



## Case Report

# Recurrent pulseless electrical activity and cardiac arrest caused by baroreceptor failure following neck irradiation

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## A B S T R A C T

**Introduction:** Baroreceptor damage and hypersensitivity can produce labile autonomic blood pressure control. Neck irradiation for malignancy is a well-known but under-recognised cause of baroreceptor failure.

**Case presentation:** We describe a dramatic delayed complication of neck irradiation treatment. Our patient developed recurrent unexplained hypotension and pulseless electrical activity cardiac arrest upon connection to intermittent haemodialysis, which he had previously tolerated uneventfully until exposure to radiotherapy.

**Conclusion:** No other cause was identified, and this case thus highlights baroreflex dysfunction as an important differential diagnosis in patients with profound hypotension.

## 1. Introduction

Baroreceptors of the carotid sinus are central to autonomic blood pressure regulation. Disease of these receptors may produce failure of the baroreflex, with potential manifestations including orthostatic intolerance, hypertension, and heart rate variability. A wide range of conditions are associated with baroreceptor failure, typically neurological disease or autoimmune processes. Radiotherapy to the head and neck is also a well-described cause of baroreceptor injury.<sup>1,2</sup> We present a case of recurrent pulseless electrical activity and cardiac arrest in a patient previously stable on chronic haemodialysis. The hypotensive episodes coincided with the patient's recent neck radiation treatment for oropharyngeal malignancy and were otherwise unexplained. The educational purpose of this report is to highlight an important and under-recognised complication of radiotherapy, and to discuss the options for workup and management of patients with baroreceptor failure. Consent for this publication was obtained from the patient.

## 2. Case Presentation

A 61-year-old male underwent 6 weeks of radiotherapy for locally invasive squamous cell carcinoma of the oral cavity. Chronic intermittent haemodialysis (IHD) had been commenced 14 months earlier for end-stage renal failure secondary to diabetic nephropathy. The

maintenance dialysis prescription was 4.5 hours of intermittent haemodiafiltration three times per week with an average inter-dialytic weight gain of approximately 3kg. Dialysis was delivered via a well-functioning left upper arm arteriovenous fistula.

Three months after completion of neck irradiation the patient developed periodic and gradually more dramatic intolerance to his usual ultrafiltration, manifesting as intra-dialytic hypotension. On one occasion, five months after radiotherapy, he developed sudden profound hypotension and pulseless electrical activity (PEA) cardiac arrest, requiring cardiopulmonary resuscitation. Return of spontaneous circulation (ROSC) occurred after 4 minutes of chest compressions and 2mg of intravenous adrenaline. This isolated episode was attributed to volume depletion from excessive ultrafiltration, although his prescription was unchanged. His only implicated medication was bisoprolol 5mg daily, which was ceased. Over the following 6 weeks the patient suffered 4 further episodes of PEA cardiac arrest during IHD. On each occasion the events had been triggered within 10 minutes of commencement of IHD with minimal ultrafiltration, and ROSC had been achieved after between 3 and 8 minutes of basic airway management, chest compressions and adrenaline. Complete recovery of consciousness occurred with each episode.

No explanation could be made for recurrent cardiac arrest despite an extensive initial workup. There was no association with fluid removal and multiple dialyser membranes and temperatures were

Peer review under responsibility of The Emergency Medicine Association of Turkey.

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<https://doi.org/10.1016/j.tjem.2019.07.004>

Received 2 July 2019; Received in revised form 25 July 2019; Accepted 26 July 2019

Available online 01 August 2019

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trialled. Three of five episodes occurred while monitored on telemetry. No significant dysthymias were identified; in two instances the patient entered transient atrial fibrillation following an adrenaline bolus. A Holter monitor and transthoracic echocardiogram were unremarkable.

The patient refused further IHD following his 5th episode of cardiac arrest. He complained of anxiety and fear of death. The nephrology team also deemed continued IHD to be contraindicated. Oral midodrine, an alpha receptor agonist, administered prior to IHD was considered as a possible pharmacological approach to prevent intra-dialytic hypotension, but it was decided that an adequate response was unlikely. A Tenckhoff peritoneal dialysis (PD) catheter was inserted urgently. The patient was managed carefully on sustained low efficiency dialysis (SLED) for several weeks while awaiting maturation of his PD catheter.

A cardiology consultation was sought, however permanent pacemaker implantation was not recommended. Regular observations while admitted to the medical ward revealed episodic, marked, unpredictable instances of postural hypotension which did not cause symptoms. Tilt table testing was planned but not performed. Orthostatic hypotension without any significant heart rate change was deemed to be suggestive of underlying autonomic dysfunction and a diagnosis of baroreceptor failure related to radiation injury was made. During SLED and the transition to PD no further PEA arrests occurred and the patient proceeded to continue treatment with PD uneventfully, with no further events at 5 months follow up.

### 3. Discussion

Baroreceptors are integral regulators of blood pressure variability. Baroreceptors are pressure sensors located throughout the aortic arch and carotid sinus which respond to vessel stretching and direct impulses to the vasomotor centre of the brainstem. This mediates efferent sympathetic stimulation, thereby increasing or decreasing heart rate and vasoconstriction accordingly.

Injury to the carotid sinus may result in acute or subacute failure of the baroreflex and carotid sinus hypersensitivity. This presents as irregular blood pressure control and orthostatic intolerance, heart rate variability, and diaphoresis. Tachycardia and hypertension are commoner features than postural hypotension or bradycardia. Manifestations are usually episodic and relate to transient paroxysmal autonomic nervous system dysfunction in the presence of a trigger.

Carotid sinus dysfunction can be triggered by lesions such as brainstem stroke, carotid atherosclerosis, peripheral neuropathy, or neurological conditions like Parkinson disease and multiple system atrophy.

There are numerous case reports of neck irradiation resulting in baroreceptor damage and autonomic failure, and the association is probably underreported. Radiotherapy causes cell death and fibrosis of vessel walls which ultimately interferes with normal interpretation by the carotid sinus mechanoreceptors. It is thought that a delay of several months is necessary before vessel fibrosis is sufficient to disrupt the carotid arterial baroreflex.

Baroreceptor failure is a difficult condition to diagnose and is often a diagnosis of exclusion. Tilt table testing may sometimes confirm the diagnosis. Absence of an appropriate increase in heart rate despite orthostatic hypotension from a tilt table signifies cardiovagal and baroreflex dysfunction and is highly suggestive of the diagnosis.<sup>3</sup> Treatment measures have been met with mixed success. The lifestyle approach includes physiotherapy and compression stockings. Useful pharmacological options are midodrine and fludrocortisone. Pacemakers are

largely ineffective as they do not counteract the problem of vasodilation.

In our case, the patient had been stably maintained on IHD for more than one year. He received neck radiation therapy for an oral cavity malignancy, and in the following months developed recurring episodes of significant unanticipated hypotension during haemodialysis. No alternative causes could be recognised. It is known that endothelial dysfunction during dialysis produces local haemodynamic changes.<sup>4</sup> We hypothesise that this trigger resulted in disruption to the normal pattern of autonomic outflow with a subsequent cardio-inhibitory and vasodepressor response. That no further episodes were provoked by PD probably reflects the fewer haemodynamic changes associated with this modality over IHD.<sup>5</sup> Finally, while this report is a case of cardiovascular collapse in a dialysis unit, it may be deduced that relevant similar situations in the context of an emergency department could be large-volume abdominal paracentesis or pleural drainage.

### 4. Conclusion

In summary, radiotherapy to the head and neck is a well-described cause of carotid sinus baroreceptor damage. To the authors' knowledge this is the first case report of PEA cardiac arrest caused by baroreflex autonomic failure. Our patient had repeated episodes correlating with connection to the dialysis circuit, which only developed after undergoing radiation treatment. This case highlights an important but overlooked complication of neck irradiation and clinicians are reminded to consider the association when encountering patients with an impaired baroreflex.

### Funding

There are no organizations or grants that have funded our manuscript.

### Author contribution statement

Everyone who contributed to this manuscript is listed as an author.

### Conflict of interest statement

There are no financial and personal relationships with other people or organizations that could inappropriately influence our work. The authors declare no conflict of interest.

### Acknowledgements

Nil.

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