Perioperative Autonomic Dysfunction in a Patient With Charcot-Marie-Tooth Disease: A Case Report

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Autonomic dysfunction can lead to unexpected hemodynamic instability during surgery, and best practices for the perioperative care of patients with this condition are not well-defined. We report the case of a 63-year-old woman with Charcot-Marie-Tooth disease who experienced perioperative autonomic dysfunction characterized by severe fluctuations in blood pressure while under spinal anesthesia. However, <1 month later, a second hip surgery performed under general anesthesia with special precautions resulted in an uncomplicated perioperative course, with only mild fluctuations in blood pressure. (A&A Practice. 2023;17:e01722.)

GLOSSARY

ASA = American Society of Anesthesiologists; **BP** = blood pressure; **CARE** = CAse REport; **CMT** = Charcot-Marie-Tooth; **GA** = general anesthesia; **PACU** = postanesthesia care unit

Autonomic dysfunction describes any malfunction of the autonomic nervous system. It may be caused by a primary autonomic disorder such as Shy-Drager syndrome, or it can be secondary to other diseases such as diabetes, malignancy, or spinal cord injury.[1] However, the interplay between anesthesia and an unrecognized autonomic dysfunction can result in unexpected perioperative hemodynamic instability.[2,3]

Charcot-Marie-Tooth (CMT) disease is a group of inherited neurological disorders characterized by chronic sensory and motor polyneuropathy.[4] The prevalence of autonomic neuropathy in patients with CMT can be as high as 65%.[5] Our knowledge on how to provide anesthesia for patients with CMT is based chiefly on case reports and case series.[6,7]

The patient provided written consent to publish this report, and the article adheres to the CAse REport (CARE) guidelines.[8]

CASE DESCRIPTION

A 63-year-old woman (weight 58 kg; height 160 cm) with CMT type 1A presented for a left total hip replacement. Her CMT symptoms had started in late adulthood and included paresthesia in the distal lower extremities followed by progressive weakness in the distal lower extremity muscles, which limited her ability to walk without support. She had begun using a wheelchair 1 year before presentation and had chronic neuropathic pain, major depressive disorder, and asthma. The patient was taking oxcarbazepine, pregabalin, fluoxetine, alprazolam, zolpidem, inhaled budesonide, and albuterol. She had a cardiac arrest after induction of general anesthesia for a knee surgery 4 years previously at a hospital in a different country. Obtaining previous medical records from that procedure was not possible, and the history was gathered directly from the patient. The cardiac arrest had been attributed to anaphylaxis and involved sudden hypotension during induction requiring resuscitation, with no bronchospasm or identifiable rash. However, the cause of anaphylaxis was not identified, and the patient reported having no known drug allergies and no history of frequent falls or presyncope events. She also had a recent pharmacologic cardiac stress test, which was negative.

The patient had been experiencing left hip pain for 1 month. Radiography showed an impacted femoral neck fracture. The patient's preoperative hemoglobin level was 11.8 g/dL, creatinine was 0.6 mg/dL, and blood urea nitrogen was 15 mg/dL. She had been fasting for 16 hours. Because of the previous cardiac arrest attributed to anaphylaxis under general anesthesia, we performed spinal anesthesia to avoid the common medications used in general anesthesia that might elicit an allergic reaction. Hence, close monitoring with noninvasive measures was deemed adequate. In the operating room, standard American Society of Anesthesiologists (ASA) monitors were attached, including a pulse oximeter, a 5-lead electrocardiogram, a noninvasive blood pressure cuff, and a facemask with end-tidal carbon dioxide capnography. The patient received intravenous midazolam (1 mg) and no additional sedation during the procedure. Spinal anesthesia was performed in the left lateral position with 12.5 mg hyperbaric bupivacaine without an adjuvant. The patient's sensory level after 10 minutes was at the tenth thoracic sensory dermatome. Mild changes in the patient's position did not affect the sensory level or substantially alter her hemodynamics. The patient had wide intraoperative fluctuations in blood pressure unrelated to surgical stimuli (Figure 1), and hypotensive episodes were

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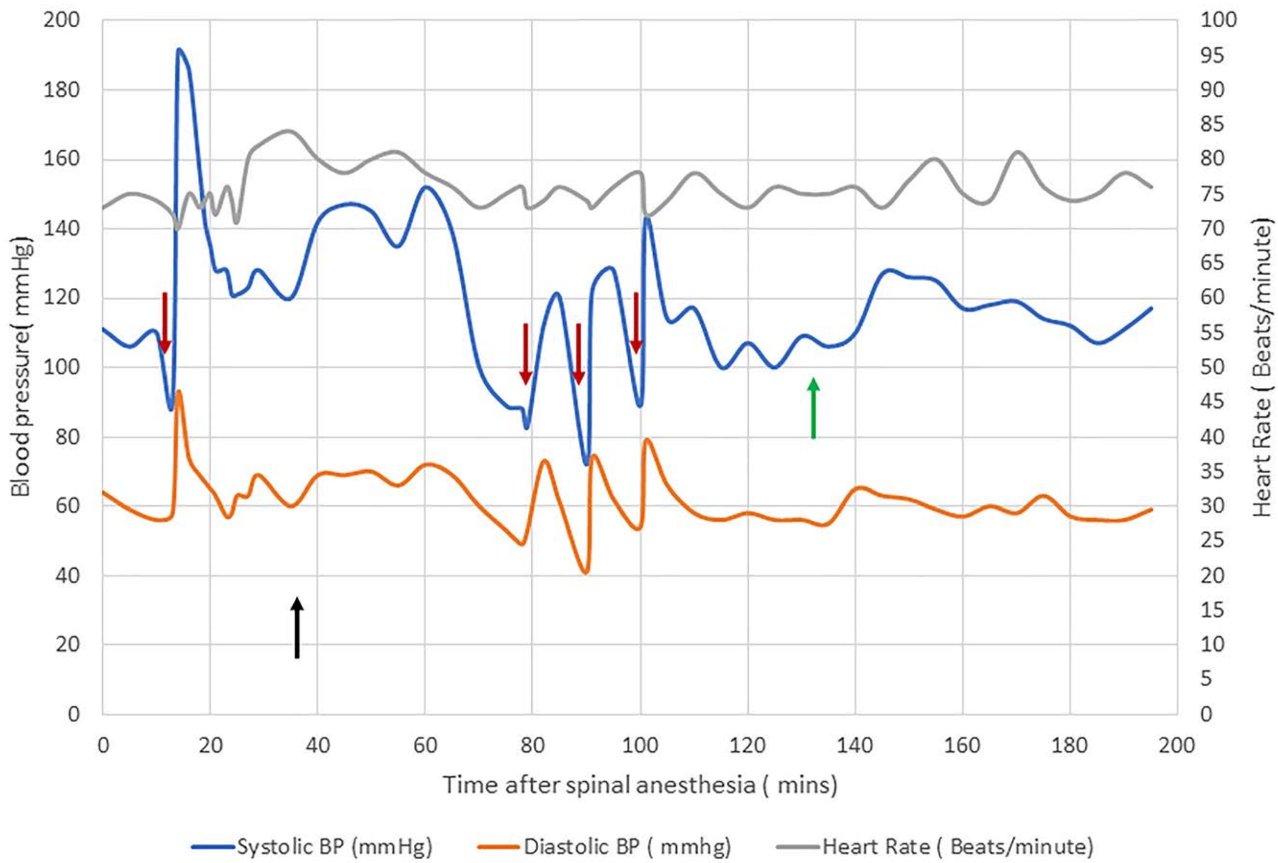

Figure 1. Changes in BP and heart rate during the first surgery under spinal anesthesia. The black arrow indicates surgical incision. The red arrows indicate when the patient received boluses of phenylephrine (100 µg). The green arrow indicates completion of 2 L crystalloid fluids. BP indicates blood pressure.

responsive to phenylephrine boluses. The patient received 2 L lactated Ringer's solution, lost approximately 500 mL of blood, and had a urine output of 0.4 mL/kg/h.

In the postanesthesia care unit, the patient felt nauseated and had severe systolic hypotension of 40 mm Hg, with a heart rate of 70 beats per minute and an oxygen saturation of 100% on room air. Her blood pressure improved with phenylephrine and crystalloid boluses. Laboratory tests showed a hemoglobin of 8.4 g/dL. The patient received a transfusion with 2 units of packed red blood cells. Results of a 12-lead electrocardiogram, a chest radiograph, and a troponin assay were all normal. At this time, the sensory level of her block was at the first lumbar sensory dermatome. The patient continued having episodes of symptomatic hypotension responsive to phenylephrine boluses over the course of 4 hours (Figure 2). A phenylephrine infusion was initiated and titrated until the mean arterial blood pressure was >65 mm Hg. She was weaned off vasopressors after 24 hours and discharged home 6 days after surgery.

After 18 days, the patient presented for a second hip surgery for a left hip periprosthetic fracture that occurred during physical therapy. Her preoperative hemoglobin was 9.9 g/dL. Considering the hemodynamic lability during the previous operation, we performed general anesthesia. We confirmed that the patient had fasted for exactly 6 hours after a light meal. She was given 1 L lactated Ringer's solution before surgery. ASA monitors were attached. An arterial line and 2 large bore intravenous lines were placed. Anesthesia was induced using fentanyl (100 µg), etomidate (14 mg), and rocuronium (70 mg). Maintenance of anesthesia was titrated using sevoflurane. A total of 1500 mL lactated Ringer's solution was administered intraoperatively, and her urine output was >0.5 mL/kg/h. Surgical requirements and blood loss were similar to the previous surgery. The patient did not have any significant perioperative hypotension or require vasopressors. Mild intraoperative blood pressure fluctuations were observed, with high blood pressures responding to increasing the depth of anesthesia (Figure 3). We used sugammadex (2 mg/kg) to reverse muscle paralysis to a train-of-four of >0.9 because the patient had 2 twitches initially measured on the ulnar nerve. The patient was extubated and transferred to the recovery room with stable vital signs. The patient's postoperative course was uncomplicated, and she was discharged home 4 days after surgery.

DISCUSSION

Our patient with CMT did not develop perioperative neurological complications during her first procedure under spinal anesthesia, but her course was complicated by severe hemodynamic instability. A 12-lead electrocardiogram and a normal troponin level ruled out a major cardiac event. Adequate oxygen saturations and lack of ventilatory

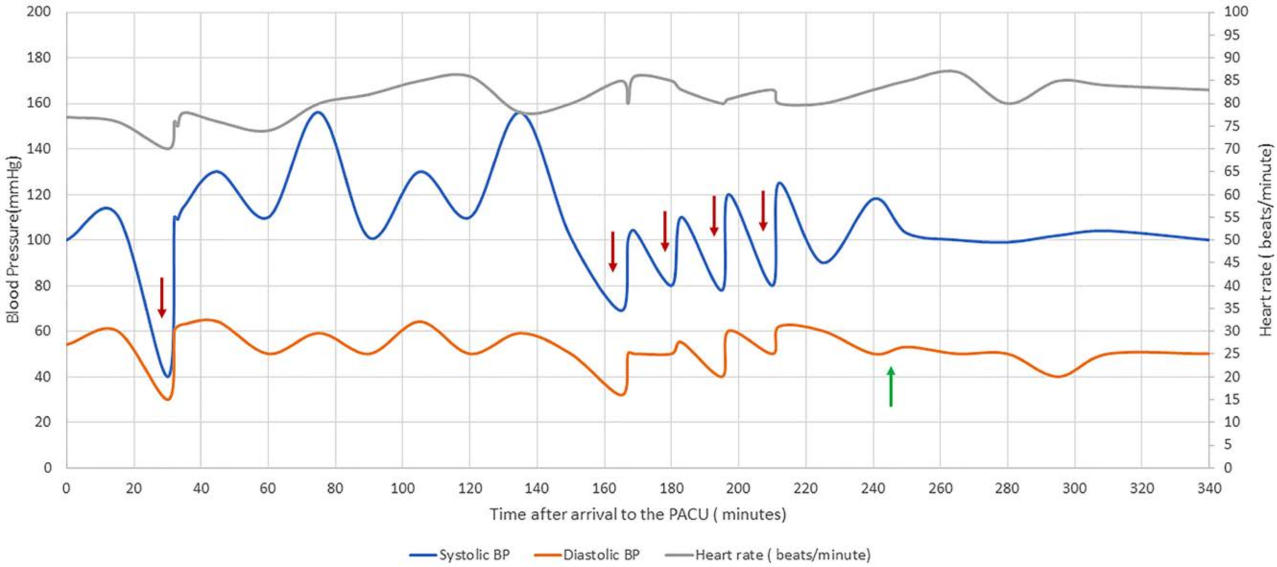

Figure 2. Changes in BP and heart rate after the first surgery while in the PACU. The red arrows indicate when the patient received boluses of phenylephrine (100 µg). The green arrow indicates initiation of vasopressor infusion. BP indicates blood pressure; PACU, postanesthesia care unit.

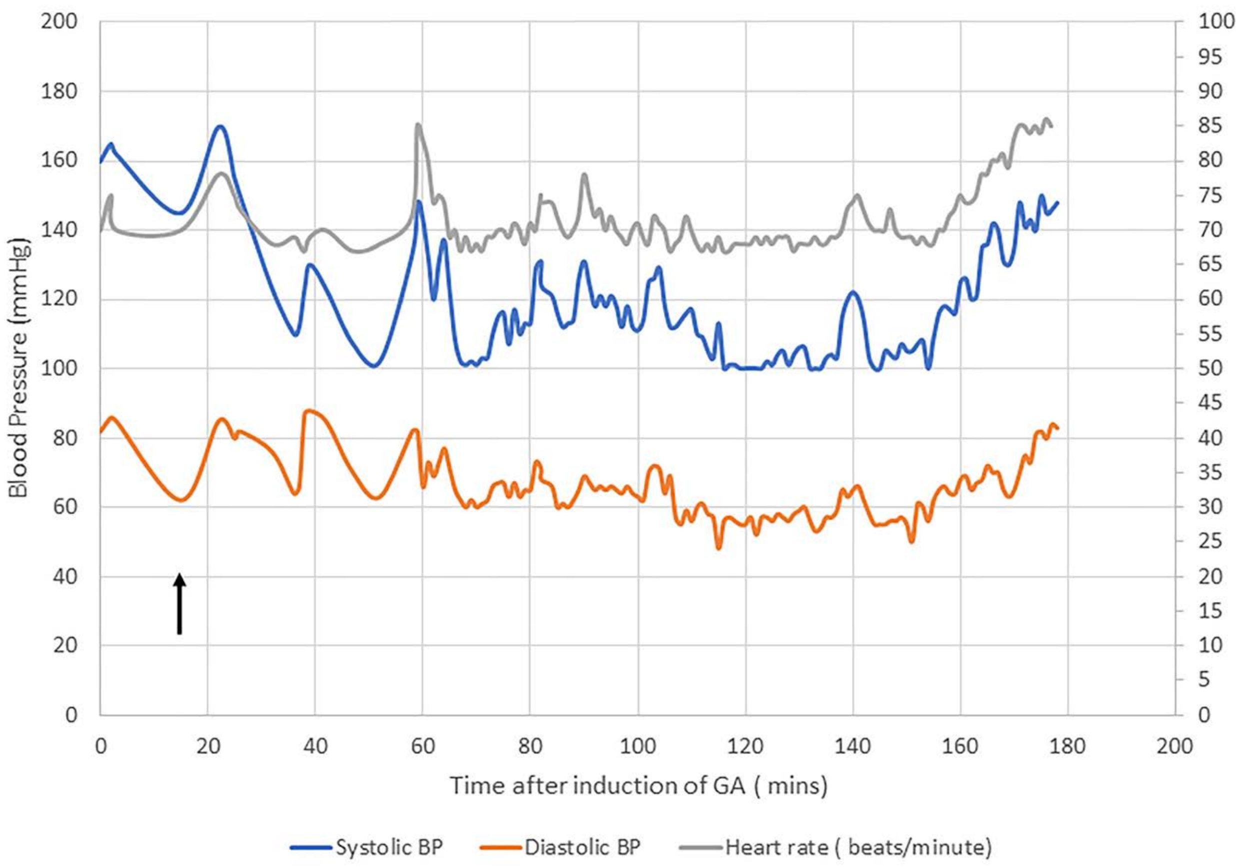

Figure 3. Changes in BP and heart rate during the second surgery under GA. The black arrow indicates surgical incision. BP indicates blood pressure; GA, general anesthesia.

distress ruled out significant lung pathology. Importantly, the patient showed no signs of angioedema, bronchospasm, or urticaria indicative of anaphylactic shock. Furthermore, high spinal anesthesia block was ruled out, as the patient was awake and responsive, and her hemodynamic instability persisted long after the effects of anesthesia had worn off. Rather, the only finding similar to her previous complicated surgical experience in another country was hypotension, which could be explained by unrecognized perioperative autonomic dysfunction.

In healthy individuals, postural changes may decrease preload, but blood pressures remain stable because of compensatory cardiovascular reflexes mediated by the autonomic nervous system. However, in patients with autonomic neuropathy, compensatory cardiovascular reflexes are compromised, and postural changes or a decrease in preload can lead to symptomatic hypotension, manifesting as syncope and presyncope events.[9] Therefore, preoperative evaluation of patients with neuropathies should include gathering a detailed history of postural syncope or presyncope and assessing orthostatic vital signs.[9] Additional perioperative tests to assess the compensatory autonomic response may be considered[1,9] (Table 1), such as the hyperventilation test, in which the patient is asked to rapidly take deep breaths for 30 seconds. In healthy individuals, the sympathetic nervous system is activated to maintain blood pressures by counteracting the hypocapnia-induced vasodilation.[1,10] However, with autonomic dysfunction, hyperventilation may lead to a drop in blood pressures because of uncompensated vasodilatation.

Because anesthesia influences preload, afterload, and autonomic responses, such as blunting the baroreflex, patients with autonomic neuropathy may show unexpected perioperative hemodynamic instability.[11] The perioperative care of patients with autonomic neuropathy entails adequate close monitoring and vigilance, including attention to hemodynamics, fluid status, blood loss, and vasopressor responses.[1,2] Fluid status should be adequately assessed by reviewing the patient's fasting duration, preoperative hemodynamics, and urine output. However, patients with autonomic neuropathies might have increased natriuresis and supine hypertension, making the determination of fluid status challenging.[1] Assessing the inferior vena cava with ultrasonography can guide fluid management (Table 2).[12] Also, a preanesthetic crystalloid fluid bolus may improve postinduction hypotension.[13] An arterial line should be considered when blood pressure lability is expected due to blood loss, hypovolemia, or specific risk factors. Additional monitoring devices can be considered depending on the patient's comorbidities (Table 2). Vasopressors should be titrated carefully, because increased sensitivity to vasopressors may occur in patients with autonomic dysfunction.[1]

The anesthetic technique for patients with autonomic dysfunction is less important than close monitoring and timely attention to fluid status.[1] The hypotension observed in our patient after spinal anesthesia might have been avoided by adequate perioperative fluid replacement with crystalloid solutions.[14] If general anesthesia is considered, we recommend using a preinduction fluid bolus, etomidate, and titration of maintenance medications in response to hemodynamic changes. Also, when the autonomic neuropathy is associated with neuromuscular weakness, as with CMT, special attention to neuromuscular blocking drugs should be considered. In our patient, neuromuscular blockade was

Table 1. Preoperative Tests for Patients With Suspected Autonomic Neuropathy

Test	Test description	Normal response	Autonomic dysfunction
Orthostatic vital signs	Blood pressure and heart rate are measured in the supine and upright positions.	Blood pressure minimally drops (systolic blood pressure <20 mm Hg and diastolic blood pressure <10 mm Hg) or is normal in the upright position with an increase (10–20 beats/min) or no change in the heart rate.	Blood pressure drops significantly (systolic blood pressure >20 mm Hg and/or diastolic blood pressure >10 mm Hg) in the upright position with little (<10 beats/min) or no change in the heart rate.
Tilt-table	The patient is secured to a table, and vital signs are measured in the supine and upright positions.	Blood pressure minimally drops (systolic blood pressure <20 mm Hg and diastolic blood pressure <10 mm Hg) or is normal in the upright position with an increase (10–20 beats/min) or no change in the heart rate.	Blood pressure drops significantly (systolic blood pressure >20 mm Hg and/or diastolic blood pressure >10 mm Hg) in the upright position with little (<10 beats/min) or no change in the heart rate.
Valsalva maneuver	The patient blows into a closed mouthpiece, with a tiny leakage (16 gauge), connected to a manometer. The patient has to maintain 15 mm Hg as measured by the manometer for 15 s.	Phase 1: Increase in blood pressure (systolic blood pressure >15 mm Hg above baseline). Phase 2: Decrease in blood pressure (systolic blood pressure below the 15 mm Hg increase in phase 1 but not below baseline systolic blood pressure) with associated tachycardia. Phase 3: Abrupt decrease in blood pressure (below baseline blood pressure). Phase 4: Increase in blood pressure (systolic blood pressure >15 mm Hg above baseline).	Phase 1: Same as normal response. Phase 2: Same as normal response but with blunted or no tachycardia. Phase 3: Same as normal response. Phase 4: No increase in blood pressure.
Cold pressor	The patient places 1 hand in a basin filled with half ice and half water.	Increase of systolic blood pressure of around 20 mm Hg above baseline after 1 min.	Blunted increase of systolic blood pressure after 1 min.
Deep breathing	The patient breathes slowly and deeply at a rate of 6 breaths/min for 90 s.	Physiological ventilatory variation in sinus rhythm: the difference between the average heart rate during inspiration and the average heart rate during expiration is >15 beats/min.	Attenuated ventilatory variation in sinus rhythm: the difference between the average heart rate during inspiration and the average heart rate during expiration is <10 beats/min in patients <40 y old or <5 beats/min at any age.
Hyperventilation test	The patient breathes deeply and rapidly at 1 breath/s for 30 s.	No significant change in blood pressure.	Significant decrease in blood pressure (no defined value, but patients usually have a systolic blood pressure decrease of >20 mm Hg below baseline).

Table 2. Advanced Perioperative Monitors for Patients With Autonomic Neuropathies

Monitor	Function	Indication
Point-of-care ultrasound of the inferior vena cava	In patients breathing spontaneously, an inferior vena cava diameter of <2.1 cm and >50% collapsibility during inspiration correlate with fluid responsiveness In intubated patients, an inferior vena cava diameter of <2.1 cm and >18% distensibility during inspiration correlate with fluid responsiveness	Perioperative or intraoperative use when fluid assessment is challenging
Arterial line	Allows continuous blood pressure monitoring	Preinduction or intraoperative use when blood pressure instability is anticipated
Central line	Allows central venous pressure assessment to guide fluid management Allows vasopressor infusion if needed	Intraoperative use when fluid status assessment is challenging or infusion of vasopressors is needed
Pulmonary artery catheter	Allows for pulmonary artery pressure, cardiac output, and pulmonary capillary wedge pressure measurements	Perioperative use in patients with known or suspected cardiovascular pathology that might contribute to hemodynamic compromise or in patients in which hemodynamic instability and major fluid shifts are expected due to the nature of the surgery
Transesophageal echocardiography	Allows assessment of ventricular structure and function, hemodynamic parameters of volume status and cardiac output, valvular structure and function, intracardiac masses, cardiac shunts, pericardial and cardiac tamponade	Perioperative use in patients with known or suspected cardiovascular pathology that might contribute to hemodynamic compromise or in patients in which hemodynamic instability and major fluid shifts are expected due to the nature of the surgery (preferred over pulmonary artery catheter)

successfully reversed with sugammadex, with no residual signs of paralysis. This contrasts with a recent case report showing residual paralysis despite sugammadex use in a patient with CMT.[15] This case sheds light on how to manage perioperative autonomic dysfunction and the potential perioperative complications that may be seen in patients with autonomic neuropathy. ■

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Name: Ahmad Oseili, MD.
Contribution: This author helped review the final draft and followed up on the postoperative outcomes of the patient.

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REFERENCES

1. Mustafa HI, Fessel JP, Barwise J, et al. Dysautonomia: perioperative implications. *Anesthesiology*. 2012;116:205–215.
2. Jang MS, Han JH, Park SW, Kang JM, Kang WJ. General anesthesia for a patient with multiple system atrophy. *Korean J Anesthesiol*. 2014;67(suppl):S34–S35.
3. Knüttgen D, Büttner-Belz U, Gernot A, Doehn M. Unstable blood pressure during anesthesia in diabetic patients with autonomic neuropathy [in German]. *Anasth Intensivther Notfallmed*. 1990;25:256–262.
4. Bird TD. Charcot-Marie-Tooth hereditary neuropathy overview. In: Adam MP, Mirzaa GM, Pagon RA, et al, eds. *GeneReviews*. University of Washington, 2023.
5. Ramchandren S, Tirella C. Dysautonomia in Charcot-Marie-Tooth disease and correlations with patient-reported disability [abstract]. *Neurology*. 2018;90(15 suppl):P2.112.
6. Antognini JF. Anaesthesia for Charcot-Marie-Tooth disease: a review of 86 cases. *Can J Anaesth*. 1992;39:398–400.
7. McClain RL, Rubin DI, Bais KS, Navarro AM, Robards CB, Porter SB. Regional anesthesia in patients with Charcot-Marie-Tooth disease: a historical cohort study of 53 patients. *Can J Anaesth*. 2022;69:880–884.
8. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Group*. The CARE guidelines: consensus-based clinical case reporting guideline development. *Glob Adv Health Med*. 2013;2:38–43.
9. Arnold AC, Ng J, Lei L, Raj SR. Autonomic dysfunction in cardiology: pathophysiology, investigation, and management. *Can J Cardiol*. 2017;33:1524–1534.
10. Schüttler D, von Stülpnagel L, Rizas KD, Bauer A, Brunner S, Hamm W. Effect of hyperventilation on periodic repolarization dynamics. *Front Physiol*. 2020;11:542183.
11. Lankhorst S, Keet SWM, Bulte CSE, Boer C. The impact of autonomic dysfunction on peri-operative cardiovascular complications. *Anaesthesia*. 2015;70:336–343.
12. Porter TR, Shillcutt SK, Adams MS, et al. Guidelines for the use of echocardiography as a monitor for therapeutic

intervention in adults: a report from the American Society of Echocardiography. *J Am Soc Echocardiogr.* 2015;28:40–56.
13. Paul A, Sriganesh K, Chakrabarti D, Reddy KRM. Effect of preanesthetic fluid loading on postinduction hypotension and advanced cardiac parameters in patients with chronic compressive cervical myelopathy: a randomized controlled trial. *J Neurosci Rural Pract.* 2022;13:462–470.
14. Bevan DR. Shy-Drager syndrome. A review and a description of the anaesthetic management. *Anaesthesia.* 1979;34:866–873.
15. Hiramatsu S, Moriwaki K, Nakao M, Tsutsumi YM. Rocuronium-induced respiratory paralysis refractory to sugammadex in Charcot-Marie-Tooth disease. *Can J Anesth.* 2022;69:364–368.