A CASE OF RENOVASCULAR HYPERTENSION WITH THE NEPHROTIC SYNDROME

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BERLYER, *Tavill* and *Barker* in 1964,¹ described 3 patients with the nephrotic syndrome and renal artery stenosis together with 10 additional cases from the literature. Of these cases 2 were children. Since they pointed out the complex of the two diseases, only one case of an infant, to our knowledge, has been reported by *Pasternack* and *Krohn*.² The present paper deals with a case of a boy with unilateral stenosis of the renal artery presumably congenital, and the subsequent nephrotic syndrome, and malignant nephrosclerosis of the contralateral kidney.

CASE REPORT

The patient, a 6 years old boy of Japanese extraction, was referred to us with chief complaints of head ache, abdominal pain, thirst, polyuria and vomiting. He was delivered at full term without complication. His progress was uneventful until 2 years of age when the first episode of abdominal pain and vomiting was encountered. Thereafter such episodes were noted at a rate of approximately once every week for 6 years. On admission he was dull and lethargic. He weighed 21 kg (normal range 21.8 ± 2.7) and his height was 115 cm (normal range 118.8 ± 5.0). No edema was present. An examination revealed marked retinal arteriosclerosis with hemorrhage and exudates, cardiac enlargement with systolic murmur, and a blood pressure of 230 mmHg systolic and 190 mmHg diastolic. Investigation showed urinary albumin to be 3.0 g per day, and a few casts and erythrocytes. Daily urine volume ranged from 600 ml to 1,000 ml.

Key Word: Renovascular Hypertension

Heamoglobin content was 10.1 g per 100 ml. Serum cholesterol 325 mg per 100 ml; serum total protein 5.0 g per 100 ml (Albumin 46.4%, α_1 globulin 14.6%, α_2 globulin 22.1%, β globulin 16.7%, γ globulin 1.0%), serum sodium 141 mEq/L, potassium 3.1 mEq/L, chloride 101 mEq/L, and total CO_2 32 m-mol/L. Serum urea nitrogen 16.5 mg per 100 ml. PSP test 34.5% at 15 min; endogenous creatinine clearance 102 ml/min/1.73sqm. Maximum specific gravity of urine 1,006. Urinary VMA negative. Urinary 17KS 2.0 mg/day, 17 OHCS 8.0 mg/day. Regitin test revealed normal.

Intravenous pyelogram showed that the right kidney was functioning poorly and the left kidney excreted contrast medium normally with normal pelvis and calyces, while stenosis of the renal artery was found in the left side by retrograde femoral aortogram. Renogram using sodium iodhipran ¹³¹I demonstrated a reduced renal blood flow and a diminished active secretory process in both kidneys indicating that not only stenotic side but also the opposite side were involved. The clinical diagnosis was renovascular hypertension with nephrotic syndrome. During the clinical course the blood pressure ranged from 210/170 mmHg to 258/208 mmHg. No response to antihypertensive drugs was observed. The patient died with bloody diarrhea and hematemesis due to intestinal perforation on the 46th day of hospitalization.

AUTOPSY FINDINGS

The heart was enlarged due to left ventricular hypertrophy. Atheromatous plaque in the coronary arteries were present. There was a bifurica-

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Fig.1. Intravenous pyelogram and aortogram of the patient. Arrow indicates arterial stenosis. Note non functioning contralateral kidney.

Fig.2. High power view of the left renal artery. Neither fibrous thickening nor atheromathous degeneration is observed.

tion approximately 1.5 cm from the aorta in the left renal artery from where the artery was separated into two pathways leading to the left kidney. When the vessels were opened, annular and valvar node was observed in the region of the

bifurcation, and thus the lumen was reduced by less than one third of contralateral renal artery in diameter. Microscopically the node consisted of a proliferation of connective tissue of the vessel without the inflammatory infiltrates. No deposition of fibrous tissue in the intimal layer was observed. The finding was interpreted as congenital rather than acquired.

The left kidney, 55 g was of normal appearance. In the right side the weight of the kidney was identical with that of left side, but the external surface was granular. The corticomedullary demarcation was obscured. The left kidney revealed glomeruli with normal tufts except for slight hyperplasia of the juxta-glomerular apparatus. The right kidney exhibited extensive vascular, glomerular and tubular damage. The arterioles, small and medium sized arteries showed marked intimal thickening due to endothelial hyperplasia and subintimal fibrosis. Fibrinoid necrosis of the entire circumference of some vessels were identified in sections stained with PTAH. Fibrinoid change was apparent in some glomeruli and some capillary loops. Many tubules were atrophied and contained hyaline, granular casts. The interstitial tissue in some places showed marked lymphocytic infiltrates. Widespread severe sclerotic degeneration of arterioles was seen in all organs except in the left kidney. Especially in the small intestine many arterioles of submucosa exhibited fibrinoid necrosis and were occluded by thrombi, which resulted in the multiple intestinal necrosis and perforation. Inflammatory infiltrates mostly of neutrophilic

Fig.3. Section of right kidney showing fibrohyaline thickening of the walls of smaller arteries. Hematoxylin and eosin.

cells accompanied these changes.

DISCUSSION

In general the pathogenesis of intrinsic renal artery stenosis are thrombosis, arteriosclerosis and syphilitic arteritis in adults^{1,3} and neurofibromatosis, fibromuscular dysplasia in children^{4,5}. Therefore it is of interest that the cause of the left arterial stenosis in the present case was an annular and valvar node in the wall and microscopic examination revealed that the node did not arise from atheromatous degeneration, fibromuscular dysplasia or inflammatory infiltration but rather from proliferation of connective tissue alone suggesting the cause to be congenital rather than being acquired. It was surmised that the renal hypertension was of a long standing. This possibility was supported by the fact that in the patient's history repeated headaches and vomiting were noted since 2 years of age. Autopsy findings in the present case were compatible with that of the malignant hypertension with nephrosclerosis of the opposite side stenosis. Although differential renal vein plasma renin activity determination or split kidney function test were not performed, the accumulated clinical⁶⁻⁸ and experimental⁹⁻¹¹ observations will give a reliable explanation for the present case as follows: the initial hypertension might be associated with the release of renin from the

occluded kidney as evidenced by the fact of hyperplasia of the juxta-glomerular apparatus in the left kidney. During the long standing chronic state, the arteries and arterioles in the contralateral kidney become hyperplastic and the form of the hypertension was changed to malignant, which, was accompanied with wider-spread severe sclerotic degeneration of arterioles in all organs except for the stenosis-side kidney.

The pathogenesis of nephrotic syndrome in association with renal artery stenosis has not been conclusively established. In the present case, it is likely that severe hypertension due to malignant nephrosclerosis and congestive heart failure on a hypertension-basis produced a gross albuminuria as high as 3.0 g per day leading to hypoalbuminemia and hypercholesterolemia, although the causal relationship between the two is still a matter of discussion. With regard to the therapy, repair of the renal artery or right nephrectomy was discussed by urologists and surgeons, but surgical treatment was thought to be contraindicated at the stage of the admission, because the contralateral kidney was severely involved as shown by pyelography and renogram. A similar conclusion was made retrospectively by autopsy findings. It is clear then that nephrectomy in unilateral renal artery stenosis can only bring favorable prognosis when the condition is discovered early.

SUMMARY

A case of a 6 year old boy is presented in which unilateral renal artery stenosis assumed to be congenital based on histological findings and subsequent malignant nephrosclerosis of the contralateral kidney and nephrotic syndrome probably due to gross albuminuria were observed.

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