The hyponatremic hypertensive syndrome in renal artery stenosis: An infrequent cause of hyponatremia

Browne WL, Nair B

Department of Geriatric Medicine, John Hunter Hospital, Hunter New England Health, Australia

Correspondence:
William Browne,
E-mail: william.browne@hnehealth.nsw.gov.au

Received : 19-04-06
Review completed : 16-05-06
Accepted : 01-06-06
PubMed ID :
J Postgrad Med 2007;53:41-3

ABSTRACT

The hyponatremic hypertensive syndrome is a rare but serious complication of reno-vascular disease. The syndrome is characterized by hypertension and profound natriuresis, leading to body sodium and water depletion. Hypertension is typically refractory to treatment. We report an 82-year-old patient with this syndrome and describe the results of an audit of the clinical records of patients admitted to a teaching hospital over a two-year period with confirmed renal artery stenosis and hyponatremia. The syndrome should be suspected in patients in whom severe hypertension is associated with hyponatremia without other apparent cause, especially in the presence of reno-vascular disease.

KEY WORDS: Hyponatraemia, hypertension, renal artery stenosis

The hyponatremic hypertensive syndrome is an infrequent complication of renal artery stenosis.[1,2] Only a small number of cases have been reported since the 1960s.[3] Associated biochemical abnormalities include hyponatremia, hypokalemia and markedly elevated plasma renin activity.[4] Patients with hyponatremic hypertensive syndrome may present with a spectrum of signs and symptoms including headache, confusion, postural dizziness, hypertensive neuropathy, polyuria, polydipsia, weight loss and salt craving.[1,2] The purpose of this case report is to highlight the existence of this rare, though possibly under-diagnosed syndrome.

Case History

An 82-year-old woman with a history of hypertension presented to a teaching hospital complaining of mild left-sided weakness. She was admitted for investigations. A magnetic resonance imaging scan six days after presentation showed no evidence of infarction. At admission, her blood pressure was 220/90 mmHg, with no postural drop. She had Grade 3 retinopathy. There was no renal bruit. The patient was hyponatremic with a serum sodium concentration of 128 mmol/l (normal range 136-144). Serum urea was 8.4 mmol/l (normal range 3.5-7.2) and creatinine was elevated at 114 mmol/l (normal range 60-100). Serum potassium was 4.6 mmol/l (normal range 3.4-4.8). Her GFR was 35 ml/min. She weighed 69 kg and was clinically euvolemic.

The patient's blood pressure was poorly controlled, despite the sequential addition of perindopril and chlorothiazide. The diuretic was stopped on the tenth day of her admission (after six days of treatment). At this time, her plasma sodium concentration had fallen to 122 mmol/l [Table 1]. A number of investigations were performed [Tables 2-3]. Plasma renin was not available. She was started on methyldopa. Nine days later, her serum sodium concentration had fallen to 114 mmol/l while blood pressure remained elevated at 210/110 mmHg with a postural drop to 190/85 mmHg. She developed lethargy, weakness, thirst and polyuria. Her weight fell to 65 kg.

A duplex ultrasonographic study of the renal vessels and kidneys showed small poorly perfused kidneys with an 80% stenosis of the left renal artery. The syndrome of inappropriate antidiuretic

Table 1: The results of serum electrolyte studies over the course of the admission

Analyte	Units	Ref. range	Day 1	Day 10	Day 12	Day 19	8 weeks
Sodium	mmol/l	136-144	128	122	118	114	132
Potassium	mmol/l	3.4-4.8	4.6	4.1	3.7	4.2	4.6
Chloride	mmol/l	103-110	93	86	90	78	96
Bicarbonate	mmol/l	24-30	27	31	29	25	28
Urea	mmol/l	3.5-7.2	8.4	12.0	10.0	6.8	7.3
Creatinine	umol/l	60-100	114	134	129	126	115
Anion gap	mmol/l	7-17	12	9	3	14	6

Table 2: Other investigations (admission day 12)

Analyte	Units	Reference range	Result
Aldosterone	pmol/l	80-1040	228
TSH	mU/L	0.4-3.90	0.54
Cortisol (serum)	nmol/l	180-720	646
Cholesterol	mmol/l	<6.5	5.8
Triglycerides	mmol/l	<2.15	1.96

Table 3: Results of analysis of 24h urine collection (admission day 12)

Analyte	Units	Reference range	Result
Urine volume	L	NA	0.739
Creatinine	mmol/L	NA	4.3
Creatinine	mmol/day	6.0-22.0	3.2
Sodium	mmol/L	NA	80
Sodium	mmol/day	60-200	59
Potassium	mmol/L	NA	52
Potassium	mmol/day	30-100	39
Urine free cortisol	nmol/day	<300	196
Urine free cortisol	nmol/L	NA	265
Urine aldosterone	nmol/day	17-69	5
Urine aldosterone	nmol/L	NA	3
Dopamine	umol/day	0.2-3.0	0.21
Noradrenalin	umol/day	<0.6	0.080
Adrenalin	umol/day	<0.1	0.011
Normetanephrine	umol/day	<4.5	1.1
Metanephrine	umol/day	<1.5	0.6

NA- Standardized reference range not available for this parameter

hormone production was excluded based on urine osmolality (173 mmol/kg). Early thiazide exposure alone could not account for the prolonged natriuresis. After consultation with a nephrologist and clinical biochemist, the hyponatremic hypertensive syndrome was diagnosed.

The patient was unfit for renal endarterectomy, angioplasty or nephrectomy. A high-sodium diet was initiated while the patient remained on atenolol, perindopril and methyldopa. A gradual fall in blood pressure and resolution of lethargy, weakness, polyuria and thirst ensued. Eight weeks later the patient's blood pressure was 150/70 mmHg and serum sodium was 132 mmol/l.

We used a coding database to identify patients admitted to a 550-bed teaching hospital with renal artery stenosis, moderate or severe hypertension and moderate or severe hyponatremia between January 1998 and December 1999. Renal artery stenosis was defined as a stenosis of 80% or more on selective angiography, MR angiography or a strongly suggestive renal duplex ultrasound study. We defined moderate or severe hypertension as a reading on at least three consecutive occasions of greater than 165 mmHg systolic or >95 mmHg diastolic. We defined significant hyponatremia as a serum sodium level of 130 mmol/l or less.

A total of 194 patients with a diagnosis of renal artery stenosis were identified and their admission records analyzed. Fourteen were found to have moderate or severe hypertension and moderate or severe hyponatremia [Table 4].

Table 4: Demographic and clinical features of patients with renal artery stenosis of greater than 80%, hypertension and hyponatremia with serum sodium of 130 mmol/l or less

Sex	Age	Imaging	Lesion	(Na) mmol/l	Diagnosed cause of hyponatremia
M	88	Duplex U/S	Right	129	Thaizide use
M	64	Angio	Bilateral	129	Thaizide use
F	74	Duplex U/S	Right	128	Thaizide use
F	79	Duplex U/S	Left	130	Thaizide use
F	76	Duplex U/S	Left	130	Thaizide use
M	74	Angio	Left	130	Thaizide use
F	76	Angio	Right	125	Renal failure
F	73	MR angio	Bilateral	130	Renal failure
F	66	Angio	Bilateral	130	Renal failure
M	56	Duplex U/S	Right	125	Renal failure
M	54	Duplex U/S	Bilateral	123	Renal failure
F	68	Duplex U/S	Right	126	CCF
F	70	Duplex U/S	Bilateral	126	CCF
F	78	Duplex U/S	Right	129	Infusion-related

M- male, F-female, Angio- renal angiography, Duplex U/S- duplex ultrasonographic study of renal arteries, MR angio- magnetic resonance imaging angiography of renal vessels, (Na)- lowest serum sodium concentration, CCF- congestive cardiac failure

Discussion

In this case report we have described a patient who developed the hyponatremic hypertensive syndrome following a stroke. Renal artery stenosis was subsequently identified. Although our patient was exposed to a thiazide diuretic, hyponatremia not only predated its use but persisted and worsened after it was withdrawn. Resolution was achieved through the combination of angiotensin converting enzyme (ACE) inhibition and a high-sodium diet.

We found a rate of 14% for significant hyponatremia and moderate to severe hypertension among 194 patients with renal artery stenosis. This largely reflected the use of thiazide diuretics and high rates of renal impairment among these patients. No additional case of the hyponatraemic hypertensive syndrome was identified.

The hyponatremic hypertensive syndrome is a consequence of multiple factors promoting sodium depletion in the presence of unilateral renal artery stenosis. Decreased perfusion of the glomerular apparatus distal to a severe renal artery stenosis leads to increased renin and angiotensin II production causing hypertension. Angiotensin II influences fluid and sodium reabsorption in the renal tubule in a biphasic, dose-dependent manner. Normal concentrations of angiotensin II, generally in the 10^{-12} to 10^{-9} mmol/l range, stimulate reabsorption. High concentrations promote water and electrolyte loss.[5] A natriuresis in the better-perfused kidney results in hyponatremia and volume depletion.

By reducing the polyuric response, widespread use of antihypertensive medications may have reduced the incidence of the syndrome.[3]

Hyponatremia and hypertension also occur in hypertensive patients treated with thiazide diuretics,[6] in patients with renin-secreting tumors,[7] acute intermittent porphyria[8] and acute or chronic renal failure.

The hyponatremic hypertensive syndrome is an infrequent cause of moderate to severe hyponatremia among patients with renal artery stenosis. The syndrome should be suspected in patients in whom severe hypertension is associated with hyponatremia without other apparent cause. Management is generally with ACE inhibitors, which can reverse both blood pressure and biochemical abnormalities.[2] Caution should be exercised however, given the risk of inducing renal failure in what is predominantly an elderly population with renovascular disease. The role of renal angioplasty is less clear,[9] although successful management of the syndrome has been achieved through this strategy.[10]

References

1. Agarwal M, Lynn KL, Richards AM, Nicholls MG. Hyponatremic-hypertensive syndrome with renal ischemia: An under recognized disorder. Hypertension 1999;33:1020-4.
2. Atkinson AB, Davies DL, Leckie B, Morton JJ, Brown JJ, Fraser R, *et al*. Hyponatraemic hypertensive syndrome with renal-artery occlusion corrected by captopril. Lancet 1979;2:606-9.
3. Tetsuou YT, Miyatake YY, Tanaka K, Suzuki T, Ohtsu F, Nagasawa K, *et al*. Hyponatremic-hypertensive syndrome associated with renovascular hypertension: A case report. Circ J. 2002;66:297-301.
4. Mailloux LU, Napolitano B, Bellucci AG, Vernace M, Wilkes BM, Mossey RT. Renal vascular disease causing end-stage renal disease, incidence, clinical correlates and outcomes: A 20-year clinical experience. Am J Kidney Dis 1994;24:622-9.
5. Wang T, Chan YL. Mechanism of angiotensin II action on proximal tubular transport. J Pharmacol Exp Ther 1990;252:689-95.
6. Abramow M, Cogan E. Clinical aspects and pathophysiology of diuretic-induced hyponatremia. Adv Nephrol Necker Hosp 1984;13:1-28.
7. Misiani R, Sonzogni A, Poletti EM, Cassinelli G, Gualandris L, Pericotti S, *et al*. Hyponatremic hypertensive syndrome and massive proteinuria in a patient with renin-producing leiomyosarcoma. Am J Kidney Dis. 1994;24:83-8.
8. Qadiri MR, Church SE, McColl KE, Moore MR, Youngs GR. Chester porphyria: A clinical study of a new form of acute porphyria. Br Med J (Clin Res Ed) 1986;292:455-9.
9. van Jaarsveld BC, Krijnen P, Pieterman H, Derkx FH, Deinum J, Postma CT, *et al*. The effect of balloon angioplasty on hypertension in atherosclerotic renal-artery stenosis. Dutch renal artery stenosis intervention cooperative study group. N Engl J Med 2000;342: 1007-14.
10. Kaneko K, Shimazaki S, Ino T, Yabuta K, Nakazawa T, Takahashi H, *et al*. Severe hyponatremia in a patient with renovascular hypertension: Case report. Nephron 1994;68:252-5.

Source of Support: Nil, **Conflict of Interest:** None declared.