Stenosing renal artery disease in children

Clinicopathologic correlation in 20 surgically treated cases

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Stenosing renal artery disease in hypertensive children encompasses a wide spectrum of clinical and pathologic parameters.[1–9] Since 1955, 20 children, 12 girls and 8 boys aged 1 to 18 years, were treated surgically at the Cleveland Clinic Hospital for renovascular hypertension (*Table*). Thirteen of the children were asymptomatic, but were noted to be hypertensive during the course of routine physical examination. Preoperative diastolic blood pressures ranged between 95 and 140 mm Hg. Eight of the 20 children had bilateral stenosing renal artery disease and three had associated extrarenal artery disease. In addition, two other children had bruits over the femoral and carotid arteries, although confirmation of stenosing artery disease by arteriography was not obtained. One girl (case 18) also had clinical von Recklinghausen's neurofibromatosis. No cases of renal artery stenosis associated with congenital rubella were encountered. Renal artery stenosis due to atherosclerosis, posttraumatic thrombosis, embolus, or extrinsic compression of the renal artery was excluded from this study. Also excluded were children in whom nephrectomy was performed without removal of the stenotic arterial segment. Surgical therapy included either revascularization or nephrectomy.

Table. Clinical results in 19 children operated on for renal artery stenosis

Lesion	Sex, age (yr)	Side	Site	Preop BP, (mm Hg)	First operation	Second operation	Results
Intimal fibroplasia							
Case 1	F 1	R	Prox	155/125	N.	...	Normotensive 9 yr
Case 2	M 10	L	Dist-B	230/120	SN	...	Recurrent mild hypertension 6 mo postop; well-controlled with medication
Case 3	F 14	R	Prox	165/115	SRA	N	Postop thrombosis of SRA; normotensive 9 yr after nephrectomy
Case 4	M 14	R,L	Prox	200/120	E(L)	E(R)	Normotensive 3 yr
Case 5	F 3	L	Prox	185/110	SRA	N	Persistent hypertension after initial surgical procedure; arteriogram revealed thrombotic stenosis at SRA; normotensive 3 yr after nephrectomy
Case 6	F 10	R,L	Prox	195/125	N(R)	...	Left renal artery stenosis diagnosed by arteriogram 15 mo postop; refused permission for second operative procedure; hypertensive 13 yr despite medication
Medial hyperplasia							
Case 7	M 15	R,L	Prox	180/105	AG(L)	AG(R)	Restenosis, left anastomosis, 10 mo postop; hypertension refractory to medication; died 11 hr after surgery; permission for autopsy not granted
Case 8	F 12	L	Mid	190/130	E	SRA	Recurrent hypertension 3 mo after revascularization; arteriogram revealed stenosis proximal to anastomosis; normotensive 4 yr after SRA
Case 9	F 9	L	Dist-B	155/125	N	...	Normotensive 9 yr
Perimedial fibroplasia							

Table —*Continued*

Lesion	Sex, age (yr)	Side	Site	Preop BP, (mm Hg)	First operation	Second operation	Results
Case 10	M 17	R,L	Dist-B (R) Dist (L)	210/120	N(R)	SRA(L)	Died 3 wk after left revascularization procedure (oliguria, hypertensive encephalopathy, spontaneous hemopericardium); permission for autopsy not granted
Case 11	M 12	R,L	Prox (R) Dist (L)	190/130	N(R)	N(L)	Recurrent malignant hypertension 8 mo after right nephrectomy required emergency surgery; revascularization technically not feasible; anephric, awaiting transplant
Case 12	F 11	R,L	Prox. (R) Mid (L)	260/140	SVG(R)	E(L)	Normotensive with medication 3 yr
Case 13	M 14	R	Prox	140/95	SVG	...	Normotensive 4 yr
Case 14	F 14	R,L	Prox (R) Mid (L)	155/110	SRA(L)	N(L)	Postoperative thrombosis of SRA; normotensive with medication 6 yr after nephrectomy
Case 15	F 10	R	Dist	175/130	E	N	Recurrent hypertension 1 mo after revascularization; normotensive 2 yr after nephrectomy
Case 16	F 4	L	Dist	170/130	SRA	...	Postoperative stenosis of splenic artery proximal anastomotic site with recurrent hypertension; normotensive with medication 1.5 yr; awaiting left nephrectomy
Case 17	F 2	R,L	Mid	170/140	N(L)	...	Nephrectomy for severe ischemic atrophy of left kidney; normotensive with medication 1 yr; to be evaluated for right renal artery revascularization after further body growth and development
Case 18	F 12	R	Prox	180/120	AG	...	Normotensive 1.5 yr
Medial dissection							
Case 19	M 10	L	Mid	195/120	SRA	...	Recurrent hypertension 2 yr after revascularization; arteriograms revealed patent anastomosis with development of distal branch disease; normotensive with medication 10 yr
Case 20	F 10	R	Prox Dist B	210/140	SVG	...	Recurrent hypertension 6 mo after revascularization; normotensive with medication 18 mo

R = right; Prox = proximal third of renal artery; N = nephrectomy; L = left; Dist = distal third of renal artery; B = primary arterial branch; SN = segmental nephrectomy with excision of stenotic arterial segment; SRA = splenorenal anastomosis; E = excision of stenotic segment with primary anastomosis; AG = bypass arterial homograft; Mid = middle third of renal artery; SVG = bypass saphenous vein graft.

The pathologic classification of fibrous and muscular renal artery disease is based upon the layer of the arterial wall involved.[10] The stenosing lesions in this series included intimal fibroplasia, medial hyperplasia, perimedial fibroplasia, and medial dissection.

Primary intimal fibroplasia (cases 1 through 6) is an extremely rare cause of renovascular hypertension in adults,[10] yet was a common variant in the pediatric group. The arterial segments with loss of internal elastica appeared on arteriograms as aneurysmal dilatation. The arteriographic appearance of segments in which the internal elastica was principally intact was that of narrowing with poststenotic dilatation (*Fig. 1*). Unlike the renal arteries of the adult counterparts, renal arteries in children with primary intimal fibroplasia were uniformly involved by fragmentation, partial absence, and reduplication of the internal elastica[11–14] (*Figs. 2 and 3*). The possibility of atherosclerosis as a cause in this group was excluded clinically by lipid profiles and histologically by the absence of demonstrable lipid with special staining techniques. Five of the six renal artery segments involved by intimal fibroplasia were narrowed in the proximal third. Two children with primary intimal fibroplasia had asymptomatic extrarenal arterial stenosis as demonstrated by repeated arteriographic examinations. One patient, a 14-year-old boy, had bilateral renal artery stenosis, superior mesenteric artery stenosis, and total occlusion of the gas-

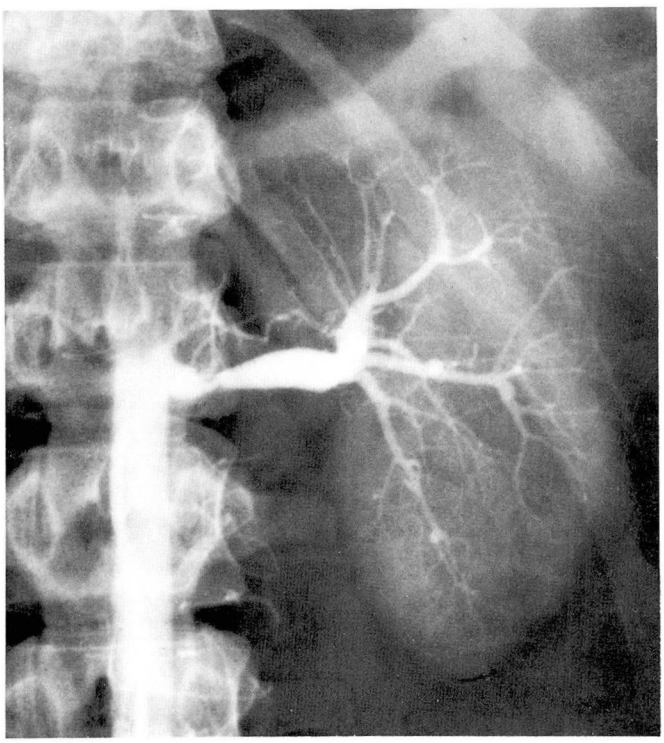

Fig. 1. Case 6. Aortorenal arteriogram. Proximal stenosis due to intimal fibroplasia. Note poststenotic dilatation.

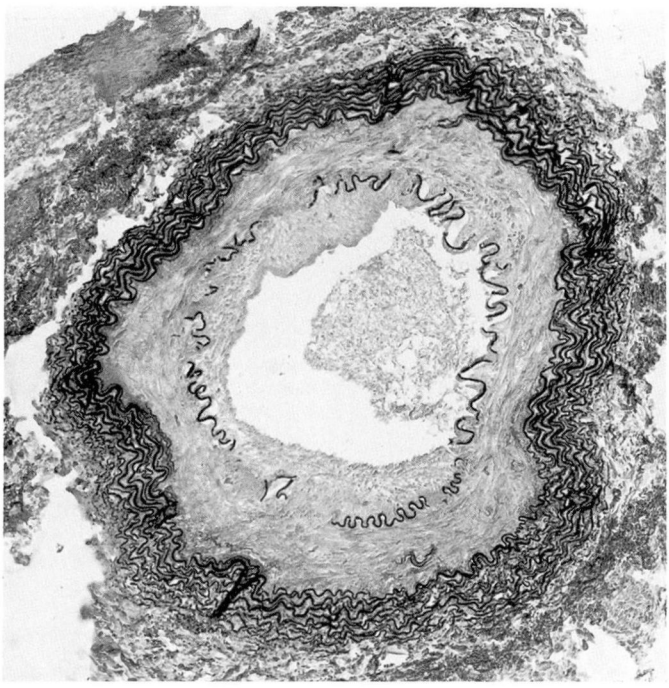

Fig. 2. Case 1. Photomicrograph cross section demonstrating intimal fibroplasia with focal fragmentation and partial absence of the elastica interna (Verhoeff elastic van Gieson, ×64).

troduodenal branch of the celiac artery (case 4); another patient, a 10-year-old girl, had left renal artery stenosis and hypoplasia of the abdominal aorta (case 6).

The arterial segments involved by medial hyperplasia (cases 7, 8, and 9) demonstrated by arteriography irregular narrowing with poststenotic dilatation. Stenosis resulted from the protrusion of proliferating smooth muscle masses admixed with a lesser amount of collagen into the arterial lumen (*Fig. 4*).

The renal artery segments involved by perimedial fibroplasia (cases 10 through 18) uniformly demonstrated a thick circumferential cuff of collagen surrounding and partially replacing the outer one half to two thirds of the media. The integrity of the lumen in arterial segments with perimedial fibroplasia was further compromised by a process of secondary intimal fibroplasia (*Fig. 5*). One of us (LJM) has previously suggested that this secondary thickening of the intima is related to slowing of blood flow through a narrowed arterial segment, with resultant platelet and fibrin deposition and subsequent fibrous organization.[11] Bilateral involvement was noted in five of nine children with perimedial fibroplasia of renal artery circulation. One of these children had vague abdominal pain and further arteriographic studies indicated significant narrowing of the inferior mesenteric artery (case 12).

The two cases of medial dissection (cases 19 and 20) were characterized on arteriogram as diffusely dilated renal arterial segments (*Fig. 6*). Pathologic examination revealed large dissecting channels in the outer one

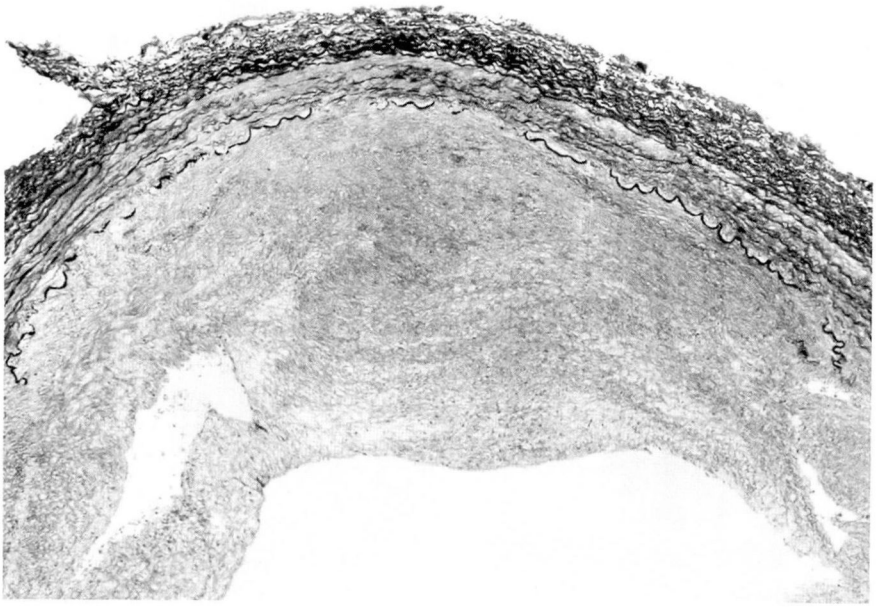

Fig. 3. Case 5. Photomicrograph cross section of severe renal arterial intimal fibroplasia with a dense cuff of intimal collagen apposed to the luminal surface of a partially disrupted elastica interna. A small recanalized channel is noted in the lower left (Verhoeff elastic van Gieson, ×50).

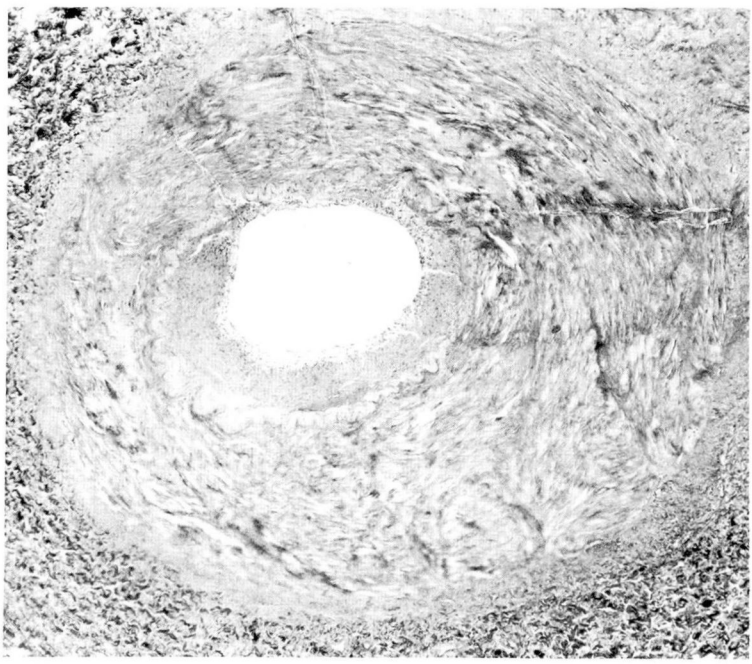

Fig. 4. Case 8. Photomicrograph cross section of medial hyperplastic process with severe compromise of renal arterial lumen (Masson trichrome stain, ×40).

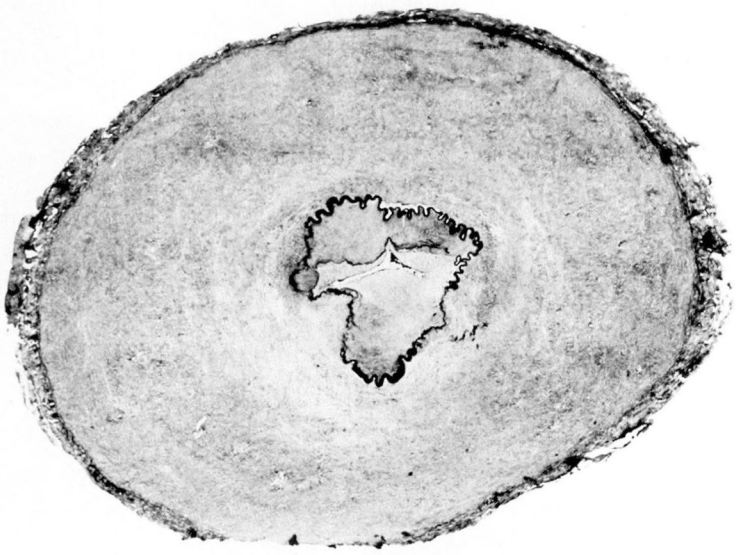

Fig. 5. Case 11. Photomicrograph cross section of perimedial fibroplasia manifested as a dense fibroplasia of the outer media with loss of the elastica externa. Note the significant secondary intimal fibroplasia (Verhoeff elastic van Gieson, ×20).

half of the media (*Fig. 7*). These lesions are thought to develop because of defects in the internal elastica with resultant medial dissection and aneurysmal dilatation.

Medial fibroplasia with microaneurysm formation is the most common cause of nonatherosclerotic renovascular hypertension in adults,[10] yet was not encountered as a histologic variant in the pediatric group. Periarterial fibroplasia, the rarest of all stenosing renal artery lesions,[10] was not represented in this series.

Considering the high frequency of bilateral renal artery stenosis in children, the main consideration regarding surgical therapy is preservation of renal parenchyma by attempted vascular repair. This protocol is based upon the premise that partial or complete nephrectomy can be performed in the future if clinical hypertension has not been relieved by revascularization. Partial or total nephrectomy in this series was performed only because of extension of the stenotic lesion into renal artery branches or because of technical inability to bypass or resect the main renal artery lesion. Revascularization procedures were least successful in patients with stenotic distal renal arterial segments in close proximity to primary renal artery branches. Postoperative restenosis of a revascularized renal artery occurred in six patients. The cause of restenosis was postoperative thrombosis in three cases. Failure to excise totally the stenotic segment, or the formation of excessive cicatrix in the healing phase at the operative site are other probable causes of restenosis.

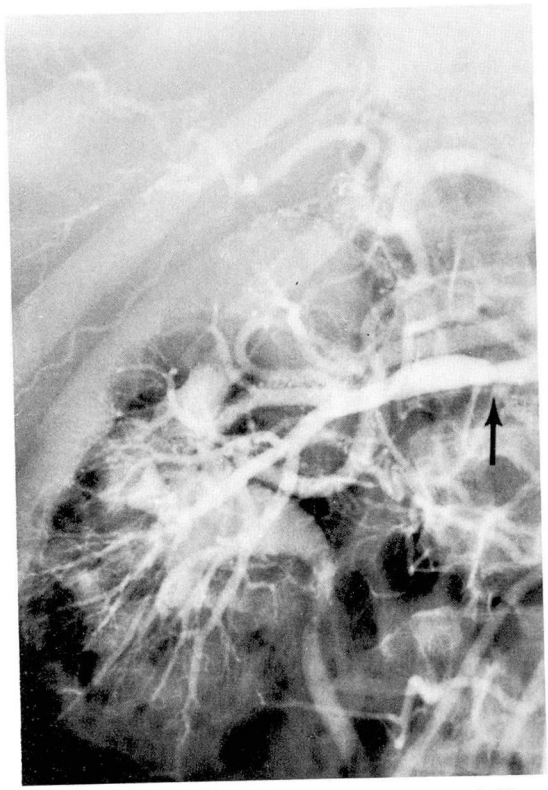

Fig. 6. Case 20. Renal arteriogram showing an elongated segmental dilatation of the renal artery due to medial dissection (arrow).

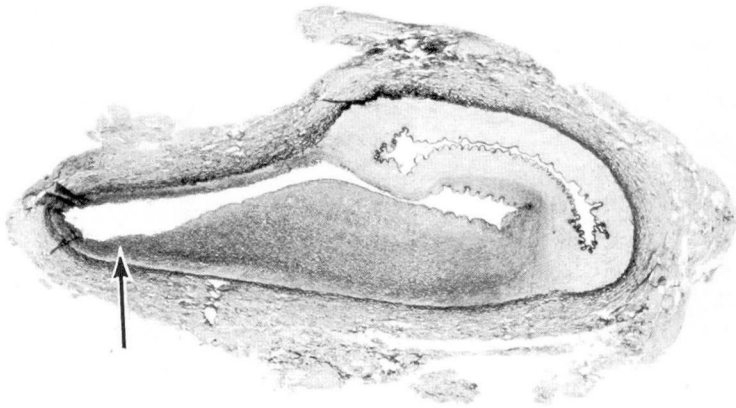

Fig. 7. Case 20. Photomicrograph tangential cross section of renal arterial segment with medial dissection. The arrow indicates the dissecting channel. The elastica interna of the true lumen is principally intact (Verhoeff elastic van Gieson, ×10).

Nine of 12 children with unilateral disease are normotensive without medication 2 to 9 years following surgery. Four of the nine children considered surgical "cures" of hypertension had revascularization only, whereas five children eventually required nephrectomy. Of the three remaining children in whom there was no relief of hypertension after surgery, segmental branch disease developed in one after revascularization, but reoperation was refused (case 19); the second child was lost to follow-up 6 months after segmental nephrectomy (case 2); a third child has stenosis of the splenic artery proximal to a splenorenal anastomosis and is presently being evaluated for a possible nephrectomy (case 16). Of eight hypertensive children with bilateral renal artery stenosis, there was only one surgical "cure" (case 4).

Regarding methods of predicting which patients will benefit from surgical therapy, we have evaluated many parameters including measurements of pressure gradients across the renal artery stenosis, ipsilateral and contralateral renal vein renin activity, peripheral venous renin activity, bilateral biopsy examination for arteriolar changes, and assessment of juxtaglomerular apparatus cellularity. In the present series, renal biopsy specimens were too small to allow for evaluation of cellularity in a significant number of juxtaglomerular apparatuses. Unlike previous observers,[15] we were unable to correlate the degree of bilateral intrarenal arterial and arteriolar sclerosis as a prognostic indicator for relief of hypertension following revascularization for nephrectomy. Our data suggest that assay of split left and right renal vein renin blood samples has proven to be the best parameter in evaluating the significance of a unilateral stenosing renal arterial lesion (ratio greater than 1.5 to 1.0).

Regarding etiology, none of these children manifested evidence of infantile syphilis or rubella. There was no history of drug ingestion. The rarity of thrombosis militates against the various arteritides. We believe these lesions to be congenital dysplasias with maldevelopment of the fibrous, muscular, and elastic tissues of the renal artery. It is a distinct possibility that the majority of patients that we have seen between the ages of 20 to 45 years with renal arterial intimal fibroplasia, medial hyperplasia, perimedial fibroplasia, and medial dissection have had undetected primary renovascular hypertension of childhood.

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