Original Paper

Renal Artery Stenosis Due To Ischemic Nephropathy

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ABSTRACT This paper approach a relatively old problem: renovascular hypertension in atherosclerotic renal artery stenosis, and a relatively new one: ischemic nephropathy. In recent years, ischemic nephropathy has been recognized as a cause of increasingly frequent chronic renal failure that requires initiation of alternate therapy failure. This has led to the develop-ment of new methods of diagnosis and treatment of vascular stenosis, such as Duplex ultrasonography, spiral CT, MRI angiography, selective renal angio-graphy that provide morphological and functional proper diagnosis in all cases. Were followed 386 patients with renal failure (203 with acute renal failure and 183 with rapidly progressive renal failure) hospitalized in Depart-ment of Nephrology, "St. John" Emergency Hospital Bucharest between 2006 and 2009. Of these, 85 patients had hypertension and were investigating the direction of possible secondary hypertension, renal origin. Only 16 were found to have renovascular hypertension and were the group of interest in this article. Have been performed screening tests for possible renal artery stenosis: with and without renal scintigraphy, Doppler ultrasound, renal arteriography. Scintigraphy changes were present in 11 of the 16 patients before Captopril administration. At four of them, the changes occurred after Captopril administration. Doppler ultrasound was performed at seven of the 16 patients watching the morphology of renal arteries, blood flow aspect, velocity and resistivity indices. Only five of the seven patients had changes suggestive, the two could not be performed because of obesity. Arteriography has been performed at all patients and showed atherosclerotic lesions at 11 patients (five of them with bilateral lesions), fibromuscular dysplasia in three patients (one with bilateral lesions), one case of abdominal aorta with dissection extended to the renal arteries and one with renal artery hypoplasia. Corrections artery stenosis was performed in seven patients: angioplasty – one case, angioplasty with stent implantation – five cases and unilateral nephrectomy with angioplasty and contralateral stent – one case. In long term were followed only six patients. Normalization of blood pressure was obtained at one patient (angioplasty on single stenosis without poststenotic dilatation), with normalization of renal function; at the other six, arterial hypertension has improved slightly, with reduction of antihypertensive drugs and stops the deterioration of renal function.

KEY WORDS *ischemic nephropathy, renal artery stenosis, renovascular hypertension, chronic renal failure*.

Introduction

Renal artery stenosis is the most common etiology of atherosclerotic renal artery disease, being associated with two major clinical syndromes: major ischemic disease and reno-vascular hypertension secondary. Renal artery stenosis (RAS), ischemic nephropathy (IN) and hypertension are combined in varying proportions. The HTA is not a constant when renal artery stenosis and renal function can be preserved for a time, despite significant anatomical narrowing of the renal artery.

In recent years, IN has been recognized as a cause of increasingly frequent and chronic renal failure requiring initiation of dialysis therapy. This finding led to the development of new methods of diagnosis and treatment of vascular stenosis, such as duplex ultrasonography, spiral CT, MRI angiography, selective renal angiography – which ensures the correct diagnosis, morphological and functional, in all cases and varied techniques of vasculature [13]. The evolution of atherosclerotic renal artery stenosis by IN and IRC is partially known, some cases of IRC in renovascular hypertension were assigned strictly hypertension. It is estimated that between 5–15% of cases of IRC is produced by SAR and IN, the proportion is even higher for patients with terminal CKD receiving dialysis.

Material and Methods

Between 2006–2009, in the study were included, at the Department of Nephrology, "St. John" Emergency Hospital, Bucharest, 386 patients with renal failure, in which 203 presented acute renal failure (IRA) and 183 with rapidly progressive renal failure. Of these, 85 patients had hypertension and were investigated systematically in the direction of possible secondary hyper-tension, primarily renal.

Only 16 were found to have renovascular hypertension and consisted of interest of this work group. Were followed clinical aspects, laboratory and treatment.

On the clinically point of view, it had the characteristics considered suggestive of diagnosis: severe hypertension or refractory to treatment; systolic-diastolic abdominal breath, acute blood pressure increase on a previous run stable, acute pulmonary edema superadded to an incompletely

controlled hypertension and a renal failure, IRA occurred during treatment of hypertension, especially with ACEI, progressive azotemia at an elderly person with severe and refractory hypertension, progressive azotemia at an elderly person with multiple atherosclerotic determinations (peripheral, coronary, cerebral, carotid).

Laboratory examination investigated in detailed kidney function: urea, creatinine, creatinine clearance, urine examination ("summary" of urine, proteinuria per 24 hours).

Renal scintigraphy has been performed in all patients with ^{99}Tc–DTPA.

Renal ultrasonography has been performed in all patients with hypertension. Were watched kidney size, thickness and appearance of parenchymal kidney, adrenal glands. Ultrasonography was completed in seven of the 16 patients with color Doppler examination in pursuing the morphology and appearance of renal artery blood flow, velocity and resistivity indices.

Arteriography-access site was femoral artery. Were used nonionic dye (Ultravist, Omnipac). The first injection of dye was made above the renal arteries to detect the ostium and juxta-aortic portion of this, and then switched to selective and supraselective renal arteriography injecting dye into the main renal arteries and their branches.

Therapy was represented by antihypertensive medications, revascularization and nephrectomy techniques. The revascularization consisted of percutaneous endoluminal angioplasty with and without implantation of stent. In some patients, dilation was followed by the introduction of stents to keep the patent vessel and prevent restenosis. Nephrectomy has been applied in antihypertensive propose, on small kidney with weak or no renal function.

Results

Of the 85-hypertensive patients, 16 were found to have renovascular hypertension, respectively single or bilateral stenosis of renal artery. The average age of patients was 60 years, seven women and nine men.

On 7/16 of patients artery hypertension were severe (systolic pressure – 190 mmHg and diastolic pressure – 110 mmHg), the 3/16 have highlighted systolic-diastolic abdominal pocket, 4/16 had recurrent pulmonary edema, 12/16 patients developed IRA mild transient after ingestion of ACE, and 4/16 had an overheating of the IRC in early stage after stroke.

On 11/16, the difference in length (on the axis of maximum) of the kidney exceeded 1.5 cm.

From the analysis of risk factors for hypertension was observed that 8/16 were suffering from systemic arterial (cerebral, coronary and peripheral), 10/16 had hypercholesterolemia, 7/16 were smokers over 10 cigarettes per day, all men.

Without and with Captopril renal scintigraphy has been performed in all patients. In 11/16 of the patients had changes suggestive of renal artery stenosis before Captopril administration: vascular and excretory slower phase, differences between kidney function and size. On 4/16, changes occurred after Captopril administration.

Doppler ultrasonography showed characteristic changes in 5/7 patients: the narrowed artery and turbulent flow accelerated, increasing in velocità stenosis, Parvus tardus. On 2/7n could not be performed because of obesity.

Three patients had resistance index of over 80% segmentation arteries, with one small kidney, under 7 cm in length. Hypertension in these patients did not respond to Captopril. Angioplasty was performed by placing the stent, TA improving slowly.

Four patients had the busiest segmentation resistivity indices below 80%. One of them had bilateral renal artery stenosis, with one small kidney less than 60 mm, hypertension failing to respond to Captopril. Kidney nephrectomy was performed for low dimensions and on the other hand, transluminal angioplasty was performed by placing a stent. Blood pressure decreased, without normalize. The other three have had kidney size over 90 mm, their blood was reduced to Captopril. Stent angioplasty was performed at one of them with single stenosis without poststenotic dilatation and at the other two, one with atherosclerotic stenoses and one with fibromuscular dysplasia, dilation was completed by placing a stent.

Table 1 – Cases of renal artery stenosis (16 patients)

Etiology	No. of cases	Bilateral lesions
Atherosclerosis	11	5
Fibromuscular dysplasia	3	1
Dissection of abdominal aorta	1	–
Renal artery hypoplasia	1	–
Overall	16	6

Table 2 – Treatment of renal artery stenosis

		No. of cases	Total
Invasive treatment	Angioplasty	1	7
	Angioplasty + stent	3 + 2	
	Nephrectomy with angioplasty and contralateral stenting	1	
Drug treatment	–	9	9
Overall			16

The number of patients treated invasive was seven and nine were drug treated.

At the drug treated patients, blood pressure was controlled satisfactorily in 5/9, with normalization of serum creatinine at four of them after discontinuation of ACEI treatment and slight decrease of serum creatinine at 1/5. At the other four (4/9), blood pressure decreased slightly (160/95 mmHg).

In patients invasive treated only one became normotensive (angioplasty on single stenosis without poststenotic dilatation), with normalization of renal function, at the other six, hypertension has improved slightly; decreasing the need for antihypertensive and creatinine was reduced, but did not return to normal (Tables 1–3).

Table 3 – Evolution of patients with renal artery stenosis

Type of treatment	No. of patients watch >1 year	No. of patients lost of evidence	Blood pressure			Levels of serum creatinine		
			Normal	*Low*	*Without influence*	*High*	*Low*	*Normal*
Invasive	6	1	1	5	–	–	5	1
Pharmacologic	9	–	–	5	4	–	5	4

Discussion

Artery stenosis often remains asymptomatic due preserved renal functional reserve, which allows a serum creatinine normal level, despite significant reduction in total glomerular filtration rate. Renal function is normal or not significantly reduced despite the fact that half of the nephrons are destroyed. SAR is often discovered by chance during angiography for other sites of atherosclerotic disease. SAR is manifested by two well-individualized clinical syndromes: renovascular hypertension and ischemic nephropathy. HTRV and IN frequently combine with each other but IN progressive renal failure may occur in the absence of hypertension [1, 2].

Clinical examination and clinical suspicion is essential. Krijnen P *et al.* [12] have developed a clinical score useful for diagnosis of SAR. This score takes into account age, gender, body mass index, presences of pocket abdominal, serum creatinine and serum total cholesterol level. This score has shown a sensitivity of 72% and a specificity of 90%. The conclusion of this study was that careful clinical evaluation of patients suspected to have renovascular hypertension makes unnecessary some investigations previously considered mandatory.

Stenosis is often consequence of atherosclerosis (75%) – in our statistics 68%, then follow fibromuscular dysplasia (15%) – in our statistics 18%. Other injuries are the arthritis-Takayashu disease, vasculitis, embolism and thrombosis renal vessels caused by abdominal trauma, post angiography, angioplasty-cholesterol embolism by fragments migrating ironing boards, atrial fibrillation, aneurysms of the aorta or renal artery dissected; post irradiation arterial fibrosis, renal artery extrinsic compression by tumors, cysts, neurofibromatosis; stenosis transplanted kidney artery.

HTARV incidence is 5% of all hypertensive patients. Is determined by:

1. Atheromatosis renal artery stenosis – 75% of HTARV. It is common in men aged over 50 years, smokers. Artheromatous lesions are located in the first third of the artery, sometimes even in the ostium of renal artery. Evolution is progressive in the absence of surgery, to complete obstruction [3, 4, 12].

2. Fibromuscular dysplasia of the renal artery-15% of HTARV. It affects mostly young women. Etiopathogenesis unknown; increased frequency of nephroptosis in these patients could not be correlated pathogenic and hyperestrogenism as stimulating collagen production is still studied. The lesion is located premedial or intimate. Angiography, areas of thickening of the wall are alternating with aneurismal areas, which cause part of a "string of beads". It is not produce complete ischemia [3, 8].

Intimate fibrodysplasia

It is characterized by endoluminal proliferation of a fibrocellular lax tissue. Phenomena is complicated by dissection and thrombosis. Appears with equal frequency in men and women.

Medial dysplasia

It is subdivided into four types:

▪ Medial fibroplasia is the most frequent predominant in women. It is characterized by the alternation of stenosis and dilation, which determines the characteristic moniliform appearance. It has a potential evolutionary variable.

▪ Medial hyperplasia is rare. This form reaches the two sexes equally and has an important evolutionary potential. This form achieves major arterial trunks and arteriography appears regularly as a renal artery stenosis.

▪ Medial fibroplasia is the second-form in terms of stenosis. Also presents a great potential evolution. Reach twice as frequently female sex, is in the form of severe multifocal stenoses often leading to thrombosis and renal infarction segmentation.

▪ Medial dissection is relatively little evolution and is often unilateral. This particular form reaches the renal artery distal segment. It may be complicated by the appearance of intramural hematoma.

Adventitial fibroplasia

It is the most rare and least known form. It is characterized by proliferation of collagen structures in the adventitia, which cause narrowing or extended stenosis.

3. Arthritis – Takayashu disease, vasculitis.

4. Embolism and thrombosis of renal vessels, which may be caused by abdominal trauma, post angiography, angioplasty, atrial fibrillation. Arterial thromboses are often consecutive of an abdominal bruising; among the most frequent causes are: trauma achieved by selective renal artery angiography, electric shock, administration of oral contraceptives. In many cases, the cause remains unknown. In children, the cause is often severe dehydration or severe sepsis. In adults, this type of thrombosis is often the result of prolonged compression, generally through a retroperitoneal tumor glomerulonephritis or amyloidosis [8].

5. Diseases of the arterial wall-dissected aneurysm of the aorta or renal arteries, arterial fibrosis post irradiation. Renal artery aneurysms represent less than 1% of all aneurysms. They are often congenital. We can distinguish four forms: sacciform, spindle, dissected and intrarenal. These aneurysms are responsible for renovascular hypertension by renal artery branches compression or thrombosis, which, in some degree, can overlap.

6. Extrinsic compression of renal artery: tumors, cysts, neurofibromatosis.

7. Transplanted kidney artery stenosis.

8. Arteriovenous fistulas. Can be congenital, presenting in the form of multiples connections acquired (renal biopsy puncture, penetrating wound, progressive rupture of a renal artery aneurysm, renal cancer surgery, arterial inflammation). Fistulae earned generally presents as a unique [4].

Ischemic nephropathy may be silent, when unilateral and contralateral kidney is healthy. Bilateral lesions (or unilateral with contralateral kidney ill or absent) leads to acute or chronic renal failure. Ischemic nephropathy is a major cause and certainly underestimated of the terminal IRC. In the latest statistics EDTA, published online in 2003, the incidence of renovascular disease as a cause of terminal renal failure in different European countries varies between 1 and 13% per year [5]. Note that in this statistic, post hypertensive nephrosclerosis is considered separately from renovascular disease. IN incidence increases with age patients: it is estimated that approximately 25% of patients over 60 years who are treated by replacement of renal function are based on an ischemic nephropathy [5, 6].

A possible renal artery stenosis should be systematically sought in two main circumstances: at the hypertensives with certain clinical features and in patients with renal failure without an obvious cause [7].

Systematic investigation of all hypertensives in the direction of any renal artery stenosis is not justified, considering the very high prevalence not HTARV [7, 8]. According to Bayes' theorem, the capacity of any diagnostic test depends on disease prevalence in the population and the sensitivity/ specificity of that test. The strategy recommends that the current first stage diagnosis "stratify" patients on clinical grounds, according to the "chances" of this disease [1, 9–11]. From this point of view were individually three categories of patients: with low clinical probability (slightly elevated blood pressure, normal renal function), medium (severe hypertension, refractory to treatment) and high (malignant hypertension, diastolic blast systolic–renal area, unexplained renal failure after ACE). Hypertensives from the group with low probability should not be specifically investigated. At those with average probability are indicated screening tests (Doppler ultrasound, MRI or CT angiography, isotopic nephrogram with Captopril). If they are positive, arteriography is the next step. In patients with high probability directly arteriography is recommended.

Conclusions

Atherosclerotic RAS is a significant cause of secondary hypertension, is responsible for a significant number of terminal IRC. The interventions of revascularization by angioplasty result in low-grade renal function improvement; angioplasty is good as long as kidney function is kept and in a few cases cures hypertension. Renal artery stenosis dilated by angioplasty reduces the number and doses of antihypertensive necessary for tension control.

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