

Uncontrolled hypertension in a hemodialysis patient – case presentation and literature update

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Abstract

We present a case study on a 60-year-old male patient with end-stage renal disease receiving hemodialysis (HD) for 7 years, diagnosed with idiopathic chronic glomerulonephritis and hyperuricemic nephropathy, as primary disease. After a long period of well-managed moderate hypertension, he started to experience severe refractory high blood pressure episodes, difficult to control, in spite of combinations of four anti-hypertensive drugs. After excluding other causes of resistant hypertension, we have diagnosed, by angio-CT scan, significant bilateral renal artery stenosis, and reconsider the therapeutic approach, by withdrawing the angiotensin converting enzyme inhibitor (ACEI). In this setting, we discuss the frequent causes of resistant hypertension in HD patients, as well as the possible therapeutic solutions of the severe, uncontrolled hypertension in this special group of patients.

Keywords: hemodialysis, uncontrolled hypertension, renal artery stenosis, therapy

Introduction

Cardiovascular complications are recognized as mortality highest mainspring in patients with end-stage renal disease (ESRD) [1-3]. Hypertension is present in more than 80% of ESRD cases, and it should be satisfactorily controlled when patients start hemodialysis (HD), together with antihypertensive treatment [4].

Prevalence of arterial hypertension in HD patients usually vary widely among studies, not only because of differences in the definition of ranges of hypertension, but also due to variability in methods/moments of measuring blood pressure (BP), either pre- and post-dialysis or using ambulatory BP recordings[5]. Multiple studies and meta-analysis have shown that more than 70% of hypertensive patients in chronic HD programs are not efficiently controlled. The target blood pressure (BP) values of < 140/90 mmHg are stated to be achieved optimally pre- and post-HD in order to reduce cardio-vascular morbidity and mortality in dialysis patients [6].

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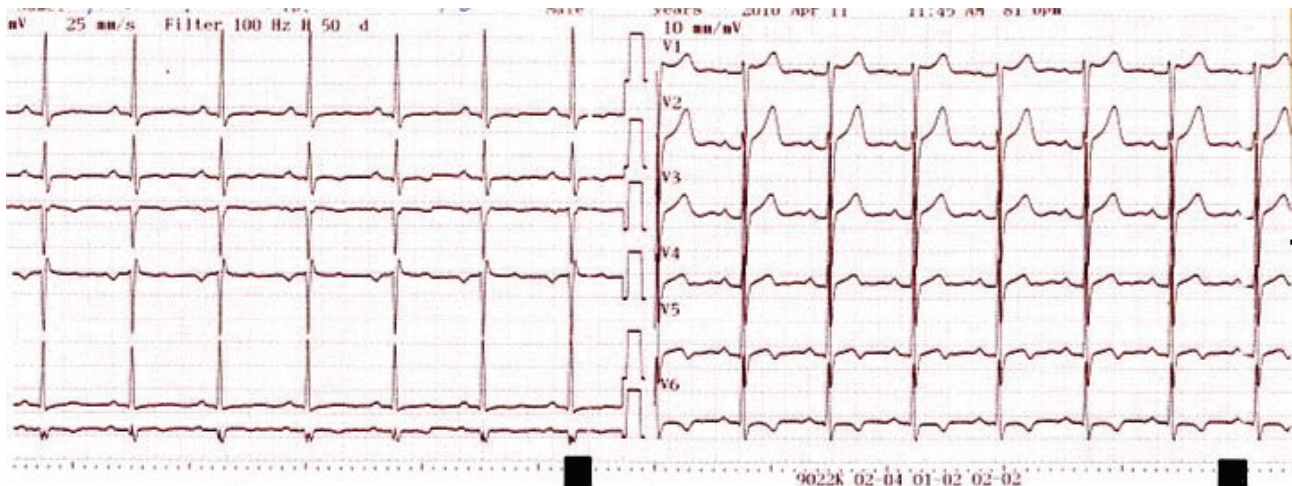


Figure 1. Patient's 12-lead ECG performed at the ER admission.

Aim

We wanted to emphasize that renal artery stenosis may be a cause of suddenly resistant hypertension in long-term hemodialysed patients, who used to be well controlled by medication and to raise the awareness of using all available methods to obtain an accurate diagnosis, for a better outcome.

Case report

We exhibit the case of a 60-years-old male patient with stage 5HD-CKD, who follows the local hemodialysis program in Constanta County Hemodialysis Department for 7 years (with a functional brachiocephalic arteriovenous fistula, since 2009). His medical history comprises primary chronic glomerulonephritis combined with hyperuricemic nephropathy, being under our nephrology evidence and surveillance since 2004. He was diagnosed with hypertension for about 10 years, with moderate-to-high values (maximal reported BP values of 180/90 mmHg), with his records showing a good therapeutic control (values around 140/90 mmHg and less). He was also diagnosed with an anxious-depressive syndrome. His current antihypertensive regimen was: quinapril 20 mg bid, moxonidine 0.4 mg bid, metoprolol succinate 50 mg bid, furosemide 40 mg bid (in the non-dialysis day), nifedipin 30 mg bid, isosorbide mononitrate 40 mg/day, aspirin 75 mg/day and atorvastatin 20 mg/day.

The patient presented to the Emergency Receiving Unit (ER) of Constanta County Hospital in non-dialysis day, with intense headache, nausea and orthopnea. Physical exam revealed white, pitting pretibial and palpebral edema and bilateral pulmonary crackles. His blood pressure was 290/140 mmHg, oxygen saturation (O₂Sat) level was 91%, and did not respond at all to furosemide 80 mg i.v. administration and captopril 25 mg sublingual in the ER. Neurological examination did not reveal any pathological finding. The 12-lead ECG

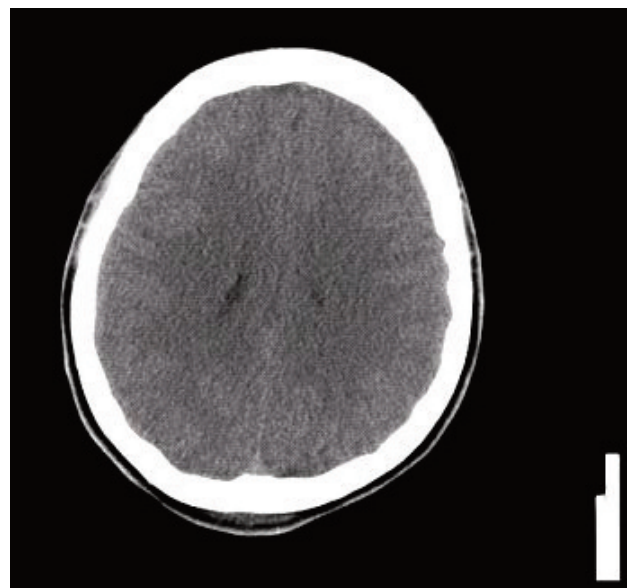


Figure 2. Brain native computed tomography at the ER admission.

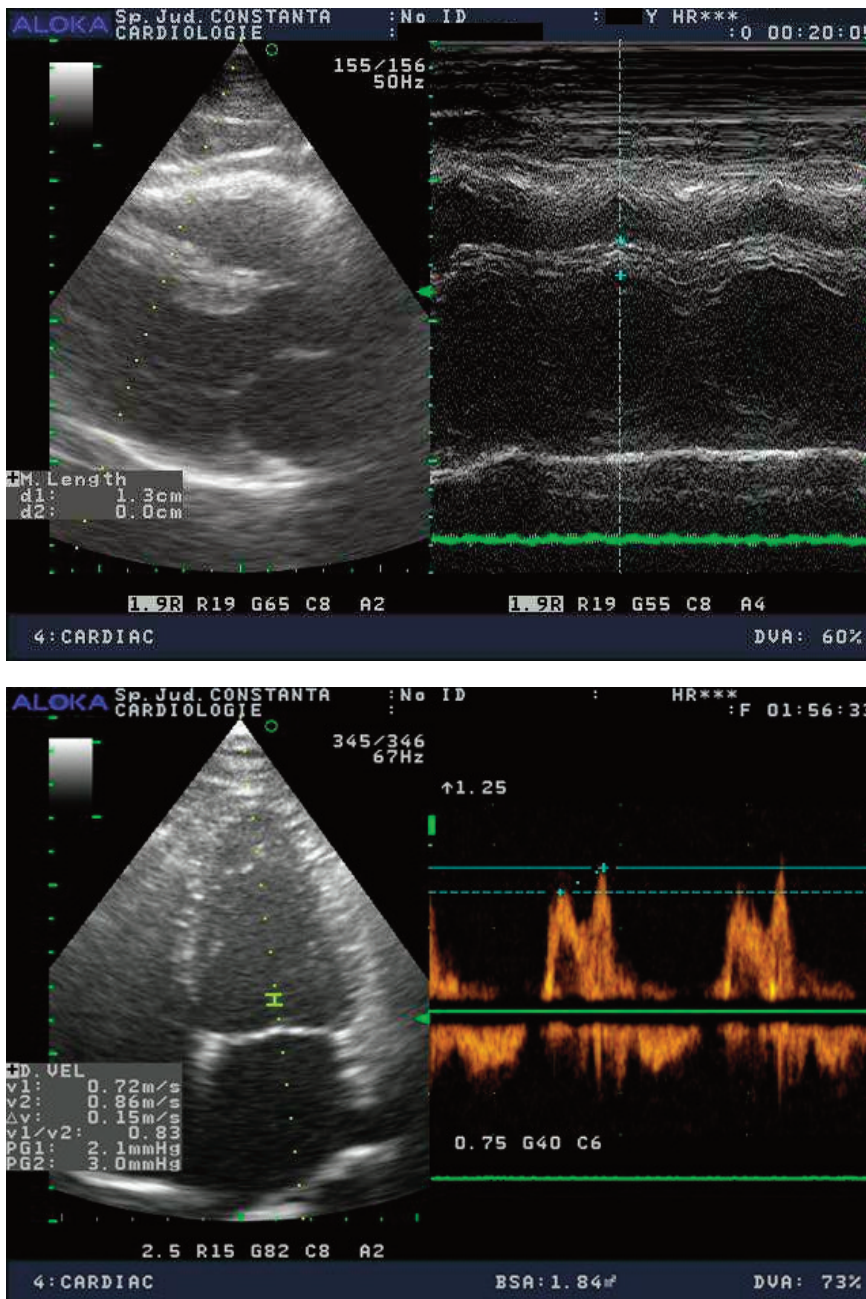


Figure 3. Ultrasound aspects from patient's standard echocardiography.

record showed sinus rhythm and signs of left ventricular hypertrophy (Figure 1). Cerebral native computed tomography pointed out slight diffuse cerebral edema (Figure 2).

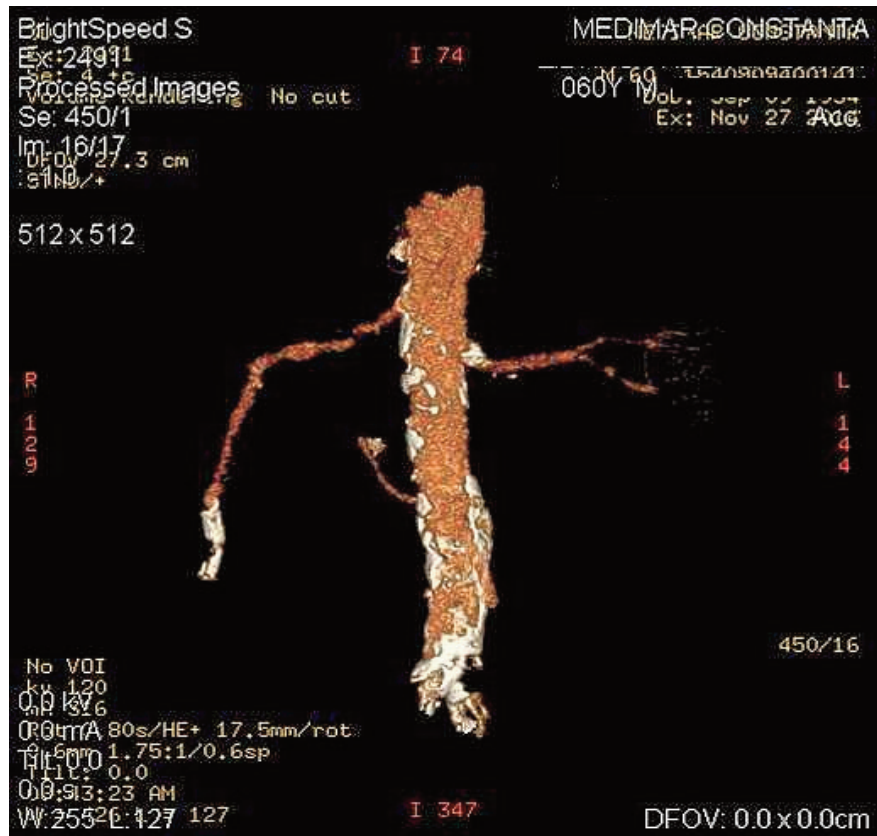
Standard echocardiography showed concentric left ventricular (LV) hypertrophy and first degree diastolic dysfunction (impaired relaxation), with preserved LV systolic function and no segmental systolic impairment (Figure 3).

Patient was initially admitted in the Cardiology Department. He received continuous intravenous infu-

sion with nitroglycerin, under which his blood pressure drop to 180/100 mmHg, and that is why he was transferred in Nephrology Department after 24 hours, to continue the therapy and perform dialysis, as scheduled.

Paraclinical investigations on admission in Nephrology department showed predialytic serum urea 128 mg/dl, serum creatinine 7.8 mg/dl, uric acid 7.1 mg/dl, iPTH 350 pg/ml, total seric calcium 9.6 mg/dl, serum phosphate 5.6mg/dl, sodium 140 mEq/dl, potassium 6.2 mE/dl, bicarbonates 15 mEq.dl. Inter-

Figure 4. Angio- CT with multiple atherosclerotic lesions on both renal arteries.



dialytic gain was only 2.3 kg and after dialysis, BP remained still uncontrolled, so we have decided to perform angio-CT scan with focus on abdominal aorta and renal arteries. Angio-CT showed multiple atherosclerotic lesions on abdominal aorta and ostial left renal artery stenosis with non-ostial right renal artery stenosis (Figure 4).

After receiving the computed-tomography angiography result, we excluded quinapril from patient's current medication and we obtain a good and sustained hypertensive control (average 142/91 mmHg, with maximum 155 mmHg systolic BP on CABPM).

Patient's medication at hospital release was: moxonidin 0.4 mg tid, metoprolol succinate 50 mg bid, furosemide 40 mg bid (in the day without dialysis), nifedipin 30 mg bid, isosorbide mononitrate 40 mg/day, aspirin 75 mg/day and atorvastatin 20 mg/day.

Discussion

Hypertension is a common finding in dialysis patients. In one multicenter trial that included 2535 adult he-

modialysis patients, the prevalence of hypertension, defined as one-week average pre-dialysis systolic BP measurements 150 mmHg or diastolic BP 85 mmHg or the use of antihypertensive medications, was 86%. In another definition of hypertension (defined by either a 44-hour inter-dialysis ambulatory BP of $\geq 135/85$ mmHg or the prescription of any antihypertensive agent) was 86% among 369 chronic HD patients [6].

Hypertension is not common only among patients who are just starting dialysis, usually due to volume overload, but persists afterwards, frequently reflecting an inadequate volume control despite the initiation of HD, mainly caused by inter-dialysis weight gain, in the context of reduced diuresis and non-compliance to salt and water restriction [7, 8].

In the randomized Dry-Weight Reduction in Hypertensive Hemodialysis Patients (DRIP) trial, dry weight was reduced progressively by additional ultrafiltration (UF), and patients with previous intradialytic hypertension who benefit of UF showed a real improvement in both intradialytic and inter-dialytic BP control [9]. At least two studies suggested that

lowering dry weight is improving inter-dialytic hypertension [10].

The definition of “resistant hypertension”, according to the 2008 American Heart Association scientific statement and the 2013 guidelines from the European Societies of Hypertension and Cardiology (ESH/ESC) is uncontrolled blood pressure that remains above goal in spite of concurrent use of at least three antihypertensive agents of different classes. Thus, patients whose blood pressure is controlled with four or more medications should be considered to have resistant hypertension. Patients with resistant hypertension are at high risk for adverse cardiovascular events and are more likely than those with controlled hypertension to have a secondary cause, which is usually at least in part reversible [11]. The most frequent causes of severe, uncontrolled hypertension in dialysis patients are: non-adherence to anti-hypertensive medication, hyperaldosteronism, erythropoietin administration, reno-vascular disease, pheochromocytoma [12]. So, the first thing before declaring a patient as having resistant hypertension is to check carefully possible secondary causes.

Atherosclerotic renal artery stenosis (RAS), already considered as a cause of chronic kidney disease (CKD), is also frequent in dialysis patients. It is generally unknown what proportion of end-stage renal disease patients on dialysis could recover kidney function if RAS were treated. Patients with CKD are often inadequately screened for RAS because of technical limitations, mainly due to the fear of contrast-induced nephropathy and nephrogenic systemic fibrosis (NSF) with gadolinium (Gd) based contrast agents (GBCA) used in magnetic resonance imaging, in those with pre-existing altered renal function [13].

RAS can determine either the syndrome of ischemic nephropathy (IN), or reno-vascular hypertension (RV-HTN). IN is a state of decreased kidney function caused by the reduction of the renal blood flow, small vessel injury and secondary nephrosclerosis. Some of the patients reaching to dialysis with RAS may have undiagnosed ischemic renal disease, sometimes with potential for regaining the renal function. RAS can coexist with other causes of CKD, mainly with diabetic nephropathy and hypertensive nephrosclerosis. Risk factors associated with RAS include: aortic and peripheral arterial disease, female gender, diabetes and congestive heart failure [14].

Patients reaching dialysis due to IN have very low survival rates (18% for 5-year survival rate, 5% for 10-year rate). Identification of the subgroup of dialysis patients with reversible IN, true candidates for renal revascularization and renal function recovery is a real challenge, especially in patients that recently started renal replacement therapy [15].

There are only few small case series and studies that have evaluated the role of revascularization for renal rescue in dialysis patients with RAS, because large, prospective, randomized multicenter trials of intervention for renal artery stenosis usually exclude patients with severe CKD [16]. Martin et al reported the most favorable outcome of angioplasty in ostial lesions of uremic patients, with improvement of renal function in 42% of cases, but this result may be explained by the low number of technically unsatisfactory angioplasties in their report: three of 79 patients, despite a large number (49 of 114 arteries) of ostial lesions treated. Other authors have not confirmed these good results and reported poor results for angioplasty in ostial lesions in comparison with those in nonostial lesions [17].

Patients with RAS have a 2.6 fold higher mortality and they require intensive medical treatment, including: smoking cessation, antiplatelet therapy, hypolipemiant drugs, and a proper control of BP. It is better to low blood pressure to levels $\leq 130/80$ mmHg, and in patients with unilateral artery stenosis the use of angiotensin antagonists is recommended in order to achieve an adequate blood pressure control, but renal function must be carefully monitored in pre-dialysis patients. A brutal increase, with $>30\%$ in serum creatinine levels, after angiotensin antagonists use, strongly suggests bilateral renal artery stenosis and needs withdrawal of these drugs. In the few studies that have compared medical conservative treatment vs angioplasty in ESRD patients, the group treated medically shown a similar outcome with those who had performed revascularization [18].

Further large, prospective studies are needed to answer unresolved issues, like:

- Which dialysis patients should be considered for reno-vascular evaluation and re-vascularization?
- Do the risks of angioplasty outweigh the potential benefit of restoring enough renal function and stop the need for dialysis?

Conclusion

Atherosclerotic bilateral renal artery stenosis can be the cause of a severe, resistant hypertension in a dialysis patient, and its proper management, either conservative, medicamentous, or angioplasty is a true challenge for both nephrologists and cardiologists.

Disclosure

The authors confirm that there are no conflicts of interest.

References

1. Levin A. Clinical epidemiology of cardiovascular disease in chronic kidney disease prior to dialysis. *Semin Dial.* 2003 Mar-Apr; 16(2):101-5.
2. Culleton BF, Hemmelgarn BR. Is chronic kidney disease a cardiovascular disease risk factor? *Semin Dial.* 2003 Mar-Apr; 16(2):95-100.
3. Mailloux LU, Haley WE. Hypertension in the ESRD patient: pathophysiology, therapy, outcomes, and future directions. *Am J Kidney Dis.* 1998; 32(5):705.
4. Agarwal R. Hypertension in chronic kidney disease and dialysis: pathophysiology and management. *Cardiol Clin.* 2005;23:237–248.
5. Agarwal R, Andersen MJ, Bishu K, et al. Home blood pressure monitoring improves the diagnosis of hypertension in hemodialysis patients. *Kidney Int.* 2006; 69: 900–906.
6. Agarwal R, Flynn J, Pogue V, et al. Assessment and management of hypertension in patients on dialysis. *J Am Soc Nephrol.* 2014; 25:1630.
7. Rahman M, Fu P, Sehgal AR, Smith MC. Interdialytic weight gain, compliance with dialysis regimen, and age are independent predictors of blood pressure in hemodialysis patients. *Am J Kidney Dis.* 2000; 35:257.
8. Nongnuch A, Campbell N, Stern E, et al. Increased postdialysis systolic blood pressure is associated with extracellular overhydration in hemodialysis outpatients. *Kidney Int* 2015; 87:452.
9. Agarwal R, Alborzi P, Satyan S, Light RP: Dry-weight reduction in hypertensive hemodialysis patients (DRIP): A randomized, controlled trial. *Hypertension.* 2009;53: 500–507.
10. Van Buren PN, Kim C, Toto R, Inrig JK: Intradialytic hypertension and the association with interdialytic ambulatory blood pressure. *Clin J Am Soc Nephrol.* 2011; 6: 1684–1691.
11. Vongpatanasin W. Resistant hypertension: a review of diagnosis and management. *JAMA.* 2014; 311:2216.
12. Malliara M. The management of hypertension in hemodialysis and CAPD patients. *Hippokratia.* 2007; 11(4): 171–174.
13. Dwyer JP1, Greco BA, Lewis JB. Evaluation of renal artery stenosis in dialysis patients. *Semin Dial.* 2009 Sep-Oct;22(5):519-23.
14. Bloch MJ, Basile J. Diagnosis and Management of Renovascular Disease and Renovascular Hypertension. *Journal of Clin Hypertension.* 2007; 9(5):381–389.
15. Garcia-Donaire JM and Alcazar JM. Ischemic nephropathy: Detection and therapeutic intervention. *Kidney International.*2005;68(99):131–136.
16. Thatipelli M, Misra S, Johnson CM, Andrews JC, Stanson AW, Bjarnason H, McKusick MA. Renal artery stent placement for restoration of renal function in hemodialysis recipients with renal artery stenosis. *J Vasc Interv Radiol.* 2008;19(11):1563–8.
17. Martin LG et al. Quality Improvement Guidelines for Angiography, Angioplasty, and Stent Placement for the Diagnosis and Treatment of Renal Artery Stenosis in Adults. *J Vasc Interv Radiol.* 2010;21: 421-430.