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CASE REPORTS / CASE SERIES

Regional anesthesia in patients with Charcot–Marie–Tooth disease: a historical cohort study of 53 patients

Anesthésie régionale chez les patients atteints de la maladie de Charcot-Marie-Tooth : une étude de cohorte historique de 53 patients

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Abstract

Purpose *Anesthetic management for patients with Charcot–Marie–Tooth disease (CMT) is controversial. Description of the use of regional anesthesia (RA) in patients with CMT is limited. Regional anesthesia has traditionally been avoided because of risk of nerve injury. We retrospectively reviewed patients with CMT who received RA at our institution.*

Methods *We performed a historical cohort study of all patients with CMT who received RA from 30 April 2010 to 30 April 2020 within our institution. Charts were reviewed for information on demographics, RA procedures, perioperative variables, evidence of neurologic complications, post-RA neurology consults, and perioperative electromyography (EMG) results. Electromyographs were reviewed by a neurologist who was blinded to the surgical and RA details.*

Results *Fifty-three patients received a total of 132 regional anesthetics during the study period. Twenty-five patients received RA on more than one occasion. Fifty-five EMGs and 14 postoperative neurology consults were performed. Two patients had neurology consults with peripheral nerve block (PNB) distribution complaints years later. Neither attributed the complaints to the PNB. The other neurology consults were for unrelated complaints. No EMG results suggested injury related to PNB.*

Conclusion *This study found no evidence of documented neurologic complications or an increased risk of nerve injury related to RA in CMT patients.*

Résumé

Objectif *La prise en charge anesthésique des patients atteints de la maladie de Charcot-Marie-Tooth (CMT) est controversée. Les descriptions de l'utilisation de l'anesthésie régionale (AR) chez les patients atteints de CMT sont limitées. L'anesthésie régionale est traditionnellement évitée en raison du risque de lésion nerveuse. Nous avons rétrospectivement passé en revue les dossiers des patients atteints de CMT ayant reçu une AR dans notre établissement.*

Méthode *Nous avons réalisé une étude de cohorte historique de tous les patients atteints de CMT ayant reçu une AR entre le 30 avril 2010 et le 30 avril 2020 au sein de notre établissement. Les dossiers ont été passés en revue pour en tirer des renseignements sur les données démographiques, les interventions d'AR, les variables périopératoires, les signes de complications neurologiques, les consultations en neurologie post-AR et les résultats de l'électromyographie (EMG) périopératoire. Les électromyographes ont été examinés par un neurologue qui n'avait pas accès aux détails concernant la chirurgie et l'AR.*

Résultats *Cinquante-trois patients ont reçu un total de 132 anesthésies régionales au cours de la période d'étude. Vingt-cinq patients ont reçu une AR à plus d'une occasion.*

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Cinquante-cinq EMG et 14 consultations postopératoires en neurologie ont été effectuées. Deux patients ont consulté en neurologie après s'être plaints de la distribution du bloc nerveux périphérique (BNP) des années plus tard. Ni l'un ni l'autre n'a attribué ces problèmes au BNP. Les autres consultations en neurologie concernaient des plaintes non liées au BNP. Aucun résultat d'EMG n'a suggéré de lésion liée au BNP.

Conclusion *Cette étude n'a trouvé aucune preuve de complications neurologiques documentées ou d'un risque accru de lésion nerveuse liée à l'AR chez les patients atteints de CMT.*

Keywords Charcot–Marie–Tooth disease · nerve injury · peripheral nerve block · regional anesthesia

Charcot–Marie–Tooth disease (CMT) is a group of hereditary motor and sensory neuropathies, affecting 1 in 2,500 population.[1, 2] Charcot–Marie–Tooth Disease may be autosomal dominant, autosomal recessive, or X-linked. Nearly 100 unique gene mutations have been identified, the most common resulting in overexpression of the peripheral myelin protein 22 (PMP22) protein.[3] These mutations may result in both nerve demyelination, and axonal loss. Phenotypic expression of CMT is heterogeneous. Patients usually present in their second to fourth decades with weakness, muscle atrophy, hyporeflexia, sensory loss, and/or skeletal abnormalities. Deformities such as *pes cavus*, hammer toes, and claw hands may require surgical intervention.

Anesthetic management for patients with CMT is controversial. Current guidelines from the American Society of Regional Anesthesia on the use of regional anesthetic techniques are limited because of sparse clinical evidence and concerns that subsequent worsening of pre-existing neuropathies secondary to the so-called double-crush phenomenon may occur.[4] Because of the lack of safety data regarding regional anesthesia (RA) in patients with CMT, RA has commonly been avoided.

Case reports and case series in the literature suggest that patients with CMT may be at risk for other types of complications when they are managed using general anesthesia (GA). Major considerations include an increased sensitivity to neuromuscular blocking agents, hemodynamic instability due to autonomic dysfunction, cardiac conduction abnormalities such as prolonged QT interval, and respiratory dysfunction due to possible CMT diaphragm involvement.[5–11]

Given the paucity of evidence related to the use of RA in patients with CMT, we sought to review all patients with CMT who received RA at our institution over the last decade with an aim of determining the risk of peripheral nerve complications in this population.

Methods

We conducted a historical cohort study in patients with CMT who received a regional anesthetic during a surgical procedure. We retrospectively reviewed patients' charts to identify new-onset neurologic injury, exacerbation or progression of CMT, or infection after surgery. Charcot–Marie–Tooth disease patients were identified through a chart search of code 356.1 of the International Statistical Classification of Diseases and Related Health Problems, ninth/tenth/eleventh revision (ICD-9/ICD-10/ICD-11). Patients who had undergone peripheral nerve block (PNB) procedures were identified by current procedural terminology billing codes (64400–64455).

Inclusion criteria were 18 yr or older, a diagnosis of CMT, and PNB for a surgical procedure between 30 April 2010 and 30 April 2020. The study period was chosen from the date of institutional review board (IRB) exemption to ten years prior as trends of RA techniques almost universally included ultrasound guidance over this time period. Records were excluded for patients who declined access to their medical records for research. This study was determined to be exempt from IRB requirements by our IRB.

Patient demographics, PNB characteristics, surgery details, perioperative complications, postoperative worsening of CMT disease, and electromyography (EMG) studies were recorded as secondary information. All EMG reports and data were initially interpreted by a neurologist electromyographer, who evaluated them to ascertain whether any EMG findings could be attributed to a PNB. The neurologist was blinded to whether the EMG study took place before or after a PNB. After reviewing all EMG studies, the neurologist was then represented with only post-PNB EMG studies to determine whether any findings could be attributable to a PNB in light of this new contextual information.

All data were analyzed using descriptive statistics using mean (standard deviation [SD]) or median [range]) and percentages for categorical data.

Results

Fifty-three patients with CMT who received a PNB were identified (Table 1). A total of 132 RAs were performed (Table 2). Twenty-five patients received a PNB on more than one occasion and nine patients received RA more than twice. One patient received seven total PNBs and one

Table 1 Patient and case characteristics for surgeries in 53 CMT patients undergoing RA

Characteristic	
Female, *n*/total *N* (%)	25/53 (47%)
Age (yr), median (range)	63 (41–88)
Surgical time (min), median (range)	110 (24–404)
Intraoperative tourniquet, *n*/total *N* (%)	27/53 (51%)
Patients with > 1 regional anesthetics, *n*/total *N* (%)	25/53 (47%)
Patients with > 2 regional anesthetics, *n*/total *N* (%)	9/53 (17%)

CMT = Charcot–Marie–Tooth; RA = regional anesthesia

Table 2 Types of regional anesthesia utilized in 53 surgical patients with Charcot–Marie–Tooth disease

Regional anesthesia type *N* = 132*	*n*/total *N* (%)
Spinal	13/132 (10%)
Epidural	2/132 (2%)
Paravertebral	2/132 (2%)
Transversus abdominis plane	1/132 (1%)
Pectoral I	2/132 (2%)
Interscalene	15/132 (11%)
Supraclavicular	10/132 (8%)
Infraclavicular	1/132 (1%)
Axillary	2/132 (2%)
Lumbar plexus	15/132 (11%)
Femoral	11/132 (1%)
Sciatic	3/132 (2%)
Adductor canal	17/132 (13%)
Popliteal	23/132 (17%)
Ankle	15/132 (11%)
Peripheral nerve catheters	40/132 (30%)
Ultrasound guidance	79/132 (60%)

*Of the 53 surgical patients with Charcot–Marie–Tooth disease, 25 (47%) received more than one regional anesthetic (cf. Table 1)

spinal for five separate procedures. Sixty percent of PNBs were performed with ultrasound guidance. The mean (SD) surgical time was 110 (73) min and 50% of surgeries utilized a surgical tourniquet.

In this patient cohort, 55 EMGs and 14 postoperative neurology consults were performed. Forty-three EMGs were performed preoperatively and 12 postoperatively. Seven patients had EMGs both before and after PNB, although only three had studies performed in the distribution of the nerve block. No EMG results suggested changes related to PNB.

Two patients had postoperative neurology consults for complaints that were grossly in the distribution of the PNB. One patient who received a popliteal block for left cavovarus deformity repair in 2017 was seen again by neurology three years later for recurrence of his deformity. Pre- and postoperative EMGs were unchanged. The other patient had a left-sided lumbar plexus continuous catheter for left total hip arthroplasty in 2004 and was seen by neurology in 2020 for left-sided lower extremity weakness and numbness. Neurology determined it was a natural progression of her CMT. Neither of these consults attributed these complaints to the PNB. The remaining neurology consults were for follow-up of CMT or unrelated neurologic complaints. The mean (SD) time of total follow-up from first PNB to end of study period was 8.0 (3.3) years. Details on the PNBs performed and dosages of local anesthetics are provided in the Electronic Supplementary Material, eTable.

Discussion

To our knowledge, this is the largest case series to date evaluating the use of RA in patients with CMT. Previous descriptions of the use of peripheral[12, 13] or central[14–19] RA in patients with CMT have been limited to small case series and case reports. In each of these cases, there was no reported neurologic complication or worsening of neuropathic symptoms. Nevertheless, prolonged nerve block was reported in two cases: a single injection epidural block with 18 mL of 0.75% ropivacaine lasted 12 hr; and a single injection supraclavicular block with 30 mL of 0.5% bupivacaine lasted 30 hr. In both of cases, it was surmised that the high local anesthetic concentration and dose played a significant role in the duration of the blocks.[12, 16] Two small case series reported three successful ultrasound-guided axillary brachial plexus blocks, and a successful infraclavicular brachial plexus block without complication. The duration of these blocks was not reported.[13]

Expert advice on the use of RA in CMT is vague at best. Kopp *et al.*[20] reviewed the available literature of hereditary peripheral neuropathies including CMT. They determined that, given the lack of clinical evidence, no definitive recommendations about the safety and use of RA in these patients could be made but caution should be used to minimize risk factors.[20] Other reports generally recommend that regional anesthesia be avoided in patients with nerve injuries or pathologies that RA could theoretically worsen the disease progression. In a review of RA in patients with pre-existing neurologic disease, McSwain *et al.*[21] advised minimizing needle manipulation to decrease potential needle trauma, utilizing ultrasound guidance to facilitate nerve identification and decrease needle passes, and reducing local anesthetic concentration and dose as these patients

may have increased susceptibility to local anesthetic toxicity.[21]

With this dearth of supportive evidence and recommendations, RA in CMT patients has traditionally been avoided in clinical practice. Nevertheless, an advantage of RA in these patients is the potential avoidance of GA, which also has been shown to be an increased risk to those with CMT.

Major anesthetic considerations for patients with CMT include an increased incidence of cardiac dysrhythmias, respiratory system dysfunction, sensitivity to nondepolarizing muscle relaxants, hyperkalemia, and malignant hyperthermia.[7] With respect to cardiac dysrhythmias, complete right bundle branch block, mitral valve prolapse with second-degree atrioventricular block, third-degree atrioventricular block, sick sinus syndrome requiring pacemaker insertion, and paroxysmal atrial flutter premature ventricular contraction giving rise to monofocal and multiple QT prolongation have all been reported.[7] In terms of respiratory system dysfunction, disorders of diaphragmatic function, abnormalities of the thorax cage leading to restricted pulmonary function, and sleep disorders have all been reported.[6, 7] Furthermore, respiratory muscle weakness may lead to perioperative pneumonia and prolonged postoperative ventilation has been reported for up to one month.[5, 7] In addition, patients with CMT may have orthopnea or difficulties lying in the supine position because of an abnormal thoracic cage.[7] With respect to the chronic denervation in CMT, involvement of all extremities can potentially lead to excessive potassium release with the administration of succinylcholine, but this was not shown to be clinically relevant in case reports.[5, 8] Finally, CMT has been associated with malignant hyperthermia.[9] Given that CMT is a diffuse neuropathy not a myopathy and that anesthetics including malignant hyperthermia-triggering agents were successful, there appears to be no association.[5] Although GA can be safely administered in CMT patients if the multiple organ systems involvement and anesthetic considerations explained above are understood, it seems prudent to avoid the physiologic perturbations associated with GA whenever possible.

To our knowledge, no previous reports have examined EMG records for subclinical evidence of neurologic injury or disease progression following RA in this patient population. In this case series, expert-blinded review of EMGs performed around the time of surgery showed no evidence of disease progression or nerve injury when EMG was performed in the same distribution of the procedure or RA technique. Although no definitive conclusions can be drawn from this EMG data, it is encouraging, nonetheless.

This study has limitations. First, as this was a historical cohort study, precise determination of neurologic function is limited to what was documented in the medical record, which was assumed to be accurate. Second, selection bias toward utilizing RA only in CMT patients with mild disease at lower risk for complication than those who did not receive RA could have occurred. This is evident by the fact that several patients over the study period had multiple regional anesthetics on different occasions. Third, this case series did not include a control group of patients with CMT who had surgery but did not receive RA. Nevertheless, we would anticipate the incidence of a nerve injury complication using GA to be less or equal to those receiving RA. Finally, the number of patients who had pre- and post-EMG and/or neurology consults was small and these patients represented only a subset of the study cohort. While being a limitation, this may further support the low likelihood of nerve injury from RA as patients with new or worse symptoms following surgery in which there was a concern for progression of disease or nerve injury would have been more likely to be referred for additional EMG testing and neurologic consultation. Nonetheless, subclinical mild nerve injury may not have been easily detected on postoperative EMGs given the underlying EMG abnormalities from CMT.

In conclusion, in this historical cohort study of 53 patients who received a total of 132 regional anesthetics, we did not find evidence of documented neurologic complication or increased risk of nerve injury related to RA in CMT patients. Ultimately, future large multicenter studies evaluating the incidence of nerve injury in patients with CMT compared with those without CMT would be valuable to further assess the risk of RA in patients with CMT and to further our decisions on the safest and most effective anesthetic technique when caring for these patients.

Author contributions *Robert L. McClain*, *Christopher B. Robards*, and *Steven B. Porter* contributed to all aspects of this manuscript, including study conception and design; acquisition, analysis, and interpretation of the data; and drafting the article. *Devon I. Rubin* contributed to the analysis and interpretation of the data and drafting of the article. *Kimmy S. Bais* and *Antonio M. Navarro* contributed to acquisition and analysis of the data and drafting of the article.

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