Nardi *et al.*
The Egyptian Journal of Internal Medicine (2023) 35:39
https://doi.org/10.1186/s43162-023-00224-1

The Egyptian Journal of Internal Medicine

CASE REPORT

Open Access

Rapidly reversible acute neurological, renal, and cardiac impairment during malignant hypertension

Giulia Nardi[1], Silvia Menale[2,3*], Valentina Scheggi[2,3] and Niccolò Marchionni[2]

Abstract

Background Malignant hypertension is a model of the rapid changes that a high afterload and renin-angiotensin levels can induce on target organs such as the heart. We present a case of a young man affected by malignant hypertension with multi-organ involvement who showed quick remission after adequate antihypertensive treatment.

Case summary A 41-year-old jazz pianist with a family history of coronary artery disease presented to the emergency department for asthenia and epigastric pain, associated with right eye visual impairment. No neurological symptoms. An echocardiogram showed left ventricular hypertrophy with severe impairment of ejection fraction (22%) due to global hypokinesia. There was renal insufficiency (creatinine 2.51 mg/dl, eGFR 34 ml/min, HS Troponin T 127 pg/dl, NT pro-BNP 22,672 pg/ml, CRP 32 mg/L, sodium 129 mEq/L with normal kaliemia. The following day, anterior T wave inversion was observed in the electrocardiogram. At a cardiac magnetic resonance. Concentric hypertrophy of the left ventricle was observed with normal myocardial T1 mapping values (1100 ± 38 ms), ruling out Fabry's disease. There was no obvious myocardial edema at T2 weighted. The viral panel for acute myocarditis resulted in negative. After the exclusion of all possible secondary causes, malignant essential hypertension was the final diagnosis, and additional tests confirmed multi-organ damage. An ophthalmological examination demonstrated hypertensive retinopathy with hemorrhages, cottony exudates, and macular lipid exudation, especially in the right eye. A brain MRI showed small areolas of T2 hyperintensity in the white matter of both cerebral hemispheres, suggestive of chronic microangiopathy, and left nuclear micro lacunar ischemia.

The patient was treated with full-dose calcium channel blockers (amlodipine 10 mg), beta-blockers (bisoprolol 10 mg), alpha2 agonists (slow-release clonidine patch), selective a1 blocker (doxazosine 16 mg), and furosemide 50 mg. After the exclusion of renal stenosis and improvement of renal function, Ramipril was added up to a final dose of 10 mg daily. In parallel with the achievement of a satisfactory blood pressure control, visual impairment disappeared with a reduction of retinal ischemic exudates and hemorrhages at the ophthalmological follow-up assessment.

At the time of discharge, an echocardiographic re-evaluation confirmed concentric hypertrophy of the left ventricle with markedly reduced wall thicknesses, with a partial recovery in left ventricular ejection function (EF 44%).

Six months after discharge, the patient is in good general condition under optimal medical therapy (without furosemide) with normalized blood pressure values (130–140/80 mmHg). At 6 months from discharge, creatinine was only mildly increased (1.5 mg/dl, eGFR 59.5 ml/min) and NT-pro BNP nearly normalized (452 pg/ml).

*Correspondence:
Silvia Menale
silvia.menale@unifi.it
Full list of author information is available at the end of the article

Discussion Malignant hypertension is a cardiovascular emergency and requires immediate and careful intervention to lower blood pressure and reduce organ injury. It is an exclusion diagnosis that can be advanced once the causes of secondary hypertension have been excluded. Remission of organ injury is possible and might be rapid under adequate antihypertensive treatment, but patients require a close follow-up.

Keywords Malignant hypertension, Antihypertensive treatment, Hypertension-related organ damage

Background

Malignant hypertension is a model of the rapid changes that a high afterload and renin-angiotensin levels can induce on target organs such as the heart. We present a case of a young man affected by malignant hypertension with multi-organ involvement who showed quick remission after adequate antihypertensive treatment.

Case presentation

A 41-year-old jazz pianist with apparently no cardiovascular risk factors presented to the emergency, presented to the emergency department for asthenia and epigastric pain with episodes of nausea and vomiting. He developed progressive fatigue and breathlessness, associated with right eye visual impairment and depression requiring therapy with benzodiazepines and paroxetine. He had suffered from recurrent tension headaches, occasionally treated with non-steroidal anti-inflammatory drugs (NSAIDs) but not recently used. He denied smoking, alcohol abuse, or use of recreational drugs.

Physical examination on admission revealed sinus tachycardia 110 beats/min, severe hypertension (205/110 mmHg), and an impaired oxygen saturation of 91%. Heart sounds were normal without detectable murmur, and jugular veins were not distended. At thoracic examination there were basal bilateral lung crackles, and no ankle oedema, the epigastric quadrant was tender to the touch. The neurological examination was negative.

Electrocardiography showed left ventricle overload. A bedside chest ultrasound showed bilateral pleural effusion. An echocardiogram showed left ventricular hypertrophy (interventricular septum and posterior wall 18 mm) with severe impairment of ejection fraction (EF) (22%) due to global hypokinesia (Fig. 1). Blood exams shown values suggestive of grade III B renal insufficiency, with creatinine values of 2.51 mg/dl

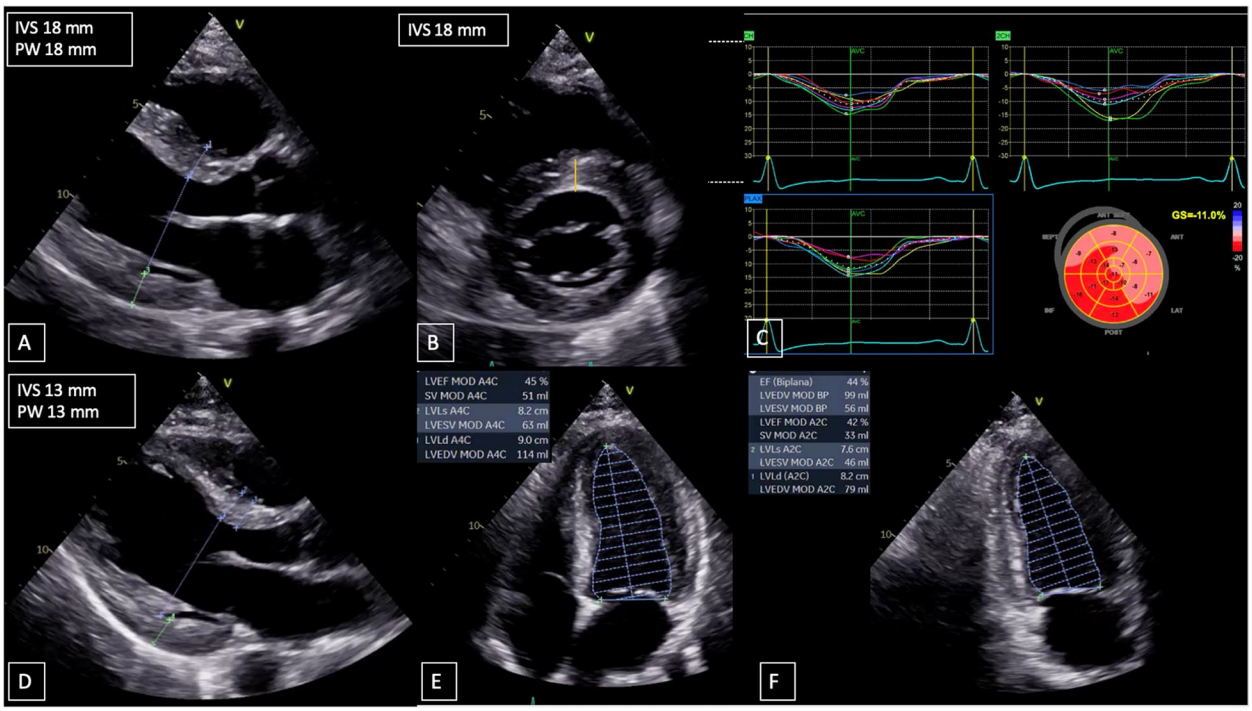

Fig. 1 Echocardiogram at the admission showed concentric left ventricle hypertrophy (**A**, **B**), reduced ejection fraction (EF 22%) and reduced [GLS – 11%] (**C**). At discharge (15 days later), the echocardiogram showed reduced wall thickness (**D**) with mild improvement in LV function (EF 45%) using Simpson's biplane method (**E**, **F**)

and estimated glomerular filtration rate (eGFR) 34 ml/min, abnormal high sensitive (HS) Troponin T levels (127 pg/dl), N terminal pro brain natriuretic peptide (NT pro-BNP) 22,672 pg/ml, C reactive protein (CRP) 91 mg/L, sodium 129 mEq/L and potassium 3.9 mEq/L, and lactate 2.5 mmol/l (Table 1).

So, the patient was transferred to the middle-intensive care unit, treated with intravenous furosemide and nitrates with improvement in systemic blood pressure control (140/100 mmHg), normalization of peripheral saturation (99%) with low oxygen support (FiO_2 32%), and reduction of lactates (0.8 mmol/l versus 2.5 mmol/l). The following day, anterior T wave inversion was observed at the control electrocardiogram. After clinical stabilization, it was considered appropriate to investigate the etiology of the clinical syndrome thought a cardiac magnetic resonance imaging (MRI), without late gadolinium enhancement because of the renal impairment. Concentric hypertrophy of the left ventricle was confirmed, normal myocardial T1 mapping values (1100 ± 38 ms), ruling out Fabry's disease. No evident myocardial edema at T2-weighted sequences was highlighted. The viral panel for acute myocarditis resulted negative.

Moreover, the patient resulted negative at the screening for metabolic diseases, comprehensive of plasma acylcarnitine, profile of blood amino acids, and urinalysis for organic acids. The autoimmune revealed traces of cryoglobulin and a weakly positive rheumatoid factor—findings of uncertain significance.

In consideration of persistently elevated pressure values, we performed second level exams to rule out secondary hypertension.

Renal ultrasound showed a small right kidney with preserved cortico-medullary differentiation and reduced vascularization. Captopril renal scintigraphy confirmed significant hypoperfusion of the right kidney. Hemodynamically significant stenosis of the right renal artery was excluded with selective arteriography of the renal arteries, showing well patent vessels with no atherosclerotic changes or alterations suggestive of fibromuscular dysplasia.

The search for urinary metanephrine and normetanephrine, and the screening for monoclonal gammopathy were also negative.

After exclusion of all possible secondary causes, the final diagnosis was essential malignant hypertension, with overt signs of multi-organ damage. In fact, an ophthalmological examination demonstrated hypertensive retinopathy with area of hemorrhage, cottony exudates, and macular lipid exudation, especially in the right eye. A brain MRI revealed small areolas of T2 hyperintensity in the white matter of both cerebral hemispheres, typically found in chronic microangiopathy, and left nuclear micro lacunar ischemia.

The patient could reach a satisfactory blood control with an amount of 6 antihypertensive drugs, including a full-dose calcium channel blockers (amlodipine 10 mg), beta-blockers (bisoprolol 10 mg), alpha2 agonists (slow-release clonidine patch), selective a1 blocker (doxazosin 16 mg), and furosemide 50 mg. After the exclusion of renal stenosis and improvement of renal function, Ramipril was up titrated to a final dose of 10 mg daily. As further optimization of heart failure with reduced ejection fraction, the patient was started on SGLT2-inhibitors (dapaglifozin 10 mg). After the exclusion of renal stenosis and improvement of renal function ramipril was up titrated to a final dose of 10 mg daily. As soon as the blood pressure (BP) values reached a normal trend, visual symptoms notably improved with a progressive reduction of retinal ischemic exudates and hemorrhages at the ophthalmological follow-up assessment (Fig. 2).

Fifteen days later, at the time of discharge, an echocardiographic reassessment showed an important reduction of the wall thicknesses (septum and posterior wall 13 mm vs 16 mm and 14 mm), with a partial recovery of the left ventricular EF (44%) (Fig. 1).

Six months after discharge, the patient was in clinically good general conditions, with an adequate BP control (130–140/80 mmHg at routine measurements). Creatinine values

Table 1 Blood exams trend from the admission, discharge, and recovery at 6-month follow-up

Lab exams	*Admission*	*Discharge*	*Follow-up*
Creatinine (mg/dl)	2.51	1.93	1.5
eGFR (ml/min)	34	42	59.5
Troponine T HS (pg/dl)	127	25	14
NT-pro-BNP (pg/ml)	22,672	906	452
CRP (mg/L)	91	13	< 5

Fig. 2 Multimodal imaging was acquired a few days after admission at the first ophthalmological evaluation, at discharge and during follow-up. In the multicolor fundus photo, we see retinal lipidic exudates, radiating along the retinal nerve fiber layer resembling a macular star, with cotton wool spots, a marker of inner retina ischemic injury in both right (**A**) and left (**B**) eye. At spectral-domain optical coherence tomography, we appreciate a serous neuroretinal detachment with intraretinal exudates at the macular level and around the optic papilla (Figs. **C** and **D**, respectively, right and left eye). At discharge, we see a reduction in neuroretinal detachment in both eyes and partial reabsorption of intraretinal exudates (**G** right eye, **H** left eye). In multicolor fundus pictures, we see partial reabsorption of cotton wool spots and lipidic exudates (**E**, **F**). Two months after the admission, the clinical picture has substantially resolved, with almost total reabsorption of lipidic exudates and absence of subretinal fluid (**M**, **N**). Only traces of lipidic exudates and cotton wool spots are left at fundus multicolor imaging (**I**, **L**)

shown a declining trend, even though still mildly increased (1.5 mg/dl, eGFR 59.5 ml/min), NT-pro BNP nearly normalized (452 pg/ml) (Table 1). At the 1-year follow-up echocardiogram, interventricular septum and left ventricle posterior wall thickness reached nearly normal values (12 mm and 11 mm respectively), and EF improved up to 50% (Fig. 3).

Discussion

Malignant essential hypertension (MHT) is defined clinically by a diastolic pressure above 130 mmHg) and acute ischemic damages on target organs (e.g., eye, brain, kidney, and heart). To be diagnosed, ocular involvement must be present, as hypertensive retinopathy grades III or IV, according to the classification of Keith, Wagener, and Barker [1]. It is accompanied by bilateral retinal hemorrhages and/or exudates, with or without papilledema. In order to aid the diagnostic process, it has been suggested to include other criteria, such as an impairment of at least three different target organs (kidney, heart, brain, microangiopathy) and out of range elevation in systolic and/or diastolic BP. In the Bordeaux registry published in 2018, 168 patients with

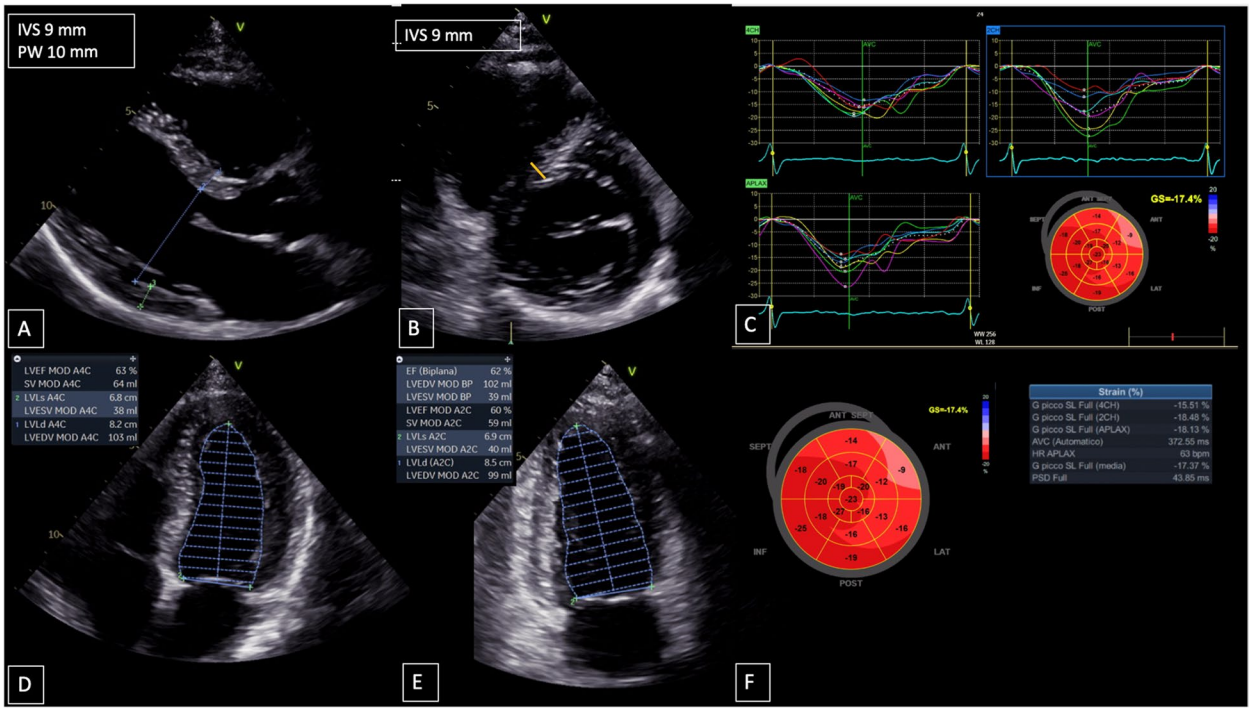

Fig. 3 Echocardiogram at 6 months of follow-up documented reduction in LV wall thickness within normal values (**A**, **B**), improvement in LV ejection fraction (EF 63%) using Simpson's biplane method (**D**, **E**), and improvement in GLS to – 17.4% (**C**, **F**)

MHT were enrolled between 1995 and 2017 systematic MRIs found significant brain damage in 93% of patients. Heart involvement was highly prevalent: 82% had a left ventricular mass greater than 60 g/m2, and 56% had systolic dysfunction, estimated by global longitudinal strain. Renal involvement was present in 55% of patients [2]. In our specific case, the initial pressure measurements were not so extreme to require acute intravenous treatment with urapidil or nitroprusside, but the neurological deficit, the acute impairment of left ventricular, and renal function were dramatic. Pathological changes at the fundoscopic exam (flame hemorrhages) as onset manifestation further confirmed the diagnosis. The pathophysiological substrate of this condition is small artery fibrinoid necrosis in the kidney, retina, and brain triggered by endothelial dysfunction and coagulative disorders [3]. Kidney damage in this context is the result of feedback mechanisms that come from a crosstalk between heart and kidney, such condition is known as type 1 cardiorenal syndrome (CRS). This is characterized by the development of acute kidney injury in a patient with a low cardiac output state. CRS is due to a complex series of events that lead to due to kidney dysfunction through the activation of neurohormonal cell signaling, oxidative stress, venous congestion, activation of the renin-angiotensin aldosterone system (RAAS), and maladaptive cell response through fibrosis [4].

Under progressive up-titration of antihypertensive treatment, according to the recent guidelines [5], we observed a rapid normalization of both cardiac and renal function. This rapid recovery has been observed by other clinicians that assessed the consequences of malignant hypertension on left ventricular function and its evolution with antihypertensive treatment [6]. They concluded that in their series of 46 patients, short-term follow-up (1–3 months) showed a rapid improvement in systolic function together with significant hypertrophy regression. With a follow-up of 11 months, on average, all patients had recovered a normal global longitudinal strain with further but incomplete regression of hypertrophy [6].

Cardiac MRI had a pivotal role to aid differential diagnosis, including LV hypertrophy phenocopies. Particularly the normal T1 values allowed to rule out Anderson Fabry disease (that was suspected because of simultaneous renal, cardiac, and neurological involvement) and amyloidosis (also because of normal free light chains levels) that commonly present reduced T1 mapping values. Metabolic and autoimmune disorders were excluded since plasma acylcarnitine, profile of blood amino acids, and urinalysis for organic acids resulted negative and the traces of cryoglobulin and rheumatoid factor were not clinically relevant. Acute myocarditis was considered in the diagnostic process, because of the

clinical presentation at the admission, but the viral panel resulted negative and the pattern described by cardiac MRI was not suggestive (no evident myocardial edema at T2 weighted sequences was highlighted). Certainly, a cardiac biopsy could have been considered in the diagnostic work-up, but the rapid clinical, instrumental, and hemodynamic recovery of the patient after adequate therapy refrain clinicians from performing an invasive examination.

Conclusions

Malignant hypertension is a cardiovascular emergency and requires immediate and careful intervention to lower blood pressure and reduce organ injury. It represents an exclusion diagnosis that can be advanced once the causes of secondary hypertension have been ruled out. Remission of organ injury is possible and might be rapid under adequate antihypertensive treatment, but patients need a strict follow-up.

Abbreviations

CRP	C-reactive protein
CRS	Cardio-renal syndrome
EF	Ejection fraction
eGFR	Estimated glomerular filtration rate
FiO_2	Fraction of inspired oxygen
IVS	Interventricular septum
MI	Myocardial infarction
MHT	Malignant essential hypertension
MRI	Magnetic resonance imaging
NSADIs	Non-steroidal anti-inflammatory drugs
NT-pro-BNP	N terminal pro-brain natriuretic peptide
PW	Pulsed wave
RAAS	Renin-angiotensin aldosterone system
SGLT2-i	Sodium-glucose cotransporter-2 inhibitors

Acknowledgements

None.

Authors' contributions

Giulia Nardi, MD: investigation, conceptualization, data curation, formal analysis, and writing. Silvia Menale, MD: data curation, formal analysis, review, and editing. Valentina Scheggi, MD: supervision, review, and editing. Niccolo' Marchionni, MD: supervision, review, and editing.

Funding

None.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

At admission, the patient signed a generic informed consent for the treatment of personal data. The case report has been completely anonymized.

Competing interests

The authors declare that they have no competing interests.

Author details

[1]Structural Interventional Cardiology, Careggi University Hospital, Florence, Italy. [2]Cardiothoracovascular Department, Azienda Ospedaliero, Universitaria Careggi and University of Florence, Largo Brambilla 3, 50134 Florence, Italy. [3]Division of Cardiovascular and Perioperative Medicine, Azienda Ospedaliero-Universitaria Careggi and University of Florence, Florence, Italy.

Received: 15 March 2023 Accepted: 31 May 2023
Published online: 05 June 2023

References

1. Chen X, Liu L, Liu M, Huang X, Meng Y, She H, Zhao L, Zhang J, Zhang Y, Gu X, Qin X, Zhang Y, Li J, Xu X, Wang B, Hou FF, Tang G, Liao R, Huo Y, Li J, Yang L (2021) Hypertensive retinopathy and the risk of stroke among hypertensive adults in China. Invest Ophthalmol Vis Sci 62(9):28. https://doi.org/10.1167/iovs.62.9.28.PMID:34283210;PMCID:PMC8300046
2. Boulestreau R, Van den Born BH, Lip GYH, Gupta A (2022) Malignant hypertension: current perspectives and challenges. J Am Heart Assoc 11(7):e023397. https://doi.org/10.1161/JAHA.121.023397. (Epub 2022 Mar 15. PMID: 35289189; PMCID: PMC9075423)
3. van den Born BJ, Löwenberg EC, Van der Hoeven NV, de Laat B, Meijers JC, Levi M, Van Montfrans GA (2011) Endothelial dysfunction, platelet activation, thrombogenesis and fibrinolysis in patients with hypertensive crisis. J Hypertens 29(5):922–7. https://doi.org/10.1097/HJH.0b013e328345023d. (PMID: 21372741. : s.n)
4. Ronco C, Cicoira M, McCullough PA (2012) Cardiorenal Syndrome Type 1: Pathophysiological crosstalk leading to combined heart and kidney dysfunction in the setting of acutely decompesated heart failure. J Am Coll Cardiol 60(12):1031–42. https://doi.org/10.1016/j.jacc.2012.01.077
5. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, Kahan T, Mahfoud F, Redon J, Ruilope L, Zanchetti A, Kerins M, Kjeldsen SE, Kreutz R, Laurent S, Lip GYP, McManus R, Narkiewicz K, Ruschitzka F, Schmieder RE, Shlyakhto E, Tsioufis C, Aboyans V, Desormais I (2018) ESC Scientific Document Group, 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). Eur Heart J 39(33):3021–3104. https://doi.org/10.1093/eurheartj/ehy339
6. Gosse P, Coulon P, Papaioannou G, Litalien J, Lemetayer P (2011) Impact of malignant arterial hypertension on the heart. J Hypertens 29(4):798–802. https://doi.org/10.1097/HJH.0b013e3283430b12. (PMID: 21178780)

Publisher's Note