SPECIAL FEATURE

Case Report/Focused Review
Fred A. Lopez, MD • Feature Editor

Brain Natriuretic Peptide Counteracting the Renin-angiotensin-aldosterone System in Accelerated Malignant Hypertension

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ABSTRACT

We describe 2 patients, a 52-year-old woman and a 57-year-old man, with rapidly progressive hypertension and marked elevation of brain natriuretic peptide who exhibited polyuria, natriuresis, hypokalemia, posterior reversible encephalopathy syndrome and left ventricular dysfunction together with retinopathy and nephropathy, which were attenuated in a short time span of 1-2 months with normalization of blood pressure after the antihypertensive treatment. The possible role of brain natriuretic peptide in the pathophysiology of accelerated malignant hypertension was discussed and a review of the literature was completed.

Key Indexing Terms: Brain natriuretic peptide; Hypokalemia; Accelerated malignant hypertension; Polyuria; Renin-angiotensin-aldosterone system. **[Am J Med Sci 2016;▮(▮):▮▮▮–▮▮▮.]**

INTRODUCTION

Accelerated malignant hypertension is a clinical syndrome of rapidly progressive elevation of blood pressure (BP) associated with retinopathy, encephalopathy and nephropathy.[1,2] The renin-angiotensin-aldosterone system (RAAS) has been shown to be critically involved in the pathogenesis of this syndrome.[1,3-5] However, the precise mechanisms by which this syndrome occurs remain to be elucidated. Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are produced from the heart, the former mainly from the atrium and the latter from the ventricle and have natriuretic, diuretic and vasorelaxant effects by activating the common natriuretic peptide receptor guanylyl cyclase A (GC-A) through production of cyclic guanosine monophosphate (cGMP) and counteract thereby the actions of the RAAS.[6-10] However, the role of ANP and BNP is not known in accelerated malignant hypertension in humans.

We report 2 cases of accelerated malignant hypertension that presented with polyuria, polydipsia, hyponatremia, hypokalemia, left ventricular dysfunction and posterior reversible encephalopathy syndrome (PRES) in the presence of renal insufficiency. Marked elevation of BNP was noted and rapidly decreased together with the amelioration of the syndrome by the therapy including angiotensin II receptor blocker (ARB) and calcium channel blocker (CCB). This article reviews the relevant literature and proposes a possible role of natriuretic peptides in the pathophysiology of this syndrome.

CASE REPORT

Case 1

A 52-year-old woman was admitted to the hospital because of headache, dizziness, nausea, polyuria and polydipsia appearing since approximately 1 month before. She had a 10-year history of hypertension and had been treated with furosemide carvedilol, angiotensin receptor blocker valsartan, and CCB nifedipine for 4 months but had stopped the medication herself 2 months before admission. Physical examination revealed BP of 292/144 mm Hg, body mass index (BMI) of 18.2 kg/m^2, heart rate of 72 beats/minute and absence of edema. Laboratory data on admission showed the markedly elevated serum BNP level (1,758 pg/mL) and plasma renin activity (PRA) (27 ng/mL/hour) together with increased serum and urinary aldosterone levels (23.9 ng/dL and 13 μg/day, respectively) and serum vasopressin level (4.1 pg/mL) but normal urinary metanephrine (0.07 mg/day) (Table). There was no renal arterial stenosis on renal angiogram. Hyponatremia (134 mEq/L), hypokalemia (2.7 mEq/L), metabolic alkalosis (arterial pH = 7.43 and base excess = +6.3 mmol/L), elevated serum levels of creatinine (1.8 mg/dL) and blood urea nitrogen (25.9 mg/dL) together with urine protein (4+) were presented (Table). Urinary volume was 2,350-2,670 mL/day. Ambulatory BP monitoring was 208/116 to 233/127 mm Hg. Electrocardiogram (ECG) showed left ventricular hypertrophy pattern (strain pattern). Echocardiogram revealed severe left ventricular hypertrophy with interventricular septum (IVS) thickness of 18.4 mm and

TABLE. Clinical data on admission and after 1 month of treatment.

Variables	Case 1 (52-year female)		Case 2 (57-year male)	
	On admission	After 1 month of treatment	On admission	After 1 month of treatment
Blood pressure, mmHg	234/128	142/84	224/120	142/80
Echocardiographic findings				
IVS, mm	18.4	16.2	16.6	15.9
PW, mm	18.4	15.4	16.6	15.9
EF, (%)	45	63	40.7	48.3
FS, (%)	28	36	19.9	24.5
Blood chemistry				
Serum albumin, g/dL	3.2	3.6	3.4	3.7
Red blood cell, $10^4/\mu L$	455	361	377	362
Ht, (%)	40.1	34.0	36.0	33.7
Platelet, $10^4/\mu L$	14.1	25.4	16.5	22.8
LDH, U/L	400	168	386	205
Serum sodium, mEq/L	134	141	136	138
Serum potassium, mEq/L	2.7	4.3	3.2	4.5
Serum chloride, mEq/L	94	104	96	101
Serum osmolarity, mOsm/L	287	291	289	291
Arterial pH	7.43		7.49	
Base excess, mmol/L	+6.3		+7.8	
Serum BUN, mg/dL	25.9	26.4	30.0	31.4
Serum creatinine, mg/dL	1.8	1.7	2.5	2.7
eGFR, mL/minute/1.73 m^2	23.9	25.4	22.4	20.7
Hormone analysis				
Serum BNP, pg/mL	1,758	37.5	1,526	190
Serum PRA, ng/mL/hour	27	7.8	8.8	7.1
Serum aldosterone, ng/dL	23.9	16.1	34.7	25.1
Serum vasopressin, pg/mL	4.1	3.3	1.8	1.1
Urine aldosterone, μg/day	13	3	16	6
Urine cortisol, μg/day	16.5		32.5	
Urine metanephrine, mg/day	0.07	11.8	0.15	
Urine				
Volume, mL/day	2,350	1,660	2,750	1,650
Sodium, mEq/L/day	186	108	195	110
Potassium, mEq/L/day	47	28	52	32
FENa, %	2.3	1.1	2.2	1.3
Protein, g/day	2.5	0.5	3.3	0.8
Osmolarity, mOsm/L	407	468	365	312

BNP, brain natriuretic peptide; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; EF, ejection fraction; FENa, fractional excretion of sodium; FS, fractional shortening; Ht, hematocrit; IVS, intraventricular septal thickness; PRA, plasma renin activity; PW, posterior wall thickness.

posterior wall (PW) thickness of 18.4 mm and diffuse hypokinesis with ejection fraction (EF) of 45% (Figure 1). Magnetic resonance imaging scan of the brain showed a high-density area in the midbrain and cerebellum consistent with PRES (Figure 2). There was a Keith-Wagener III retinopathy with hemorrhages and exudates. She was given ARB olmesartan of 20-40 mg/day, CCB nifedipine of 40-60 mg/day and aldosterone receptor blocker spironolactone of 12.5 mg/day in gradually incremental doses on dietary sodium of 100 mEq/day. Her BP and urinary volume decreased gradually to almost normal range (142/83 to 148/85 mm Hg and 1,580-1,665 mL/day, respectively) and hypokalemia, hyponatremia, increased levels of PRA, serum and urinary aldosterone and serum BNP also were improved or almost normalized after 1 month of these medications (Table). Echocardiography revealed a reduction of the left ventricular thickness (IVS = 16 mm and PW = 15 mm) and improvement of wall motion (EF = 63%) (Table), together with marked amelioration of strain pattern on ECG.