Case report

**Sport activity in Charcot–Marie–Tooth disease: A case study of a Paralympic swimmer**

Giuseppe Vita, Stefania La Foresta, Massimo Russo, Gian Luca Vita, Sonia Messina, Christian Lunetta, Anna Mazzeo

*Unit of Neurology, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy*

**Abstract**

This study reports the positive physical, emotional and psychosocial changes induced by sport activity in a Paralympic swimmer with Charcot–Marie–Tooth (CMT) type 4A. When we compared evaluations before initiating sport activity with those after five years of competitive activity, we found: i) increased proximal muscles strength of upper limbs; ii) augmented ability to propel wheelchair independently; iii) improved quality of life; iv) reduced trait anxiety and striking improvement of depression; v) enhanced self-esteem. Longitudinal studies in large cohorts to evaluate the positive effects of sport activity are needed to support provision of evidence-based advice to patients and families.

© 2016 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

**Keywords:** Charcot-Marie-Tooth; Sport; Swimming; Paralympic record; Quality of life; Self-esteem

1. **Introduction**

Sport activity is a valuable tool to improve sense of wellness, quality of life and to break down social barriers of discrimination for disabled individuals [1]. Apart from the issue of autonomy of the individual, many physical, psychological and social benefits arise from sporting participation, which can translate into reduced health-care costs [2]. Available evidence reveal also a positive impact of sports on areas of self-esteem, self-efficacy and mental health [3].

The main impairment types in Paralympic sports include amputation or limb deficiency, cerebral palsy, spinal cord-related disability, visual impairment, and intellectual impairment. A sixth group, known as *les autres*, accommodates those athletes with physical impairments who are not covered by the other groups [2]. It is commonly accepted that subjects with a single disabled body segment are those preferentially prone to a sport activity. In this context, individuals with a progressive and severe genetic neuromuscular disorder are believed able to perform sports, with the exception of those competitive and with a full-body workout.

Charcot–Marie–Tooth (CMT) disease, the most common inherited neuromuscular disorder, has a quite variable course because of genotypic and phenotypic heterogeneity. CMT type 4A is caused by mutation in the gene encoding ganglioside-induced differentiation-associated protein-1 (GDAP1) on chromosome 8q21. The recessive disorder is a severe neuropathy of childhood characterized by early age of onset, rapidly progressive distal weakness and atrophy of the limbs leading to inability to walk in late childhood or adolescence, mild sensory loss with abolished deep tendon reflexes, and frequent vocal cord paresis [4].

We report here a wheelchair-bound woman with CMT type 4A who became a Paralympic champion swimmer. Longitudinal observation allowed to demonstrate, after five years of intensive aerobic physical exercise and sprint distance swimming competitions with many wins, improved proximal muscles strength with increased ability to propel wheelchair independently, enhanced quality of life (QoL) and self-esteem, remarkable improvement of depression, reduced trait anxiety.

2. **Case report**

An adult woman was referred to our clinic for a long history of muscle weakness. She started to walk at 18 months. At three
years of age, because of frequent falls, she was seen by a
neuropediatrician who noticed claw hands and a steppage gait.
Her gait improved after bilateral Achilles tendon lengthening.
By 14 years of age she developed dysphonia. She continued to
have progressively increased difficulty in walking and at 25 years of age started to walk with the help of one stick and
at age 28 she became wheelchair-bound. On neurological
examination, at age 31 years, she was able to walk only for 1–2
meters with bilateral support. There were dysphonia for
bilateral vocal cord paresis, rare dysphagia for liquids, inability
to go from supine to seated position without assistance, severe
claw hands and bilateral pes cavus. The patient had muscular
hypotonia, mild proximal weakness and severe distal weakness
(Muscle Research Council – MRC – strength grade 4 in deltoid,
biceps and triceps muscles and 0 in forearm and hand muscles;
at lower limbs, grade 4 in ilioopsoas, 2 in quadriceps and biceps
femoris, 0 in tibialis anterior, peroneus longus and hallucus
extensor longus). She also displayed reduced-to-absent deep
tendon reflexes and deep sensory loss at legs and feet. Barthel
Index (BI), which is a widely used measure of functional
disability assessing the capacity of an individual to care for
him/herself and to move independently or with assistance in
the activities of daily living, was 55/100, and modified BI (mBI)
60/100. Nerve conduction studies showed evidence of a severe
axonal sensory-motor polyneuropathy. CMT Neuropathy
Score (CMTNS) resulted 33/36. Genetic study revealed that
she was homozygous for a c.173_174 insA mutation in the
GDAP1 gene, determining the introduction of a premature stop
codon (p.P59AfsX3). Father, mother and the brother were
heterozygous for the same mutation and had a normal
neurological examination.

On the occasion of the visit at age 31, the patient was
also evaluated by a psychologist. The 36-item short-form
questionnaire (SF-36) [5,6] assessed QoL by eight specific
categories of physical and emotional scores, then summarized
in two scores: physical composite score (PCS) and mental
composite score (MCS). Previous studies in CMT patients
showed that very low scores for PCS indicate severe physical
dysfunction, distressful bodily pain, frequent tiredness and
unfavorable evaluation of health status. Very low scores for
MCS indicate frequent psychological distress and severe social
and role disability due to emotional problems [7,8]. Anxiety
was evaluated by State-Trait Anxiety Inventory (STAI) [9].
Beck Depression Inventory II (BDI-II) was used to evaluate
depression symptoms [10]. Rosenberg Self-Esteem Scale
(RES) measured global self-worth by evaluating both positive
and negative feelings about the self [11]. All SF-36 QoL
domains were markedly deteriorated with respect to the Italian
normative sample, especially physical function, role physical,
social function and mental health (Fig. 1). There were also high
scores of state and trait anxiety, high level of somatic and
cognitive elements of depression, and low self-esteem (Fig. 1).

We suggested the patient to perform physical activity. At that
time, she was not able to swim, but at age 32, she was persuaded
by a close friend to attend a swimming pool. She started to
develop a real passion for swimming and progressively
increased her workout from 25–50 m to 1200–1500 m in each
pool session of approximately 1.5 hour duration, four times a
week. In addition, physical training included two to three
sessions of weight and aerobic exercise per week, of 90 minutes
duration each, in a gymnasium. She started to play in national
Paralympic competitions. As a swimmer with severe physical
disability, she was classified in S3 category (range 1–10, with 1
corresponding to the most severe type of disability). In 2013
she gained the following positions at Italian Paralympic Games:
silver medal, 50 m backstroke in winter; gold medal, 50 m
backstroke (Italian record) and silver medal, 50 m backstroke
(category record) in summer. In 2014: gold medal, 50 m
backstroke; gold medal, 50 m freestyle in winter; gold medal,
100 m backstroke in summer. In 2015: gold medal, 50 m
freestyle; bronze medal, 50 m backstroke, in winter (Fig. 2).
Moreover, in 2014 she arrived 4th in 50 m backstroke at the
International Championships in Berlin, Germany.

In 2015, at age 36, after 5 years of intensive sport activity,
she had a follow-up visit in our clinic. We noticed an increased
muscle strength in deltoid, biceps and triceps bilaterally (MRC
grade 5-), whereas biceps femoris muscle strength decreased to
grade 1. CMTNS diminished to 31/36 with reduced score from
4 to 3 in the items “Motor symptoms (arms)” and Strength
(arms)”. BI was unchanged (55/100) but mBI increased to
64/100 with improvement in the wheelchair ambulation (from
almost total dependence from others except short distance on
flat surface to ability to propel wheelchair independently at
least 50 meters).

Psychological evaluation revealed an improvement of all
SF-36 domains except for a stable vitality (Fig. 1). State
anxiety, as transitory emotional state, slightly increased but
trait anxiety, including feelings of apprehension, tension and
worry as stable personality trait during daily living activities,
decreased almost reaching the normal cut-off. BDI–II showed
quite decreased levels of pessimism, past failures, punishment
and guilt feelings, self-dislike and worthlessness with presence
of ups and downs. Self-esteem returned to normal range
(Fig. 1).

Finally, the revised form of Behavioural Regulation in
Exercise Questionnaire (BREQ-2) [12] demonstrated a strong
self-determination as a result of high intrinsic and identified
motivation regulating exercise behavior. Despite her physical
problems, she exhibited strong self-determined motivation,
which was suitable for her to engage in high levels of physical
activity. The patient perceived increased self-esteem and self-
efficacy as a consequence of sport events, which were
experienced as supporting her autonomy and promoting her
competence.

3. Discussion

A recent systematic review to evaluate benefits and risks of
exercise in CMT showed that the optimal exercise modality
and intensity as well as the long-term safety of exercise still
remain unclear [13]. However, it appears that exercise in CMT
patients may be effective in improving some components of
health and fitness without harmful effects in the short-term.
The majority of published studies investigated resistance
training interventions, which were found to result in positive modifications in strength, functional activities, and muscle fiber size. Similarly, aerobic training led to favorable changes in some measures of strength and functional activities, as well as an increase in aerobic capacity. Combined exercise intervention studies found positive changes in ankle flexibility, balance, agility, and mobility [13]. Respiratory function has been rarely investigated in CMT patients and found minimally abnormal compared to healthy subjects, and with no amelioration after combined rehabilitation treatment [14]. Conversely, neuromuscular recovery after a fatiguing task has been found to be impaired in the vastus lateralis muscle, but not in the biceps brachii muscle, of functionally independent CMT type 1A patients, compared with healthy individuals [15]. This difference was thought due to a prevalent involvement of the lower limbs.

There are concerns that exercise may cause overwork weakness (OW), characterized by a progressive muscular weakening due to exercise, work, or daily activities in people with CMT disease, and this topic is the subject of ongoing debate with contradictory results. We have tested the OW hypothesis in 271 CMT1A patients recruited in the Italian/UK multicenter trial of ascorbic acid and did not find effect of OW over time resulting in greater weakness in dominant muscles with increasing age or in more severely affected patients [16]. The main consequence of these results is that exercise is not harmful for CMT1A patients, and possibly for the overall CMT population. Since a detrimental effect of supramaximal exercise cannot be excluded, most authors encourage physical activity in CMT patients, but recommend aerobic exercises at a submaximal work level [14,17,18]. However, the best training to adopt (e.g. endurance? explosive strength?) by CMT patients is not known. By definition, muscular endurance refers to the ability to perform a specific aerobic muscular action for a prolonged period of time, whereas explosive strength refers to the ability to exert strength or force as rapidly as possible in a given action with a short, very high intensity anaerobic exercise [19]. A recent study on two novel outcome measures for CMT disease, the 6-minute walk test and StepWatch™ Activity Monitor (SAM), which is an activity measuring accelerometer, showed that several SAM outputs, all reflecting the higher speed, were significantly related to the main score of physical aspect of QoL: the higher the explosive performance, the better the physical QoL. [20].

Fig. 1. (A) SF-36 domain results before initiating sport activity and after five years of swimming activity. Pointed line indicates the mean of the Italian normative sample. (B) State-Trait Anxiety Inventory (STAI) score before and after sport activity. A higher score indicates greater anxiety, with a cut-off of 40 (pointed line). (C) Beck Depression Inventory II (BDI-II) score before and after sport activity. The pointed line indicates normal cut-off per each score. (D) Rosenberg Self-Esteem Scale (SES) score before and after sport activity. The pointed area delineates the normal self-esteem range.
Although it is an anecdotal observation, the present case study leads to two main comments. First, neuromuscular experts have not so far directed too much attention to disability sport. Based on available literature, very rarely they suggest patients to perform sport activity and, when they do, they recommend avoiding supramaximal exercise. Our patient, severely affected by CMT, not only was able to carry out regularly intensive aerobic swimming workout with progressive increase of covered distance, but she also competed in sprint distance events, in which anaerobic activity is prevalent to endurance, with many wins in national championships. After five years of sport activity, deltoid, biceps and triceps muscle strength increased from MRC grade 4 to 5- with improved mBI and CMTNS and increased ability to propel her wheelchair independently. It might be related to strengthening of deconditioned muscles which were not severely affected. The polymorphic disabilities involving people with CMT disease may lead to deconditioning and a lower tolerance for physical activities. Even a short physical performance battery is an efficient and safe tool in producing some improvement in proximal limb muscles [13,14,21].

The second conclusion of our report is that such an intensive muscular training induced a marked improvement of QoL, removal of depression, and reduced trait anxiety. Thanks to sport practice, the patient experienced increased self-esteem and self-efficacy leading to interpret existing situations as more autonomy-promoting and to organize her actions on the basis of personal goals and interests rather than controls and constraints [22]. A 2-year prospective study of QoL in CMT1A showed no worsening of QoL despite worsening in muscle strength and sensory function, most likely due to development of compensatory strategies that help patients cope with the slow progression of the disease [23]. We postulate that coping strategies together with the beneficial and gratifying effects of sport caused a considerable improvement of mental, emotional and psycho-social health in our patient.

Sport activity may be considered a complementary therapy of CMT, despite the present lack of proven efficacy. Longitudinal studies of its effects are needed to confirm our experience and to support provision of evidence-based advice to patients and families. Continued involvement in physical activity for both functionally independent and dependent CMT patients should be supported by clinicians.

Acknowledgment

We express our deep gratitude to the patient, Ms. Giusi Barraco, who gave her permission for the publication of the Case Report. The study was partially supported by a grant from Telethon Foundation (GUP 13006).

References

[1] DePauw K, Gavron S. Disability sport. 2nd ed. Champaign (IL): Human Kinetics; 2005.
[2] Webborn N, Van de Vliet P. Paralympic medicine. Lancet 2012; 380:65–71.
[3] Blauwet C, Willick SE. The Paralympic Movement: using sports to promote health, disability rights, and social integration for athletes with disabilities. PM R 2012;4:851–6.
[4] Pareyson D, Marchesi C. Diagnosis, natural history, and management of Charcot-Marie-Tooth disease. Lancet Neurol 2009;8:654–67.
[5] Ware JE Jr. SF-36 physical and mental health summary scales: a user’s manual. Boston (MA): The Health Institute, New England Medical Center; 1994.
[6] Apolone G, Mosconi P. The Italian SF-36 Health Survey: translation, validation and norming. J Clin Epidemiol 1998;51:1025–36.
[7] Padua L, Apire I, Cavallaro T, et al. Variables influencing quality of life and disability in Charcot Marie Tooth (CMT) patients: Italian multicentre study. Neurol Sci 2006;27:417–23.
[8] Padua L, Shy ME, Apire I, et al. Correlation between clinical/neurophysiological findings and quality of life in Charcot-Marie-Tooth type 1A. J Peripher Nerv Syst 2008;13:64–70.
[9] Spielberger CD, Gorsch RL, Lushene R. Manual for the state-trait anxiety inventory. Palo Alto (CA): Consulting Psychologists Press; 1983.
[10] Beck AT, Steer RA, Brown GK. Manual for Beck Depression Inventory-II. San Antonio (TX): Psychological Corporation; 1996.
[11] Rosenberg M. Society and the adolescent self-image. Princeton (NJ): Princeton University Press; 1965.
[12] Markland D, Tobin V. A modification of the behavioural regulation in exercise questionnaire to include an assessment of amotivation. J Sport Exercise Pay 2004;26:191–6.
[13] Sman AD, Hackett D, Fiatarone Singh M, Fornusek C, Menezes MP, Burns J. Systematic review of exercise for Charcot-Marie-Tooth disease. J Peripher Nerv Syst 2015;20:347–62.

[14] Maggi G, Monti Bragadin M, Padua L, et al. Outcome measures and rehabilitation treatment in patients affected by Charcot-Marie-Tooth neuropathy: a pilot study. Am J Phys Med Rehabil 2011;90:628–37.

[15] Menotti F, Bazzucchi I, Felici F, Damiani A, Gori MC, Macaluso A. Neuromuscular function after muscle fatigue in Charcot-Marie-Tooth type 1A patients. Muscle Nerve 2012;46:434–9.

[16] Piscosquito G, Reilly MM, Schenone A, et al. Is overwork weakness relevant in Charcot-Marie-Tooth disease? J Neurol Neurosurg Psychiatry 2014;85:1354–8.

[17] Lindeman E, Leffers P, Spaans F, et al. Strength training in patients with myotonic dystrophy and hereditary motor and sensory neuropathy: a randomized clinical trial. Arch Phys Med Rehabil 1995;76:612–20.

[18] White CM, Pritchard J, Turner-Stokes L. Exercise for people with peripheral neuropathy. Cochrane Database Syst Rev 2004;(4):CD003904.

[19] Mikkola J, Rusko H, Nummela A, Pollari T, Häkkinen K. Concurrent endurance and explosive type strength training improves neuromuscular and anaerobic characteristics in young distance runners. Int J Sports Med 2007;28:602–11.

[20] Padua L, Pazzaglia C, Pareyson D, et al. Novel outcome measures for Charcot-Marie-Tooth disease: validation and reliability of the 6-min walk test and StepWatch™ Activity Monitor and identification of the walking features related to higher quality of life. Eur J Neurol 2016; DOI:10.1111/ene.13033. [Epub ahead of print].

[21] Ramdharry GM, Pollard A, Anderson C, et al. A pilot study of proximal strength training in Charcot-Marie-Tooth disease. J Peripher Nerv Syst 2014;19:328–32.

[22] Ng JY, Ntoumanis N, Thøgersen-Ntoumani C, et al. Self-determination theory applied to health contexts: a meta-analysis. Perspect Psychol Sci 2012;7:325–40.

[23] Padua L, Pareyson D, Aprile I, et al. Natural history of CMT1A including QoL: a 2 year prospective study. Neuromuscul Disord 2008;18:199–203.