

CASE REPORT



# Recurrent syncope secondary to autonomic dysfunction in spinal cord injury: a case report

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High-level spinal cord injuries are often associated with autonomic impairment, which can result in orthostatic hypotension and syncope. Persistent autonomic dysfunction can manifest with disabling symptoms including recurrent syncopal events. We describe a case of autonomic failure resulting in recurrent syncopal events in a tetraplegic 66-year-old man.

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## CASE REPORT

### Presentation

A 66-year-old man was admitted to our service for spinal rehabilitation, 6 months after sustaining a C6-ASIA-A spinal cord injury in a mountain bike accident. He had fallen forwards while going over a jump and sustained a hyperextension injury to the neck, with immediate onset bradycardia, hypotension and tetraplegia. He had initially been admitted to his local acute tertiary hospital for a C3–T3 posterior decompression and fusion, before being transferred to the statewide acute spinal unit, and then to our service for rehabilitation. Neuroimaging of his spinal injury on admission to rehabilitation (6 months after injury) is presented in Fig. 1.

Prior to arrival at our service, his acute admission had also entailed management for a concomitant traumatic brain injury with 36 days of post-traumatic amnesia, from which he had recovered well with no significant cognitive deficits. He also sustained facial fractures requiring surgical repair, dislocation of the right middle finger PIP joint, and facial lacerations. In addition, he contracted COVID-19 during an outbreak in the brain injury service, which was complicated by hypoxia secondary to mucous plugging. He received 10 days of dexamethasone, as well as clindamycin and piperacillin-tazobactam to treat superimposed bacterial pneumonia. His admission was prolonged due to recurrent viral shedding requiring negative viral cultures before he could be deisolated.

During his acute admission, and shortly after arriving at the spinal rehabilitation unit, he experienced a number of syncopal events which significantly limited his participation in therapy. These occurred almost daily and mostly lasted less than 1 min and resolved either spontaneously or with positioning (tilting back in the chair and raising the legs). There was sometimes a coarse tremor of the upper limbs immediately prior to the events occurring, often associated with him becoming somewhat vague beforehand, and then becoming non-responsive. There were no clear findings suggestive of a post-ictal state. Blood pressure was often very low (less than 80 mmHg systolic) during these events but resolved spontaneously, usually within less than 2 min. It was

noted that during his acute admission, he had been commenced on regular fludrocortisone at night and PRN midodrine for a presumptive diagnosis of orthostatic hypotension. Neurology and cardiology opinions had been sought, both of which indicated no additional cause was felt to be likely. At that stage, the episodes had been described as possible 'dystonia', possibly from salbutamol administration but no clear cause was identified. He also had global hypokinesia on a transthoracic echocardiogram with reduced left ventricular function, felt to be due to the fludrocortisone which was ceased.

After he was deisolated from COVID-19, he was transferred to our unit for spinal rehabilitation. The syncopal events continued in the same manner as described, and occurred at a frequency that significantly interfered with his rehabilitation (in particular resulting in a number of therapy sessions being terminated, as well as a wheelchair collision). Concerns were raised by his family regarding his ability to discharge home if his recurrent syncope would necessitate 24-h supervision.

### Investigations and management

Baseline blood tests including full blood count, electrolytes/urea/creatinine, liver transaminases, calcium/magnesium/phosphate, B12, folate, iron studies and morning cortisol yielded no significant abnormalities. C-reactive protein was not elevated. There was mild subclinical hypothyroidism in serial thyroid function studies. COVID-19 PCR testing was performed weekly in accordance with the institutional infection control policy in force at the time; most results were reported as positive but had very high cycle thresholds and were considered inconsistent with ongoing infection. Supine aldosterone levels were 66 pmol/L (normal range 61–980), and supine renin level was undetectable (normal range 4.4–46.1 mU/L).

Assessment of cardiac function was performed by way of a 24-h Holter monitor, which was reported as showing sinus rhythm with an average rate of 64 bpm, no significant pauses, and rare atrial and ventricular ectopics. A brief run of slow, non-sustained VT was noted. 24-h ambulatory blood pressure monitoring showed labile blood pressure, with systolic BP ranging from 66 to 180 mmHg

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(Fig. 2). Blood pressure was more stable overnight, with the widespread daytime fluctuation likely related to orthostatic changes. A repeat transthoracic echocardiogram was performed and reported as showing a non-dilated left ventricle with preserved systolic function, no hypertrophy and a borderline dilated left atrium. A second cardiology opinion at a specialist syncope clinic was sought; the advice was that a pacemaker would be of limited utility and was not recommended, and that autonomic dysfunction as a cause of the syncope should be considered.

A second neurology opinion was also sought, and on the neurologist's advice, a sleep-deprived EEG was performed which showed a slow, symmetric background with low amplitude, at 6–7 Hz. Light sleep and photic stimulation provoked no dysrhythmia. Review of an MRI brain scan previously performed in the acute admission identified restricted diffusion and magnetic



**Fig. 1** Sagittal STIR MRI performed 6 months after injury showing myelomalacia with volume loss of the cord at C5–C6 levels.

susceptibility including multiple sites, which were felt to be related to multifocal diffuse axonal injury from the initial head trauma (Fig. 3). A small number of periventricular and subcortical white matter T2/FLAIR hyperintensities with no correlation to the microhaemorrhages were seen and were considered nonspecific. The opinion of the consulting neurology service was that a neurological cause of the syncopal events was most unlikely.

In addition to the above, carotid dopplers were obtained, which only revealed minimal plaque in the left internal carotid artery, with normal bilateral antegrade vertebral arterial flow.

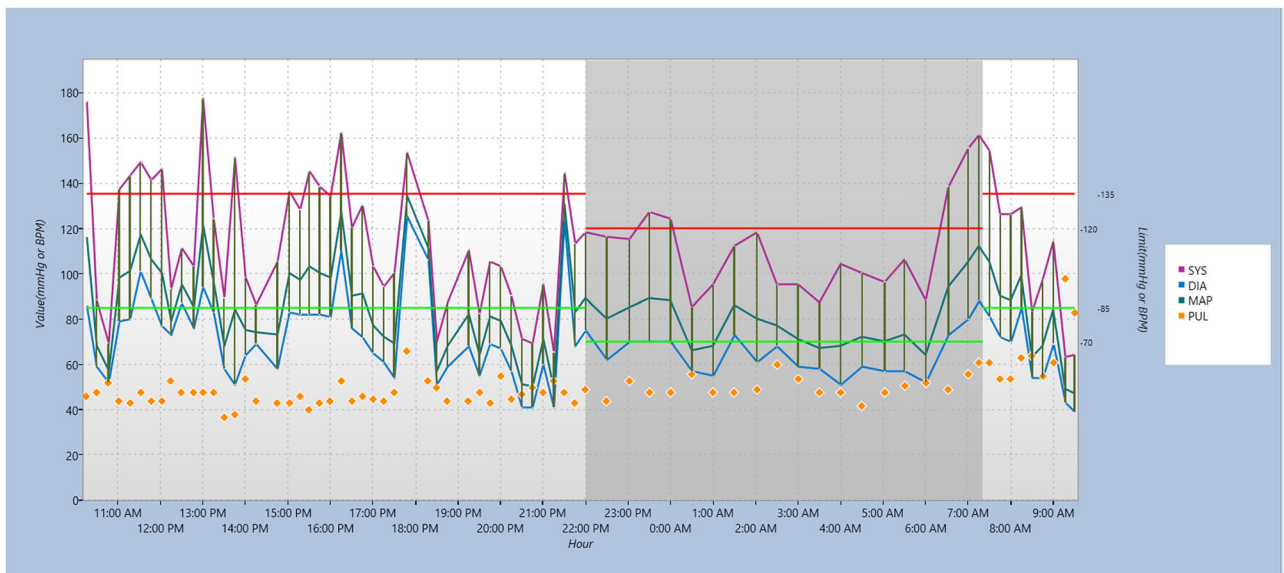
In the context of the lack of a definitive cardiac or neurological cause, and the possibility of autonomic dysfunction being a contributor, bedside autonomic function testing was performed, which suggested a lack of sympathetic autonomic or cardiovascular responses to multiple stimuli (Table 1). The statewide autonomic laboratory was not able to accommodate tetraplegic patients and hence formal autonomic testing was not performed.

In the context of possible autonomic dysfunction, undetectable renin and no other clear cause, the patient was treated on a working diagnosis of severely impaired sympathetic function including a failure of autonomic renal supply to the kidney. Midodrine was increased to 5 mg twice daily and aggressive oral hydration was provided each morning. Compression stockings were applied, and therapy times were changed to be at least 1 h after each meal and preferably longer, to mitigate the effects of post-prandial hypotension.

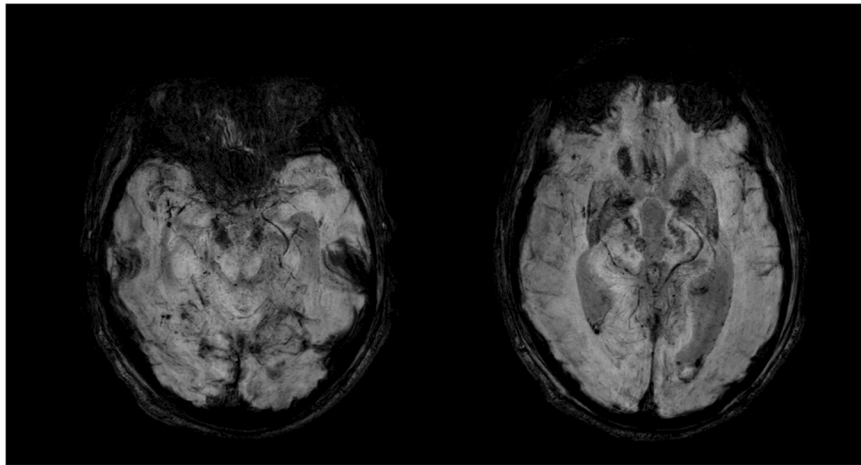
### Outcome

Within 1 week of the new treatment plan being implemented, the number of syncopal events began to decline considerably to less than once per week. The patient unfortunately developed a recurrent dehiscence of an upper lip surgical wound requiring transfer back to the acute hospital for repeat grafting and surgical monitoring. At the time of transfer to the acute hospital, a nasogastric tube was inserted.

After his return from the acute hospital, he remained syncope-free for 1 month, until the nasogastric tube was removed. He then had two syncopal events within 48 h, leading to speculation that insufficient oral electrolyte intake may have been a contributing factor. To address this, midodrine was further increased to 10 mg twice daily and oral sodium chloride tablets (1200 mg twice a day) were added. His frequency of events stabilised again at less than once a week. He continued multidisciplinary spinal rehabilitation



**Fig. 2** Twenty-four-hour ambulatory BP monitor. Significant fluctuation in systolic BP (66–180 mmHg) is noted, with reduced lability overnight.



**Fig. 3** Susceptibility-weighted imaging at 2 months after injury, showing multifocal sites of magnetic sensitivity related to diffuse axonal injury.

**Table 1.** Results of bedside autonomic function testing.

Test protocol	Results
Mental Stress Test (sympathetic response) BP and HR checked before test, and then instructed patient to start at number 1000 and perform serial subtractions of 17. BP re-checked at 2 min	Initial: BP 80/56 mmHg; HR 47 bpm Final: BP 80/50 mmHg; HR 49 bpm
Cold Pressor Test (sympathetic response) BP and HR checked before test, and then right hand placed in ice-cold water for 3 min. BP re-checked at 3 min	Initial: BP 84/58 mmHg; HR 48 bpm Final: BP 87/58 mmHg; HR 47 bpm
Deep Breathing Test (cardiovagal response) Deep breathing performed at 6 cycles per minute guided by a metronome, with continuous heart rate monitoring	Mean expiration/inspiration difference in heart rate over 6 inspiration/expiration cycles at 6 breaths per minute was 0.4 bpm.

with a view towards discharge into the care of his family. While his syncopal events still occur intermittently, they are short-lived (less than 30 s) and self-terminating.

## DISCUSSION

Disruption of the autonomic system is a common complication of spinal injury, with orthostatic hypotension being a particularly common manifestation of the same [1]. This is most commonly associated with complete injuries above the T6 level, which is also the level associated with an increased risk of autonomic dysreflexia [1–3]. The pathophysiological mechanisms of this are multifactorial, but include impaired sympathetic response to stimuli which would ordinarily cause an increase in BP (e.g. positioning), and derangement of salt-water balance [3]. Traditionally, it was felt that orthostatic impairment secondary to spinal injury improves slowly over time, although newer evidence suggests it can be prolonged and can last years after the injury [1]. Management options include the mineralocorticoid fludrocortisone, which increases intravascular volume, the alpha-agonist midodrine, which increases vascular tone, and non-pharmacological agents including abdominal binders, salt intake, and compression stockings [1, 4]. Although some level of orthostatic impairment would be expected at the level of injury experienced by our patient, it is nevertheless highly unusual for it to manifest with syncope at the frequency observed in this case.

The role of plasma renin activity in hypovolaemic orthostatic hypotension has been described previously, with low renin being associated with a marked reduction in intravascular volume [5]. Nondetectable renin in our patient, in the absence of any clinically confirmed hypertension, suggests reduced renin activity, possibly

due to impaired sympathetic supply to the kidney, likely played a role in the pathogenesis of our patient's symptoms. Indeed, activation of the renin-angiotensin system is a possible mechanism for reduced orthostatic hypotension in chronic spinal patients, which may have been impaired in our patient [6]. Unfortunately, sitting renin and aldosterone levels were not collected in this patient's admission, and so a postural change in renin or aldosterone levels could not be confirmed.

The impact of the patient's COVID-19 is worthy of some consideration, although its precise contribution to his symptoms is difficult to quantify. Autonomic impairment after COVID-19 has been recognised as a common finding [7], but is believed to be mostly transient and mild in nature. Our patient had a prolonged period of viral shedding, which may suggest that some level of residual viral activity was ongoing, which could favour increased inflammation and autonomic dysfunction as a result. However, definitive confirmation of this as a contributor would be extremely difficult.

The potential causes of syncopal events are many, and it is particularly debilitating symptom that impairs activities of daily living, is a source of anxiety and makes safe mobility in the community much more challenging, even with appropriate assistive technology. Frequent syncopal events of this nature had the potential to greatly limit our patient's participation in rehabilitation, due to therapist concerns regarding safety of participation in multidisciplinary therapy, and the very real risk of wheelchair collision, which occurred on multiple occasions. The prospect of driving for our patient was also severely curtailed; Australian guidelines preclude driving for a minimum of 12 months after two or more episodes of syncope of undetermined nature [8]. As such, a comprehensive investigation of its cause, which may

be a time-consuming process involving multiple diagnostic procedures and consultations, is nevertheless warranted in almost all cases of recurrent syncope.

## CONCLUSION

We report on a case of refractory syncope likely secondary to major autonomic impairment occurring in the context of combined brain and spinal cord injury. Autonomic dysfunction is a common manifestation of spinal cord injury, which can cause debilitating syncopal events. Detailed medical investigation including cardiogenic, neurogenic and autonomic causes of syncope in spinal cord injury is often warranted.

## DATA AVAILABILITY

All relevant data related to this case are available as part of the article. Clinical data related to this case are retained by the medical records department at Royal Rehab, and are unavailable for release due to legislative requirements regarding patient confidentiality.

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## AUTHOR CONTRIBUTIONS

LS and RH were both involved in the clinical management of the patient's care. LS authored the initial manuscript and RH provided a review and comments.

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No external funding was received for the production of this manuscript. LS and RH are both employees of Royal Rehab, which was not involved in the creation, content or decision to publish this manuscript.

## COMPETING INTERESTS

The authors declare no competing interests.

## CONSENT FOR PUBLICATION

Informed consent was provided by the patient for publication of this case.

## ADDITIONAL INFORMATION

**Supplementary information** The online version contains supplementary material available at <https://doi.org/10.1038/s41394-023-00585-3>.

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