

Afferent Baroreflex Failure Following Neck Radiation: A Case Report

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Abstract

Afferent baroreflex failure is a rare but serious complication of neck irradiation that causes extreme blood pressure variability. We present the case of a 72-year-old man with oropharyngeal cancer treated with chemotherapy and neck radiation who developed severe blood pressure lability several years after therapy. After a thorough workup ruled out other possible causes, a clinical diagnosis of afferent baroreflex failure was made, despite the absence of formal autonomic testing. Management included long acting central sympatholytics together with as needed medications to treat both hypotensive and hypertensive episodes. This case demonstrates a physiology based treatment strategy as outlined by the Vanderbilt Autonomic Dysfunction Center in the absence of formal guidelines.

Introduction

The baroreflex provides constant and immediate regulation of blood pressure. Baroreceptors are stretch sensitive nerve endings in the carotid sinus and aortic arch. When blood pressure rises, afferent signals increase. This stimulates parasympathetic activity and reduces sympathetic output. Disruption of these pathways by injury to the carotid sinus nerves or autonomic ganglia can cause exaggerated hypertensive responses and heightened sensitivity to vasopressors (1–4).

Neck irradiation is responsible for nearly all cases of afferent baroreflex failure (5). Subclinical impairments may appear soon after radiation therapy (6, 7). Clinically significant dysfunction occurs years later due to progressive fibrosis and damage to the baroreceptor pathways (8). The incidence of this complication remains uncertain.

Afferent baroreflex failure is marked by severe blood pressure instability with alternating hypertensive

crises. Patients often experience hypertensive episodes triggered by mental stress or exertion (9). These episodes are frequently accompanied by facial flushing (10). All patients exhibit hypertension but only some also experience hypotensive episodes. The absence of hypotensive events in some patients may be due to compensatory mechanisms involving aortic baroreceptors and vestibular afferents (11).

Diagnosis of afferent baroreflex failure is primarily clinical and depends heavily on a thorough history, particularly prior neck surgery or radiation, along with the exclusion of alternative diagnoses such as essential hypertension, pheochromocytoma, sympathomimetic drug use, panic disorder, and postural tachycardia syndrome. Ambulatory monitoring of blood pressure and heart rate can reveal the hallmark feature of marked blood pressure variability accompanied by an inappropriate or absent heart rate response. A definitive diagnosis typically requires formal autonomic testing with continuous hemodynamic monitoring during pharmacologic provocation using agents such as phenylephrine and nitroprusside. Patients with afferent baroreflex failure exhibit exaggerated blood pressure responses without the expected compensatory changes in heart rate, reflecting impaired afferent baroreceptor signaling.

Case Presentation

A 72-year-old man presented with significant blood pressure variability. His medical history included severe aortic stenosis, type 2 diabetes mellitus, atrial fibrillation, hypothyroidism, and dyslipidemia. Importantly, the patient received definitive chemotherapy and radiation without surgical resection for stage T2N1M0, p16-positive squamous cell carcinoma of the right tonsil with extension into the soft palate and involvement of right level II lymph nodes. Intensity-modulated radiation therapy was

delivered to a total dose of 6,750 centigray in 30 treatment sessions. The radiation plan included contouring of the primary tumor in the right tonsil with extension into the soft palate, as well as involved right-sided lymph nodes, with dose calculations accounting for adjacent normal tissues. Cisplatin was administered weekly during the course of radiation therapy.

Approximately 4 years after radiation, he began to experience marked blood pressure lability. The patient completed chemoradiation in June 2018. Symptoms of labile blood pressure began in late 2022. He was first evaluated in December 2022. A 24-hour ambulatory blood pressure reading was performed in April 2023. Symptoms have been persistent through the present.

Upon presentation, home readings showed systolic values ranging from 71 to 192 mmHg. Hypotensive episodes were often postural and associated with dizziness, headache, and near syncope. His symptoms were initially attributed to severe aortic stenosis, but they persisted despite surgical valve replacement. At the time of presentation, his antihypertensive regimen included daily oral lisinopril 20 mg and metoprolol succinate ER 200 mg.

Ambulatory blood pressure monitoring revealed a systolic variation of 120 mmHg over a single day, with preservation of the normal nocturnal dip. Figure 1, 24-hour ambulatory blood pressure and heart rate monitoring, displays the 24-hour ambulatory blood pressure and corresponding heart rate data, demonstrating significant blood pressure variability without appropriate compensatory changes in heart rate. Further evaluation included a 24-hour urinary fractionated metanephrine test, which was within normal limits. Laboratory studies showed a creatinine level of 1.2 mg/dL, sodium 133 mmol/L, potassium 5.0 mmol/L, and TSH 2.57 mIU/L. Urine studies revealed an albumin-to-creatinine ratio of 45 mg/g, 24-hour urine creatinine of 1.201 g, and urine sodium of 108 mmol. Urinalysis was unremarkable, and renal artery duplex imaging showed no evidence of renovascular disease.

Discussion

The characteristic blood pressure lability and delayed onset of symptoms following neck irradiation, along with the exclusion of other potential causes, supported a diagnosis of afferent baroreflex failure.

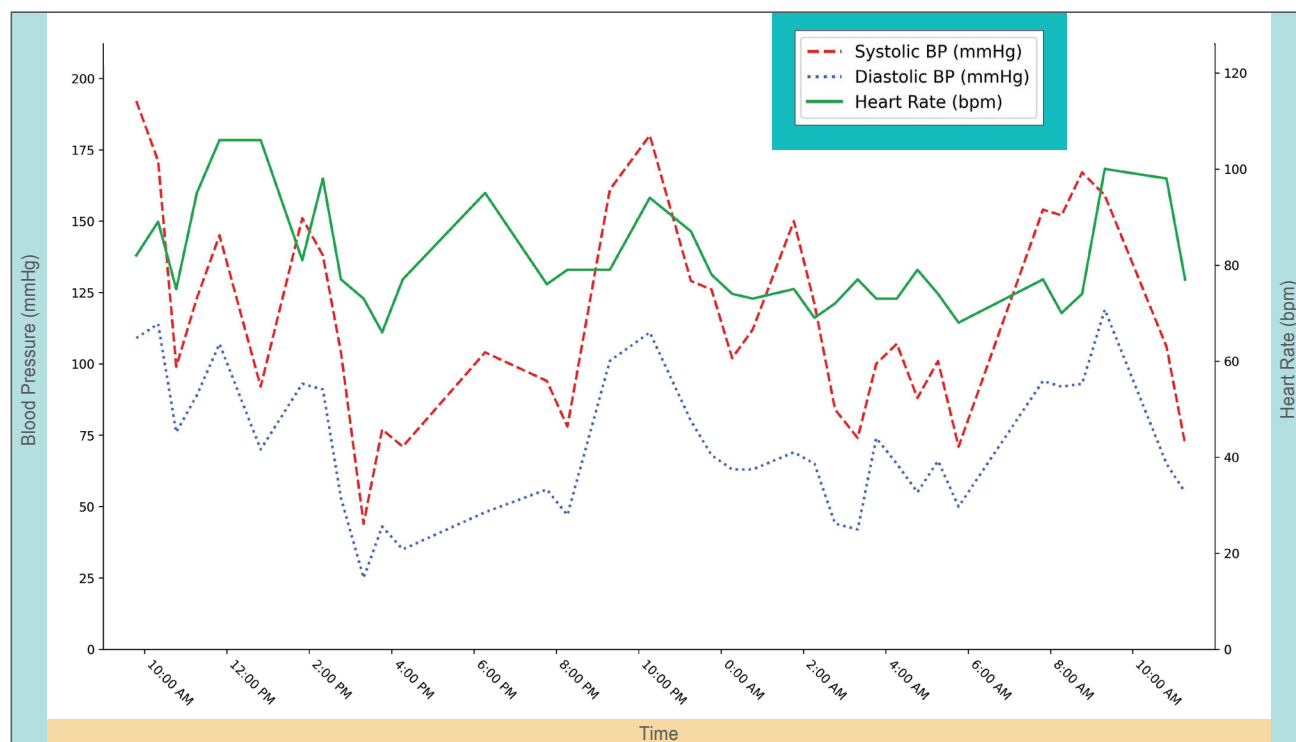


Figure 1. 24-hour ambulatory blood pressure and heart rate monitoring

Although formal autonomic testing was not conducted, the clinical presentation was highly suggestive of afferent baroreflex failure, warranting intervention due to recurrent episodes of both hypertension and hypotension. Nonetheless, the absence of formal autonomic testing remains a significant limitation of this study.

Managing afferent baroreflex failure is challenging due to the unpredictable nature of blood pressure fluctuations. While there are no formal guidelines, the Vanderbilt Autonomic Dysfunction Center outlines a comprehensive, physiology-based treatment strategy in their 2019 JACC review article titled “Blood Pressure Management in Afferent Baroreflex Failure.” This approach focuses on reducing blood pressure variability and improving patient quality of life (11).

The primary treatment involves the use of long-acting central sympatholytic agents, such as guanfacine or methyldopa, to mitigate sympathetic surges. These medications help prevent significant hypertensive spikes. Short-acting sympatholytics, like clonidine, are generally avoided due to the risk of rebound hypertension, though they may be considered for acute hypertensive episodes triggered by stress or exertion.

For managing hypotension, the strategy includes increasing salt and fluid intake, the use of midodrine, employing physical counter-maneuvers, and maintaining a supine position with legs elevated. Additionally, for hypertensive crises induced by stress, interventions such as biofeedback, benzodiazepines, or cannabinoids may be beneficial. The overarching goal is not to normalize blood pressure but to reduce the amplitude of hypertensive spikes and minimize episodes of hypotension, thereby enhancing patient well-being.

Our patient is currently being treated with lisinopril 10 mg orally once daily, metoprolol succinate 100 mg orally once daily, amlodipine 5 mg orally twice daily, and guanfacine extended release 1 mg orally at bedtime. As needed, labetalol 100 mg orally is used for hypertensive crises, and midodrine 2.5 mg orally is administered for symptomatic hypotension. Since initiating amlodipine and guanfacine, hypertensive episodes have become less frequent. Mild afternoon hypotension still occurs but is better managed with intermittent midodrine.

Conclusion

Afferent baroreflex failure is a rare but serious late complication of head and neck radiation. Diagnosis requires detailed clinical history, exclusion of mimicking disorders, and recognition of its hallmark feature of marked blood pressure variability years after radiation therapy. Management focuses on attenuating sympathetic surges and preventing hypotensive symptoms. This case highlights the diagnostic and therapeutic complexities of afferent baroreflex failure and the importance of individualized, physiology driven treatment strategies.

Disclosures

The authors have no disclosures.

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