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Management of Labile Blood Pressure due to COVID-19 Infection and Radiation Induced Baroreceptor Dysfunction

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INTRODUCTION

The baroreceptor reflex is responsible for beat-to-beat blood pressure (BP) regulation and its failure results in different clinical syndromes that manifest with blood pressure dysregulation.[1] Baroreceptor dysfunction can be caused by neck irradiation, neck surgery, repeated neck trauma, and more recently COVID-19.[2,3] In patients with hypertension, baroreceptor dysfunction can lead to extremely labile blood pressures that are difficult to manage.[3]

Head and neck cancers account for more than 900,000 yearly cases of cancer.[4] From this population, 4% develop lower cranial nerve deficits from radiotherapy that results in baroreceptor failure. More recently, autonomic dysfunction, including that of the baroreceptor reflex, has been identified as part of the post-COVID-19 syndrome.[5,6] Cases of both new autonomic dysfunction and worsening of existing dysfunction have been described.[2,6,7]

A case of labile blood pressure due to damage to their baroreceptors by radiation is presented, which became significantly worsened after COVID-19 infection. Within this case, the challenges and approach to manage such uncontrolled blood pressures were discussed.

CASE REPORT

A 76-year-old male veteran with a history of hypertension, basal cell carcinoma with radiation therapy to the neck in 2015, orthostatic hypotension (OH), congestive heart failure, coronary artery disease, type 2 diabetes, chronic obstructive pulmonary disease, gastroesophageal reflux disease, and recent COVID-19 infection presented with complaints of severe "charley horse-like" pain in his chest. He reported that his blood pressures over the last month have fluctuated rapidly from greater than 220 mmHg to below 100 mmHg systolic causing him to have significant orthostatic hypotension. On review of medical records, he had three emergency department (ED) visits during the prior month with similar complaints and findings. The only significant change in his medical history was a COVID-19 infection one month prior to this admission. The patient stated his blood pressure was manageable prior to his COVID-19 infection, averaging 100-130 mmHg systolic. Review of his home medications revealed a blood pressure control regimen of: lisinopril 20 mg BID, metoprolol tartrate 50 mg BID, and isosorbide mononitrate 30 mg daily.

In the ED, the patient had a sitting blood pressure of 226/109 mmHg, but his other vital signs were normal and physical examination was unremarkable. Complete metabolic panel and complete blood count were unremarkable. He had elevated troponins of 0.061 ng/ml (normal range of 0-0.033 ng/ml) and his electrocardiogram was unremarkable.

In response to his severely elevated blood pressure, the patient received IV hydralazine 10 mg which adequately lowered his blood pressures. He was admitted for hypertensive emergency given his chest pain, elevated troponins, and elevated blood pressure. The cardiology service was consulted for his elevated troponins and their final disposition attributed the troponins to a type II myocardial infarction secondary to his severely elevated blood pressures.

Upon admission, the patient's home regimen of metoprolol tartrate 50 mg BID was continued, lisinopril was changed from 20 mg BID to 10 mg TID, hydralazine 10 mg was added as needed for standing systolic blood pressures greater than 160 systolic two hours after lisinopril, and isosorbide mononitrate 30 mg was discontinued. During this hospital course, his fluctuating standing blood pressure measurements had no correlation to time of day or any other triggers. Within the one to two days of admission, the patient's standing systolic blood pressures ranged from 97-214 mmHg (Figure 1). His blood pressures remained difficult to control and, in response, clonidine 0.1 mg was added. For one day only, his standing blood pressures were controlled tightly between 96-125 mmHg (Figure 1).

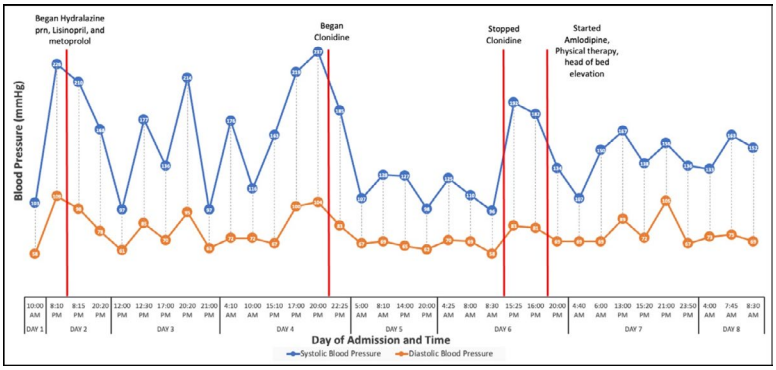

Figure 1. Blood pressure measurements and interventions were charted throughout the hospital course.

The patient experienced symptoms of lightheadedness and dizziness when his systolic blood pressure dropped below 100 mmHg. During this hospital stay, he had extensive work up for secondary causes of hypertension. His workup for cardiac dysfunction with an echocardiogram, adrenal insufficiency and Cushing Syndrome with 24-hour cortisol test, pheochromocytoma with metanephrines and catecholamines, and renal artery stenosis with renal ultrasound were all unremarkable (Table 1). Nephrology/hypertension specialists were consulted, and they discontinued clonidine, started amlodipine 5 mg, recommended the patient to elevate the head of the bed at 30 degrees, started physical therapy for strengthening exercises, and gave the patient compression stockings. With these recommendations, the patient's standing blood pressures over the course of two days, never peaked more than 160 mmHg systolic and never dropped lower than 107 mmHg systolic (Figure 1).

Table 1. Key patient characteristics, laboratory, and imaging findings during the hospital course.

	Description	Result	Normal Ranges
Anthropometrics	Weight	88.95 kg	
	Height	182.88cm	
	Body Mass Index	26.6 kg/m^2	
Relevant Laboratory Tests			
	Hemoglobin A1c	8.30%	
	Creatinine	0.94 mg/dL	0.7-1.3 mg/dL
	Plasma free metanephrine	30 pg/mL	(≤ 57 pg/mL)
	Plasma Normetanephrine fraction	60 pg/mL	(≤ 148 pg/mL)
	Plasma metanephrine total	90 pg/mL	(≤ 205 pg/mL)
	Troponin peak	0.061 ng/mL	(0-0.1ng/mL)
	BNP	142 pg/mL	(HF likely, > 400pg/mL)
	TSH	3.74 IU/mL	(0.5-5.0 UI/mL)
	AM Cortisol	3.9 ug/dL	(3.7-19.4 ug/dL)
	Aldosterone (supine AM)	9 ng/dL	Supine: (3-16 ng/dL)
Imaging and Other Studies	Renal ultrasound	No sonographic evidence of significant renal artery stenosis	
	Echocardiogram	LVEF: 50% Trace TR, MR, AI	

Abbreviations: BNP-Brain Natriuretic Peptide, HF-Heart Failure, TSH-Thyroid Stimulating Hormone, AM-Morning, LVEF-Left Ventricular Ejection Fraction, TR-Tricuspid Regurgitation, MR-Mitral Regurgitation, AI-Aortic Insufficiency.

In a three-month follow-up with the cardiology service, they recorded his average blood pressure at 136/72 mmHg, with systolic blood pressure highs of 160's and lows of 100's. The patient closely adhered to the medication regimen, went to all his physical therapy appointments, and had little to no symptoms of OH.

DISCUSSION

Management of labile blood pressure due to baroreceptor failure remains difficult. It is challenging to establish a floor and ceiling for these patients as their blood pressure remains chronically volatile.[8] Baroreflex nerve lesions can cause drastic changes in systolic blood pressures that can exceed 300 mmHg.[9,10] This dangerous volatility was demonstrated in our patient with systolic blood pressures that ranged from the 90s to the 230s mmHg within a span of 20 minutes (Table 1). This established the difficulty of controlling a patient's blood pressure in a range that was safe and allowed the patient to be asymptomatic. For this patient, a specific regimen of pharmacologic and nonpharmacologic treatments showed promising control of this labile blood pressure.

For pharmacological management, clonidine was discontinued as this patient began to have significant drops in his blood pressure. Some patients with baroreflex failure can be treated effectively with clonidine.[8] Clonidine was compared against phenoxybenzamine and showed that clonidine was effective at reducing both the frequency and severity of hypertensive and tachycardic surges. For our patient, clonidine was effective at controlling his hypertensive episodes, but exacerbated his hypotensive episodes. Antihypertensives such as clonidine could cause precipitous drops in blood pressures and as a result, it was not an appropriate choice for this patient.

Our patient was started on amlodipine 5 mg QD with goals of titrating upwards. Amlodipine was the antihypertensive choice because the medication could control his elevated blood pressure and did not drop this patient's blood pressure. Rivasi et al.[11] showed that calcium channel blockers (CCB) can have a protective effect against orthostatic blood pressure in older people. The study explained that a dihydropyridine CCB frequently can induce a compensatory increase in heart rate, which serves as a counteraction against a drop in blood pressure. Furthermore, CCBs have little to no association with causing orthostatic hypotension.[12,13]

Lisinopril 10 mg TID was used to control his blood pressure in our patient. Angiotensin-converting-enzyme inhibitors (ACEi) and angiotensin II receptor (ARBs) blockers were not associated with OH and may have protective effects, which are attributed by the improvement of baroreceptor sensitivity and vascular compliance.[14-18]

For nonpharmacological management, the patient should have his bed elevated at least 30 degrees. Elevating the head of the bed in treatment of labile blood pressure decreases nocturnal hypertension and nocturnal diuresis.[19] The mechanism behind this demonstrated that fluctuations in blood pressure due to lying down may affect the body's regulation of arginine vasopressin, an anti-diuretic hormone, which, in turn, can affect nocturnal blood pressure and diuresis.[20] The increase in diuresis could affect further how the body regulates our blood pressure.

Physical and occupational therapy were recommended for strengthening exercises and can control this patient's OH. Deconditioning from lack of exercise worsens OH.[21,22] To combat deconditioning, physical therapy was a good choice to promote safe and supervised physical activity and mild physical exercise can improve orthostatic tolerance by decreasing venous pooling.[22]

Our patient's blood pressure variations during admissions prior to and after he suffered from COVID-19 revealed increased lability in his blood pressures after the infection. He received radiation to his neck for basal cell carcinoma five years prior to this presentation which may have resulted in baseline autonomic dysfunction. His baroreceptor dysfunction was worsened by COVID-19 based on the temporal associations.[5,23] Regular and frequent follow-ups with his primary care physician and nephrologist for monitoring and adjusting of medications were recommended because of the lack of literature on the natural history of COVID-19 induced baroreceptor dysfunction. Improvements in baroreceptor function over time could necessitate treatment adjustments.

Recommendations for patients struggling with labile blood pressures due to autonomic dysfunction are to approach their management with an individualized, multifaceted strategy. For our patient, it proved important to individualize blood pressure control targets based on symptoms, response to therapy, and empiric ceilings to minimize end organ damage. Drugs were avoided that were associated more frequently with orthostasis like clonidine and antihypertensives were chosen that were associated less frequently with orthostasis such as CCB, ACEi, and ARBs. Non-pharmacologic interventions were included such as elevation of the head of the bed and physical therapy to decrease changes in orthostatic blood pressure and deconditioning.

It was difficult to control this patient's blood pressure due to its unpredictable and fluctuating nature. There were significant limitations in antihypertensives that we could choose because his blood pressure could bottom out. At the same time, medications such as midodrine or fludrocortisone could not be given because they could exacerbate his hypertensive episodes.[24] Overall, the goal of management for this patient was to avoid high and low blood pressures, while minimizing symptoms with the realistic understanding that it was not expected that his blood pressure would be consistently in the normal range. This regimen of pharmacologic and nonpharmacologic interventions allowed this patient to maintain his blood pressure with a ceiling that was safe and a foundation that prevented symptomatic OH.

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