

“Apparent” heart failure: a syndrome caused by renal artery stenoses

C G Missouriis, A-M Belli, G A MacGregor

Abstract

Objective—To report on renal artery stenosis presenting as congestive heart failure.

Design—Case series.

Setting—Tertiary referral centre.

Patients—Nine hypertensive subjects (five male, four female) seen in the blood pressure unit, St George’s Hospital, between 1991 and 1997 with clinical signs and symptoms of congestive cardiac failure but without overt coronary or valvar heart disease. Mean (SEM) age was 67 (3) years. Eight patients had renal artery revascularisation with percutaneous angioplasty and one had surgery.

Results—Renal revascularisation was followed by a large fall in blood pressure from 191/94 (7/3) to 150/75 (8/5) mm Hg two days after intervention ($p < 0.01$). There was also a large natriuresis and weight reduction. One week after revascularisation there was a mean loss in weight of 3.8 (0.6) kg. The largest fall in weight was seen in those patients with stenosis in a single functioning kidney. Furthermore, plasma atrial natriuretic factor fell from 120 (28) to 48 (9) pg/ml ($p < 0.05$; $n = 6$; normal value = 8.6 (0.8) pg/ml), and serum creatinine fell from 200 (37) to 140 (11) $\mu\text{mol/l}$ ($p < 0.025$). The clinical signs and symptoms of heart failure resolved and the diuretics were then withdrawn in all patients. On long term follow up, patients remained free from symptoms and signs of heart failure and the blood pressure was better controlled.

Conclusions—In hypertensive patients with symptoms and signs of congestive heart failure who do not have obvious ischaemic or valvar heart disease, renal artery stenosis should be considered as a possible underlying cause. Relief of the stenosis can result in resolution of the apparent heart failure.

(Heart 2000;83:152-155)

Keywords: renal artery stenosis; heart failure

Congestive heart failure is a syndrome characterised by changes in left ventricular function which can ultimately result in reduced exercise tolerance, impaired quality of life, and a five year mortality in excess of 50%.¹⁻³ Epidemiological studies have clearly shown that hypertension is one of the most important modifiable precursors of congestive heart failure.⁴⁻⁶

The great majority of patients with hypertension have primary elevation of blood pressure which can be ameliorated only by life long treatment with pharmacological agents. Renal artery stenosis has been thought to be a rare cause of hypertension. It is now realised that in patients with vascular disease elsewhere, atherosclerotic narrowing of the renal artery is extremely common.⁷⁻⁸ Indeed, renal artery stenosis is the most common curable cause of hypertension and progressive renal failure.⁹ It is also a rare cause of acute recurrent pulmonary oedema in patients with hypertension.¹⁰ We report nine patients with symptoms and signs of moderate to severe congestive heart failure in whom stenosis in a single functioning kidney or bilateral renal artery stenoses appeared to be the underlying cause for their symptoms.

Methods

Many hypertensive patients are referred to the blood pressure unit at St George’s Hospital from local general practitioners and general hospital physicians. In addition, all patients

with peripheral vascular disease who, on aortography, are found to have coexistent renal artery stenosis are referred to us for further management.

We studied nine white hypertensive subjects who were seen in the blood pressure unit between 1991 and 1997 with clinical signs and symptoms of congestive cardiac failure (New York Heart Association class II to IV) but had no overt coronary or valvar heart disease. Of these, five were male and four female. Their mean (SEM) age was 67 (3) years. In four patients, renal function had deteriorated after treatment with an angiotensin converting enzyme (ACE) inhibitor.

Supine blood pressure was recorded three times, two minutes apart, using a semiautomated ultrasound sphygmomanometer (Arteriosonde, Roche, Welwyn Garden City, UK) two days before renal percutaneous angioplasty or surgery and every other day for a week after renal revascularisation. Patients were weighed wearing the same clothing, and non-fasting venous blood samples were taken with the subjects seated and without stasis for determination of serum electrolytes, creatinine, and plasma atrial natriuretic factor (ANF). Blood samples for ANF measurements were spun immediately at 4°C and plasma stored at -20°C until assay. Plasma ANF was measured by radioimmunoassay.¹¹

Four patients were studied on a constant daily sodium intake of 150 mmol (diet of 30

St George’s Hospital
Medical School,
Cranmer Terrace,
London SW17 0RE, UK
C G Missouriis
A-M Belli
G A MacGregor

Correspondence to:
Dr Missouriis

Accepted 16 September 1999

Table 1 Clinical characteristics and biochemical measurements of nine patients with "apparent" heart failure before and after renal percutaneous angioplasty or surgical revascularisation

Patient, age, sex	Pre-treatment supine BP (mm Hg) (n drugs)	Supine BP 48 h post-intervent (mm Hg) (n drugs)	Recent supine BP (months post-intervent; n drugs)	Baseline serum creatinine ($\mu\text{mol/l}$)	Se creatinine ($\mu\text{mol/l}$) 7 d post-intervent	Se creatinine ($\mu\text{mol/l}$) post-intervent	Plasma ANF (pg/ml) pre-intervent	Plasma ANF (pg/ml) (d post-intervent)	Na excr 24 h post-intervent (mmol)	Weight loss in 1 week post-intervent (kg)	Angiographic findings in renal arteries
1, 65, F*†	180/105 (4)	158/90 (4)	—	482	154	125 (24)	—	—	—	5.2	Occl right RA; severe left RA stenosis
2, 51, M	180/106 (3)	160/100 (3)	138/87 (38; 3)	162	109	129 (38)	—	—	538	6.4	Occl right RA; severe left RA stenosis
3, 73, M	194/96 (4)	125/70 (4)	176/95 (2; 3)	172	169	135 (2)	133	88 (7)	485	5.5	Occl left RA; severe right RA stenosis
4, 62, F*	191/94 (3)	168/90 (3)	177/86 (23; 2)	196	137	159 (23)	98	44 (4)	560	3.2	Occl left RA; severe right RA stenosis
5, 60, F	186/95 (4)	103/68 (4)	160/99 (4; 1)	148	105	78 (3)	—	—	—	5.1	Occl left RA; severe right RA stenosis
6, 70, M	229/92 (3)	168/60 (3)	115/71 (23; 2)	205	187	112 (23)	53.2	43 (3)	—	3.1	Bilateral severe RA stenoses
7, 77, F	220/84 (3)	163/64 (3)	162/71 (24; 3)	102	102	116 (21)	250	21 (6)	316	1.8	Bilateral severe RA stenoses
8, 76, M	162/95 (2)	141/61 (2)	128/86 (32; 2)	124	116	117 (33)	86.9	46.6 (4)	—	2.2	Bilateral severe RA stenoses
9, 72, M	174/76 (2)	163/69 (2)	151/69 (36; 2)	213	185	175 (36)	98.4	46.6 (4)	—	1.5	Bilateral severe RA stenoses
Mean (SEM)	191/94 (7/3)	150/75 (8/5)	151/83 (8/4)	200 (37)	140 (11)	127 (9)	120 (28)	48 (9)	—	3.8 (0.6)	

*On renal replacement therapy; †deceased 5 years after renal revascularisation. ANF, atrial natriuretic factor; BP, blood pressure; excr, excretion; Na, sodium; occl, occluded; post-intervent, after intervention; pre-intervent, before intervention; RA, renal artery; Se, serum.

mmol, supplemented by 12 Slow Sodium tablets each containing 600 mg of sodium chloride; CIBA, Novartis Pharmaceuticals, Frimley, UK). In these patients continuous 24 hour urine collections were performed from day -2 to day 7 following renal percutaneous angioplasty.

During the study period (day -2 to 7), the patients who had renal percutaneous angioplasty performed were maintained on the same dose of blood pressure lowering drug treatment and no intravenous fluids were prescribed. Eight patients had renal revascularisation with percutaneous angioplasty, and one had surgery (reversed saphenous graft from left external iliac artery to renal artery) after unsuccessful renal angioplasty. Renal percutaneous angioplasty was performed using 40 ml of Iopamidol 300 as a contrast medium, which contains 0.08 mmol of sodium as disodium calcium edetate.

Mode echocardiograms were performed before renal revascularisation in the partial left decubitus position using a 2.25 MHz transducer of the Hewlett Packard echogram (1000 C; Hewlett Packard Inc, Andover, Massachusetts, USA). Measurements of the septum, ventricular cavity, and posterior wall in systole and diastole were made according to the American Society of Echocardiography leading edge convention¹² by one trained observer blinded to the clinical data. Five cardiac cycles were used and values averaged.

The patients were reviewed at two weeks, one month, and at three monthly intervals after renal revascularisation. Measurements of blood pressure and serum creatinine were performed. At the same time patients were also assessed for symptoms and signs of heart failure.¹³

All patients gave informed consent for the investigations, which were approved by the hospital ethics committee.

STATISTICAL ANALYSIS

Results are given as means (SEM). Paired measurements were compared using the Wilcoxon sign rank sum test. A p value of < 0.05 was considered as statistically significant.

Results

The clinical and hormonal indices of patients studied are shown in table 1.

BEFORE RENAL REVASCLARISATION

Before renal revascularisation all patients had signs of moderate to severe heart failure (New York Heart Association class II to IV) despite treatment with diuretics. Mean (SEM) supine blood pressure was 191/94 (7/3) mm Hg (on treatment with at least two blood pressure lowering drugs), and serum creatinine was 200 (37) $\mu\text{mol/l}$. In eight patients, good quality echograms showing continuous echoes of the interventricular septum and left ventricular posterior wall were obtained and were included in the final analysis. Mean left ventricular measurements were as follows: interventricular septum in diastole 1.2 (0.1) cm; ventricular cavity in systole 5.0 (0.2) cm, and in diastole 3.6 (0.4) cm; and posterior wall in diastole 1.1 (0.1) cm.

Plasma concentrations of ANF were available in six subjects. These were markedly raised with a mean value of 120 (28) pg/ml (normal value = 8.6 (0.8) pg/ml).

AFTER RENAL REVASCULARISATION

Renal revascularisation was followed by a large fall in blood pressure from 191/94 (7/3) mm Hg to 150/75 (8/5) mm Hg two days after intervention ($p < 0.01$). Furthermore, there was a large natriuresis and weight reduction (table 1). One week after revascularisation there was a mean loss in weight of 3.8 (0.6) kg. The largest fall in weight was seen in those patients with stenosis in a single functioning kidney. At the same time serum creatinine fell to 140 (11) $\mu\text{mol/l}$ ($p < 0.025$). The clinical signs and symptoms of heart failure resolved and the diuretics were then withdrawn in all patients. The improvement in clinical symptoms and signs was associated with a significant fall in plasma ANF concentrations (to 48 (9) pg/ml, $p < 0.05$; $n = 6$).

Figure 1 shows the individual values of blood pressure, weight, plasma ANF and 24 urinary sodium (while on a constant daily sodium

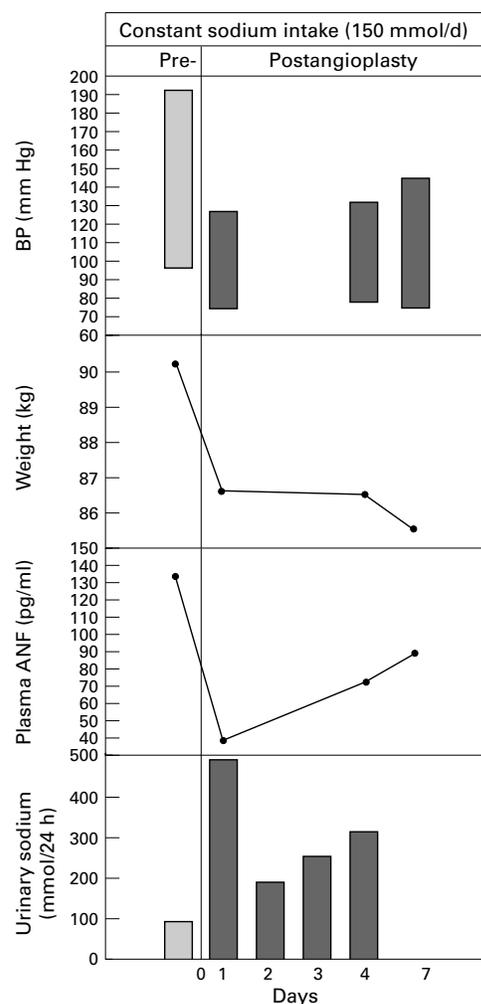


Figure 1 Individual values of blood pressure, weight, plasma atrial natriuretic factor (ANF), and 24 hour urinary sodium (while on a constant daily sodium intake of 150 mmol/l) in a typical patient (case 3) whose symptoms and signs of heart failure resolved after renal artery percutaneous angioplasty to a single functioning kidney.

intake of 150 mmol/l) in a typical patient whose symptoms and signs of heart failure resolved after renal artery percutaneous angioplasty to a single functioning kidney.

LONG TERM FOLLOW UP

On follow up, patients remained free of symptoms and signs of heart failure, and the blood pressure was better controlled (table 1). In all but two patients the early improvement in renal function was maintained long term. The patient who had surgical renal revascularisation died five years after the procedure from end stage renal failure and septicaemia.

Discussion

Recent studies have described an association between renal artery stenosis and recurrent pulmonary oedema in patients with hypertension.^{10 14 15} In 1987 Sutters *et al* reported a patient with stenosis in a single functioning kidney who developed a large diuresis and postural hypertension after a technically successful angioplasty.¹⁶ Furthermore, in a case report, we have previously described the resolution of symptoms and signs of apparent heart failure in two patients with stenosis in a single functioning kidney.¹⁷

Our present study clearly shows that renal artery stenosis can be a reversible cause of apparent congestive heart failure in hypertensive patients in the absence of overt coronary or valvar heart disease. This syndrome appears to develop in those patients with stenosis of the renal artery in a solitary kidney or in those with severe bilateral renal artery disease. We believe that this clinical entity is separate from heart failure that is caused by high blood pressure alone. This is because in the former there is much more pronounced sodium and water retention as a direct result of a narrowed renal artery. This clinical observation is consistent with the experimental evidence provided by the sodium and water retention that occurs in rats with one kidney—one clip Goldblatt hypertension.¹⁸

In all patients studied, relief of the stenosis caused a large loss of sodium and water and resolution of the symptoms and signs of heart failure. There was also an improvement in blood pressure and renal function and a significant fall in plasma concentrations of atrial natriuretic factor. Indeed, the baseline and post-treatment plasma ANF values were comparable to those obtained in a separate group of nine patients who were admitted to our institution with untreated moderate to severe heart failure resulting from ischaemic or valvar heart disease (pretreatment plasma ANF, 136 (26) pg/ml; post-treatment plasma ANF, 77 (19) pg/ml, $p < 0.025$).¹⁹

It is important to identify the patients with renovascular disease and apparent heart failure, as there is now no doubt that when ACE inhibitors are prescribed they may have profound effects on glomerular filtration in the stenosed kidney.²⁰ The effect is usually reversible on stopping the drug, provided that thrombosis has not occurred.

Retention of sodium and water also occurs in renal parenchymal diseases, such as acute nephritic syndrome. In this condition, the mechanisms of renal sodium retention are poorly understood, but include a reduced filtered sodium load as well as enhanced sodium reabsorption at the distal nephron caused by increased pressor activity of circulating angiotensin II. Retention of sodium is also seen in other clinical conditions associated with reduced blood flow to the kidneys, such as congestive heart failure, nephrotic syndrome, and cirrhosis. In these patients, the sodium retention appears to be independent of the renin-angiotensin system, and it is likely that some other overriding mechanism is responsible for the sodium retention.^{19 21 22}

Clearly further studies are required to establish the importance of neurohumoral factors such as the sympathetic nervous system, the renin-angiotensin system, and factors such as vasopressin and endothelin in the pathophysiology of sodium retention in patients with renal artery stenoses.

In summary, we suggest, therefore, that in patients with heart failure without overt ischaemic or valvar heart disease, renal artery stenosis to a single functioning kidney or bilateral renal artery stenoses should be considered as a possible underlying cause. This is particularly likely if patients have hypertension, renal impairment, and evidence of peripheral vascular disease.^{7 8} Treatment of the stenosed artery can result in resolution of the apparent heart failure.

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