elevated blood pressure. In Case 3, the first symptom was hemianopsia binasalis. It was one year after the visual onset, that his hypertension was first detected. A loss of axillary and pubic hair and a decrease in libido were also noticed. The other 5 patients were essentially asymptomatic, and hypertension was incidentally detected on a routine physical examination in their schools or companies.

Physical findings were unremarkable except the high blood pressure and hypertensive changes in the ocular fundi. Their systolic blood pressures ranged from 160 to 225 mmHg in 6 out of 7 cases. Severe hypertensive changes corresponding to Keith-Wagener III were found in 3 cases, mild changes in 2 cases and normal in only one case. Case 3 had bilateral optic nerve atrophy. An abdominal bruit was heard in only one (Case 7).

All patients had received one or several kinds of antihypertensive drugs, but in 6 out of 7 patients no effect on blood pressure was observed.

(2) Laboratory Studies

Urinalysis showed albuminuria in 3 cases, but no abnormalities in sediment. Remaining 4 cases had normal urine. The concentrations of serum potassium were 3.7~4.7 mEq/L. Routine renal function studies were performed in all patients. Phenolsulfophthalein test and blood urea nitrogen were normal in all cases. Creatinine clearance was reduced slightly in 2 cases, and para-amino hippuric acid clearance was also reduced in 4 cases. Electrocardiogram showed left ventricular hypertrophy in 5 cases, but enlargement of cardiac shadow in chest-X-ray film was found in only one.

Intravenous pyelography was carried out in all cases. The pyclocaly-
Table I. Histories and Clinical

<table>
<thead>
<tr>
<th>Case</th>
<th>History</th>
<th>Blood pressure</th>
<th>Ocular fundi (KW)</th>
<th>Abdom. bruit</th>
<th>Urine prot.</th>
<th>Gly.</th>
<th>I.V.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 M 16</td>
<td>Trauma on abdomen</td>
<td>224/128</td>
<td>III</td>
<td></td>
<td>+</td>
<td>-</td>
<td>Size R&gt;L (2.5 cm)</td>
</tr>
<tr>
<td>2 F 23</td>
<td>Routine exam.</td>
<td>165/110</td>
<td>I</td>
<td></td>
<td>-</td>
<td>-</td>
<td>Size R&gt;L (1.0 cm) Scalloping</td>
</tr>
<tr>
<td>3 M 31</td>
<td>Loss of pubic hair, Decrease of libido</td>
<td>225/130</td>
<td>Optic atrophy</td>
<td></td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>4 M 12</td>
<td>Routine exam.</td>
<td>208/150</td>
<td>III</td>
<td></td>
<td>+</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>5 F 14</td>
<td>Routine exam.</td>
<td>180/120</td>
<td>I</td>
<td></td>
<td>-</td>
<td>-</td>
<td>Size R&gt;L (2.0 cm)</td>
</tr>
<tr>
<td>6 M 17</td>
<td>Routine exam.</td>
<td>160/84</td>
<td>0</td>
<td></td>
<td>-</td>
<td>-</td>
<td>Normal</td>
</tr>
<tr>
<td>7 M 21</td>
<td>Routine exam.</td>
<td>214/130</td>
<td>III</td>
<td></td>
<td>+</td>
<td>+</td>
<td>Size R=L Scalloping</td>
</tr>
</tbody>
</table>

The length of the right kidney was 2.5 cm less than the left in Case 1, 1.0 cm in Case 2, and 2.0 cm in Case 5. In Case 1, opacity of the lower pole of the right kidney was decreased. Ureteral scalloping was recognized in Case 2 (Fig. 1) and Case 7 in whom the size of both kidneys was equal. The diagnostic usefulness of intravenous pyelography in this type of renovascular hypertension could be observed in 4 out of 7 cases. In remaining 3, this radiologic study failed to show any difference or abnormality between the kidneys.

Radioisotope renography ($^{131}$I-Hippuran) was examined in 6 cases. An abnormal finding was obtained only in one (Case 4) in which the initial spike and the peak value dropped in the affected kidney. On the other hand, normal renogram was found in 5 cases.

Radioisotope renoscintigraphic study ($^{203}$Hg-Neohydrin) was performed in 5 cases. Case 1 showed a decrease in radiomercury uptake in the lower pole of the right kidney (Fig. 2). In other 4 cases, no abnormal finding was
Split renal function studies were carried out in 4 cases. It was very difficult to collect exactly the urine through the ureteral catheterization. Therefore, the tubular rejection fraction ratio by Rapoport calculated from urinary concentration of creatinine and sodium from each kidney was used as an index of the divided renal function. The ischemic pattern was obtained in only one (Case 2). In other 3 cases, no ischemic pattern was found.

(3) Angiography

Angiographic studies with serial abdominal aortography and selective renal angiography were done in all cases in a retrograde manner through the femoral artery. Aortogram of Case 1 showed normal bilateral main renal arteries. However, a posterior branch of the right renal artery was not demonstrated (Fig. 3). In this case, a decrease of radiomercury uptake was found in the lower pole of the right kidney by renoscintigraphic study. From these findings, a posterior infarction of the right kidney resulting from total occlusion of posterior branch artery was considered.

Multiple renal arteries were found in Case 2 (Fig. 4). This patient had
Fig. 1. Excretory urogram of Case 2.

Fig. 2. Renoscintigram of Case 1.
Fig. 3. Aortogram of Case 1.

Fig. 4. Aortogram of Case 2.
Fig. 5. Selective renal angiogram of Case 2.

Fig. 6. Periureteric collateral circulation of Case 2.
Fig. 7. Aortogram of Case 7.

Fig. 8. Selective renal angiogram of Case 7.
Fig. 9. Selective left renal angiogram of Case 3.

Fig. 10. Selective right renal angiogram of Case 3.
3 renal arteries on the right kidney. Two of them (middle and inferior branches) were occluded, and their blood flow was supplied from collateral circulations developed around the pelvis originated from a superior branch (Fig. 5). The periureteric collateral circulation also developed in this case (Fig. 6). Aortogram of Case 7 revealed an extra-renal branch stenosis with poststenotic dilatation (Fig. 7). The peripelvic collateral circulations were observed in this case (Fig. 8).

Renal arterial branch aneurysm was detected in 4 cases. One of them (Case 3) had bilateral multiple intra-renal aneurysms (Figs. 9, 10). Cerebral angiogram in this case also revealed large aneurysms of bilateral internal carotid arteries which compressed the pituitary gland resulting in his hypopituitarism. The other 3 patients (Cases 4, 5, and 6) had an aneurysm of the right renal arterial branch (intra-renal in 2 cases, Fig. 11 and extra-renal in one). No collateral circulation was detected in these cases of renal branch aneurysm.

(4) Plasma Renin Activity

Measurement of plasma renin activity (PRA) in both peripheral and renal venous blood was carried out by the modified method of Pickens and
his associates. Resting peripheral venous blood PRA was measured on specimens collected from fasting patients in recumbent posture in the early morning. To evaluate the reaction of renin secretion, intravenous injection of furosemide (60 mg) followed by taking on upright posture for 2 hours was loaded. Peripheral venous blood PRA was estimated before and after this procedure. Renal venous blood was obtained through the percutaneous transfemoral retrograde catheterization. Estimated values of PRA in peripheral and renal venous blood in these cases are given in Fig. 12.

Resting peripheral venous blood PRA was estimated 13 times in 7 cases. The activity ranged from 3 to 180 ng/ml. As shown in Fig. 12, marked elevation of resting peripheral vein PRA was observed in only 2 (Cases 3 and 4). In Case 4, PRA was estimated 4 times and the activity elevated markedly in 3 occasions, and slightly in one. Other 5 patients had upper normal or slightly elevated peripheral vein PRA at rest.

Stimulation of renin secretion by injection of furosemide and upright posture was carried out in 3 cases having normal resting PRA. Apparent enhancement in renin secretion after this load was found in 2 out of 3 cases. Renal vein blood PRA was measured in 13 patients with essential hypertension as controls. The difference between higher and lower sides of PRA ranged from 0.5 to 10 ng/ml (mean 3.53), and the ratio between both sides ranged from 1.05 to 1.45 (mean 1.23). In 3 out of 6 cases with unilateral branch arterial stenosis, there was a significant elevation of PRA in the af-
fected sides. The ratio between both sides was above 2.0 in these patients. However, remaining 3 cases showed no difference in renal vein PRA between affected and unaffected sides.

(5) Surgical Treatment

Five out of 7 patients underwent a surgical operation for relief of hyper-

![Graph showing blood pressure, plasma renin activity, and albuminuria](image)

**Fig. 13.** Pre- and post-operative course of blood pressure, plasma renin activity and albuminuria in Case 2.

![Section of the extirpated kidney](image)

**Fig. 14.** Section of the extirpated kidney in Case 2.
tension. In Case 2, an attempt was made initially to revascularize the ischemic kidney. The reconstruction of a new vessel with 2 branch arteries (middle and inferior) and the end to side anastomosis of this vessel to aorta with Dacron graft were performed. After the operation, systemic blood pressure suddenly rose from 170–180/120 mmHg to 220–230/180–190 mmHg and peripheral venous blood PRA elevated remarkably (Fig. 13). Albuminuria appeared and rapidly increased. Patient complained of severe headache. On the fifth postoperative day, papilloedema was observed in ocular fundi. Nephrectomy was subsequently performed. A fresh thrombus was observed in the lumen of the reconstructed vessel. The extirpated kidney was demonstrated in Fig. 14. Extensive necrosis was observed in apical, upper and middle segments of this kidney. Renin content in necrotic infarcted area decreased below 1 ng/mg of tissue/hr, but it increased markedly in ischemic area near infarct to the level of 240 ng/mg of tissue/hr. After nephrectomy, her blood pressure returned to normotensive. However, one month
after discharge, her blood pressure again became slightly elevated requiring antihypertensive drug (thiazide) for control. This patient remained in normal blood pressure with this drug one year after the operation.

On the other hand, nephrectomy was chosen for the initial treatment in 4 patients including 2 cases of right renal arterial branch aneurysm (Cases 4 and 5), one of intra-renal branch arterial occlusion (Case 1) and one of extra-renal branch arterial stenosis (Case 7). All 4 patients were normotensive and asymptomatic postoperatively. The extirpated kidney of Case 1 showed sharply localized cureiforme infarct in the lower segment of this kidney (Fig. 15).

There were 2 non-operated cases in the present series (Cases 3 and 6). Because Case 3 had bilateral multiple branch arterial aneurysms, the reconstructive surgery was thought to be impossible. This patient was treated with α-methyl-dopa and propranolol which suppressed renin secretion from the kidney. In remaining one (Case 6), hypertension was well controllable by drug therapy.

**DISCUSSION**

Evidence that systemic hypertension is caused by segmental renal ischemia or infarction has been accumulated in many experiments on animals. In 1946, Loomis\(^5\) observed that hypertension was developed in all rats when more than 25% of normal renal tissue was deprived by renal infarction. Approximately one third of these rats showed blood pressure above 200 mmHg. In his experiment, the more the normal renal tissue was reduced, the severer the hypertension turned to be. This observation was also confirmed by Klapproth\(^6\) in dogs.

In human subjects, however, little is known about whether or not renal segmental infarction or ischemia give rise to hypertension. Although the association of hypertension and renal infarction has been reported occasionally, only few papers were found in which hypertension was proved to be due to partial infarction or ischemia of the kidney. In 1940, Hoxie and his associate\(^7\) reviewed the protocols of 14,411 autopsies performed at the Los Angeles County Hospital, and selected 205 patients with renal infarcts. They found that 34 patients (16.6%) out of them had the blood pressure above 140/90 mmHg. However, no evidence could be obtained that their hypertension was, with no doubt, due to the renal infarction. In 1969, Benraad and his associates\(^3\) reported a case with acute severe hypertension caused by segmental infarction in whom hypertension was satisfactorily treated by antihypertensive drugs. On the contrary to this, there were few publications in which patients with
segmental renal ischemia were relieved from their high blood pressure by nephrectomy or partial nephrectomy of the affected kidney.\(^8\),\(^9\) In 48 cases of renovascular hypertension in our clinic, approximately 15 per cent of cases belonged to this type of hypertension. This value seemed to be unexpectedly high and it should be emphasized that almost all these patients were asymptomatic resembling essential hypertension.

In 1970, Arakawa\(^10\) found a transient elevation of plasma renin activity after attacks of renal infarction in 3 cases of cardiac valve lesions. However, no significant elevation in their blood pressure was observed. The similar case was reported in 1971 by Morimoto and his associates.\(^11\) As mentioned above, severe hypertension developed rapidly with remarkable increase in peripheral vein plasma renin activity in Case 2. Plasma renin activity increased 100 times of preoperative level following renal infarction by thrombus formation in the reconstructed vessel. After nephrectomy, her blood pressure and plasma renin activity returned to normal range. From these findings, it was convincing that renin played a role in the origin of hypertension in this case.

Generally speaking, diagnosis of renovascular hypertension could be established by means of clinical features (abdominal bruit) and the laboratory examinations including intravenous pyelography, radioisotope renography, renoscintigraphy, split renal function test, estimation of plasma renin activity, and angiography.\(^12\) We believed that it was not difficult to detect the typical renovascular hypertension due to constriction of main renal artery with com-

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**Fig. 16.** Frequency of abdominal bruit and abnormal laboratory findings.
bination of these procedures. However, it was very difficult to detect the particular type of renovascular hypertension due to segmental renal ischemia or infarction. Renography, renoscintigraphy and split renal function study were of little value in screening the patients of this type (Fig. 16). From the present study, we concluded that most available diagnostic procedures for the diagnosis of this type of renovascular hypertension were angiographic examinations (serial abdominal aortography and selective renal angiography) and provocation test of renin secretion by i.v. injection of furosemide followed by upright position.

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