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Renovascular and renal parenchymal arterial hypertension: clinical considerations

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Abstract

Parenchymal renal disease (PRD) is the main cause of secondary arterial hypertension (AH) and renovascular (RV) AH is the leading cause of potentially curable hypertension. On the other hand, primary AH is frequently responsible for progressive renal disease, as well as damages in other target organs. When hypertension develops as a result of renal disease, it is the predominant risk factor for accelerated loss of renal function. In Venezuela, the prevalence of AH has been estimated between 8.1% and 23.58% in the general population, but the prevalence of secondary AH due to PRD or RV disease is not known. In this review article that has been made in view of the importance of the subject, we present some clinical and epidemiological considerations about these two forms of AH, based upon current bibliographic data in the field and also in some experience that we have acquired from the management of in-patients with such pathologies, who were attended in a public hospital in Venezuela in the last 20 years. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

At present, it is well known that PRD is the main cause of secondary AH and that renovascular (RV) AH is the leading cause of potentially curable hypertension [1]. On the other hand, primary AH is a frequent cause of progressive renal disease, as well as damages in other target organs. In addition, when hypertension develops as a result of renal disease, it is the predominant risk factor for accelerated loss of renal function [2,3]. In the USA, the incidence of terminal renal failure (TRF) is rising in an alarming rate in spite of impressive advances in the management of end-stage renal disease (ESRD) [4]. TRF secondary to AH follows diabetic nephropathy for type 2 diabetes mellitus which is the main cause [5,6].

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From the clinical point of view, AH and chronic renal disease (CRD) may coexist in two different settings. First, primary AH is an important cause of nephroangiosclerosis in nontreated or badly treated patients or in those with accelerated or malignant forms of hypertension. Second, CRD is usually associated with systemic AH [1,2,7,8]. Unilateral renal disease (URD) is not an infrequent cause of AH and is also another potentially curable form of secondary hypertension like other pathologies such as renovascular disease, aortic coarctation and adrenal tumors. The exact prevalence of RV-AH in the general population is not known and the diagnosis is probably missed in the majority of patients [9]. RV-AH is not only the most common curable form of hypertension at any age, but also one of the few potentially reversible causes of chronic renal failure (CRF). In this review article, we present some clinical and epidemiological considerations about AH secondary to RPD and RV disease, based upon current bibliographic data in the field and also in some experience that we have acquired from the management of patients with such pathologies in Venezuela in the last 20 years.

2. General considerations

In Venezuela, the prevalence of AH has been estimated between 8.1% and 23.58% in the general population [10], but the prevalence of AH secondary to PRD or RV disease is not known. In our Service of Medicine that is one of the three Internal Medicine Services that we have at the Hospital Vargas (Caracas, Venezuela), which is on the other hand, a type IV general hospital in our Health System, we have discharged in the last 20 years a total of 1642 patients (1029 females and 613 males) with diagnosis of AH (Table 1), which represents approximately the 25% of total in-patients attended in those years (1980–1999). The mean age of the hypertensive population was 53.3 years with S.D. of 17.3 and a range of 11–95 years. The 58.6% (963 patients) were considered primary forms and the remaining 679 (41.4%) as secondary forms of AH. An accelerated or malignant course was found in 207 cases, the majority of them being primary forms. In 539 patients, the AH was considered as secondary to PRD or RV disease (Table 2); in the remaining 140 patients with secondary forms, the leading cause was type 2 diabetes mellitus without evidence of clinical diabetic nephropathy (Mogensen stages I–III). CRF was present in 372 cases; cerebrovascular disease (472 cases) and hypertensive/

Table 1
Arterial hypertension: general data from 1642 in-patients (Vargas Hospital, Caracas, Venezuela, 1980–1999)

	Number	Percentage
Total patients	1642	100.0
Male	613	37.0
Female	1029	63.0
Primary arterial hypertension	963	58.6
Secondary arterial hypertension	679	41.4
“Benign” forms	1435	87.4
Accelerated or malignant forms	207	12.6

Table 2
Arterial hypertension: target organ complications in 1642 hypertensive in-patients and secondary arterial hypertension in 679 cases (Vargas Hospital, Caracas, Venezuela, 1980–1999)

	Number	Percentage
Target organ complications		
CRF	372	22.7
CVD/Strokes	472	28.7
ICM/HCM	702	42.8
Secondary arterial hypertension	679	41.4
Parenchymal renal disease	530	32.3
Reno vascular AH	9	0.5
Others	140	8.6

CRF: chronic renal failure. CVD: cerebrovascular disease. ICM/HCM: ischaemic cardiomyopathy/hypertensive cardiomyopathy. AH: arterial hypertension.

ischaemic cardiomyopathy (702 cases) were found more frequently as target organ complications.

3. Systemic arterial hypertension and parenchymal renal disease

Systemic AH is common in patients with PRD. Approximately 85% of patients with ESRD have hypertension, which is responsible, at least in part, for the high incidence of cardiovascular events and deaths in these patients [11,12]. AH, without any doubt, is an important factor in the progression of renal disease and it is a predictor of coronary artery disease in uremic patients more than cigarette smoking and hypertrigliceridemia [11,13,14].

The pathogenesis of AH in patients with PRD and in those undergoing chronic dialysis is multifactorial. It varies in relation to the type of renal pathology and its treatment is difficult. Several factors have been incriminated in the development and maintenance of high blood pressure (HBP) in patients with renal disease: increased volemia and sodium excess, activation of the renin–angiotensin–aldosterone system (RAAS), participation of the sympathetic nervous system (SNS), action of vasodepressive and vasoconstrictor substances from the endothelium, use of erythropoietin, divalent ions and parathyroid hormone, natriuretic atrial peptide, structural changes in arteries, preexisting primary AH and miscellaneous factors (anemia, arteriovenous fistulae, vasopressin, serotonine, thyroid hormones and calcitonin-related gen) [11]. The activation of the RAAS, sodium retention and volume expansion as a consequence of the reduction of nephron mass secondary to RPD, have been considered for a long time as the most important factors in the development of AH in patients with CRD [2]. Nevertheless, in the last 25 years, significant evidence has emerged that in grand part, the HBP in these patients is due to increased activity of the SNS; experimental studies have demonstrated that afferent stimulus from lesioned kidneys towards the central nervous system could activate the SNS for complex interactions between the two systems, IL-1β and nitric oxide [11]. Renal failure progress independently of the underlined cause, in direct relationship with mean blood pressure; the intrarenal increase of angiotensin II (AII) and other factors maintain glomerular filtration rate by

means of transglomerular pressure increased by glomerular efferent arteriole resistance. Such an increase of the resistance reduces blood flow toward peritubular capillaries and vasa recta, inducing tubular ischaemia with additional loss of nephrons. The remnant nephrons increase in size as an attempt to modulate the elevation of filtered charge by a single nephron.

PRD is the most frequent cause of secondary AH, representing between 2.5% and 5% of all causes of hypertension [1]. PRD could be bilateral (B) or unilateral (U) with different probabilities from the therapeutic viewpoint. In our selective series of hospitalized patients, PRD represented the 32.3% (530 patients) of the 1642 patients discharged with the diagnosis of AH and the 78.1% (530 out of 679) of the total of patients with secondary AH. Only 3 of the 530 patients presented UPRD.

3.1. Arterial hypertension secondary to unilateral renal parenchymal disease (U-RPD)

The best chance of cure in patients with AH related to U-RPD probably lies with a tumor of the juxtaglomerular apparatus (hemangiopericytoma) and with Wilms tumor [1]. Wilms tumor is usually observed in children younger than 4 years of age. The hemangiopericytomas are rare and they are difficult for diagnosis and should be suspected in young adults with hypertension and hyperreninemic hyperaldosteronism with hypokalemia. Thirty-five percent of patients with renal adenocarcinomas present HBP that could be cured by nephrectomy. Reflux nephropathy is generally bilateral, but in isolated unilateral cases with AH, there is a potential benefit with the nephrectomy if there is unilateral renal scarring, renal hypertrophy of the contralateral kidney without other lesions and when the affected kidney contributed less than 25% to overall renal function [1].

In our series, only three patients presented AH related to UPRD. In one of them, HBP was associated to unilateral renal scarring secondary to unilateral vesico-ureteric-renal reflux (VURR), but there was not a formal indication of nephrectomy. In another female patient, there was unilateral renal scarring due to chronic pyelonephritis without evidence of VURR. In the third, a male patient, the intravenous urogram showed an ileopelvic ectopic kidney; nephrectomy of such a kidney did not cure HBP but improved AH which had a previous malignant behavior.

3.2. Arterial hypertension secondary to bilateral renal parenchymal disease (B-RPD)

Up to 40% of patients with HBP could be observed in series of cases with diagnosis of acute renal failure (ARF). In such cases, AH is more common when ARF is secondary to intrarenal vascular disease rather than acute tubulonecrosis or acute interstitial nephritis [8]. The AH secondary to B-RPD represent nearly 5% of all causes of hypertension and could be caused by almost all kinds of renal parenchymal diseases [8,15]. Focal and segmental glomerulosclerosis is the most common cause of AH among primary glomerulonephritis (GN), followed by mesangiocapillary (membranoproliferative) GN and a third of the cases with primary crescentic GN [1,2,8].

Postinfectious GN, GN secondary to systemic vasculitis and some forms of lupus GN are the most frequent causes of AH due to secondary GN [1,2,16]. Primary diabetic glomerulopathy is the most frequent pathology responsible for AH among all glomerular diseases

[8,17,18]. Eclamptic glomerulopathy is also a frequent cause of AH due to PRD [19]. Polycystic kidneys and chronic pyelonephritis are the main causes of AH among pathologies that primarily affect renal tubules and the interstitium. In minimal glomerular changes, membranous GN and in the majority of cases of tubule-interstitial renal disease, AH is an infrequent finding [1,8].

In our series, 527 patients had AH due to B-PRD. The majority of them (204 patients) were type 2 diabetics with Mogensen stages IV and V of diabetic nephropathy without clinical signs of accelerated or malignant hypertension but CRF at different stages. A significant number of diabetics without clinical manifestations of diabetic nephropathy (Mogensen stages I, II or III) had HBP. AH due to primary GN was found in 43 cases only; 83 patients had hypertension due to lupus GN.

4. Renovascular arterial hypertension (RV-AH)

The prevalence of RV-AH has been considered to be between 0.2% and 5% in the general hypertensive population. Its prevalence in stage III (WHO) AH is probably higher, reaching 32% when only accelerated or malignant forms of HBP are considered [9]. In these forms, the prevalence is 43% in whites and 7% in blacks. In the majority of the series with studies of hypertensive patients selected from a general population, systematic assessment with accurate methods for diagnosis of RV-AH such as Ecodoppler Renal Ultrasonography or Selective Renal Angiography are not carried out for medical or economical reasons [9,20]. In view of this fact, it is generally accepted that there exists an underscore registry of RV-AH in large series of nonselected population with AH. Indeed, that could probably be one of the reasons why in only nine patients from our series of 1642 hypertensive in-patients, RV pathology was demonstrated as the cause of the AH. In the majority of these nine patients, AH had an accelerated or malignant course. Nevertheless, systematic searching by accurate methods for the diagnosis of this form of hypertension was carried out in only a small proportion of the 207 patients with accelerated or malignant clinical behavior because of economical limitations in our public hospital. Fibromuscular dysplasia was the renovascular lesion that was found more frequently (seven out of the nine cases).

5. Final considerations

Parenchymal renal disease (PRD) is the main cause of secondary arterial hypertension (AH) and renovascular (RV) AH is the leading cause of potentially curable hypertension. On the other hand, primary AH is frequently responsible for progressive renal disease and when hypertension develops as a result of renal disease, it is the predominant risk factor for accelerated loss of renal function. In Venezuela, AH is a public health problem; its prevalence has been estimated between 8.1% and 23.58% in the general population, but the prevalence of secondary AH due to PRD or RV disease is not known.

According to our experience in Venezuela, secondary AH due to RPD is frequently seen in patients hospitalized in wards of an Internal Medicine Service. As in other countries, diabetic nephropathy is the leading cause in such a hypertensive population

followed by some forms of primary and secondary GN such as focal and segmental glomerulosclerosis and lupus GN. RV-AH is not frequent, but an underscore registry probably exists due to the lack of systematic assessment by accurate methods for the diagnosis of RV pathology in the population at risk.

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