Complex assessment in progressive multiple sclerosis: a case report

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Abstract
The study presents the case of a patient with progressive multiple sclerosis in relapses (PPMS) and proposes a comprehensive neuromuscular and biomechanical evaluation in order to achieve a predictive picture of gait evolution and balance disorders with disease progression. Patient and Methods: The evaluation included: clinical, functional and neuromuscular evaluation by tensiomyography (TMG) and biomechanics (by RSscan platform force). Elements evaluated included the calf muscle groups (tibialis anterior and gastrocnemius) and the following parameters were assessed from neuromuscular point of view: contraction time, sustain time, delay, relax time and displacement amplitude after electrical stimulation. Biomechanically, we assessed the subtalar angle, foot loading in metatarsian area, foot balance and pressure center distribution. Results and Conclusions: From neuromuscular point of view, we concluded that the right anterior tibial muscle developed compensatory muscle fibers resistant to fatigue. TMG analysis can estimate the possibility of developing gait disorders even in the absence of visible clinical manifestations. We also noted an increased muscle tone in the muscles of bilateral twins. Biomechanical evaluation revealed a symmetrical, abnormal gait, explained by the difference in the angle of left and right foot and in subtalar angle, which expresses the degree of coordination and control of foot gait initiation and execution. In this context, there is an exorotation of both feet.

Keywords: progressive multiple sclerosis in relapses, tensiomyography, neuromuscular.

Introduction
Progressive multiple sclerosis in relapses (PPMS) is a clinical form of MS characterized by progressive development of the disease in relapses with complete remission. Steady deterioration of nerve function begins with the initial appearance of symptoms that appear and disappear, but nerve damage is continuous [1–4].

The most commonly encountered pathology issues are:
- Multiple demyelinating plates, disseminated over large areas, developed especially in perivenous area;
- Coexistence of active demyelinating plates (soft, edema, poorly delimited, pink) with old plates (rough, hard, gray);
- In the early stage, there are predominantly macrophages containing myelin (granulocyte-plump body cells), subsequently adding lymphocytes, and perivenously astrocytes and oligodendrocytes proliferate;
- In the old plates – absence of inflammatory cells, predominance of demyelinated fibers and astrocytic gliosis.
- Plates located mainly in the optic nerves, periventricular white matter, brainstem, cerebellum, white matter in the frontal lobes and posterior cervical spinal cords.

Each patient with multiple sclerosis (MS) has only one type of damage, although there is great variation between the types of damage seen in different patients [5]. Based on these different patterns, the authors postulate that MS has several pathological mechanisms or etiologies, thus arguing hypothesis that MS is a collection of heterogeneous syndromes, which raises implications for individual patient therapy. In addition, the clinical course may differ, pattern II is often associated with relapsing-remitting multiple sclerosis (RRMS) and type IV with progressive multiple sclerosis relapse (SMPP).

In SMPP, there is a pathological and immunopathological type IV, resulted from an oligodendropathy with subsequent demyelination [6].

Patient and Methods
Based on the above-mentioned issues, we propose the presentation of a PPMS case with a comprehensive assessment meant to offer the clinician a predictive image of the evolutionary potential of such cases. Specifically, although this case does not record any clinically detectable abnormal gait disorders, these disorders exist and have evolutionary potential demonstrated by the results of our assessments.

Patient D.M., female, aged 28 years, from urban environment, diagnosed with multiple sclerosis, PPMS, with disease onset at the age of 18, has the following symptoms: local and general fatigue, balance disorder, no gait disturbance, paresthesia of the lower limbs without pathological personal or family history to suggest a possible link with disease pathogenesis.

In this study, we proposed a comprehensive assessment from clinical, functional, neuromuscular and biomechanical point of view.
We made a complex evaluation regarding clinical examination that involve also neurologic examination for collect information about muscle strength, muscle tone, gait and static/dynamic balance, visual and auditory disorders. In the same time, we have data about MRI examination that reveal multifocal lesions of different ages. For functional evaluation, we used Hamilton score, ADL scale and Kurtzke scale. Kurtzke’s Expanded Disability Status Scale (EDSS) records progression of disease, clinical status on a scale of 0 to 10 [7]. ADL Scale (Activities of Daily Living) refers to activities performed routinely by a person during the day [8]. Hamilton Scale evaluates overall anxiety and contains 14 items, each being rated on a scale of five anchors from 0 to 4 (a score over 14 indicates a clinically significant anxiety) [9].

The new aspect of this research is the neuromuscular assessment, which was performed by tensiomyography (TMG), a technique that allows the assessment of contractile properties of striated muscle using a displacement sensor for selective detection of transverse muscle strains on electrical stimulation [10]. By this method, it is possible to monitor contractile properties of skeletal muscle fibers through the isometric contraction due to electrical stimulus applied to the maximum relief area of the muscle and at the same time, the rate of shortening of the muscle during the contraction produced by electrical stimulation [11–15].

From TMG response, there were extracted five parameters that related to:

- Maximum displacement (Dm) [16]: the amplitude of muscular displacement in transverse direction – Dm [mm] is a parameter that is also correlated with Tc values and depends on the flexibility of muscular tissue; therefore, Dm values increase when explosive force is developed and thus, movement amplitude is higher, and decrease under the conditions of a high muscular tone;
- Delay time (Td) [ms]: the time between the moment of stimulation and the moment when we obtain 10% of the muscular contraction;
- Contraction time (Tc) [ms]: the time between the moment when the muscular contraction is 10% and the moment when the contraction reaches 90% out of maximum. The value of contraction time depends on the percent of fast or slow fibers found [17] in the studied muscle. Thus, the values decrease once the percent of type II fibers increases, and they increase when the percent of fibers of type II is reduced and that of type I fibers increased;
- Sustain time (Ts) [ms]: the time between the moment when the muscular contraction is 50% and the moment when the relaxation reaches 50%;
- Relax time (Tr) [ms]: the time between the moment when the relaxation is 50% and the moment when the relaxation is 90%.

TMG method also analyzes lateral and functional symmetry and muscle adaptation to exercise, with normal value over 85% [18]. TMG is an evaluation method for the morphofunctional potential of the muscle, which allows the detection of the muscular reaction to electrical stimulation. Through this method, we may appreciate the ratio between type I (fatigue-resistant) and type II (white, fast-twitch, with low resistance to fatigue – this phenomenon appearing before the completion of the electrical stimulation process) muscular fibers. In order to complete the data supplied by the clinical and paraclinic examination, we suggested the use of TMG as an evaluation method for muscular fatigue and skeletal muscle composition, which took place within MS and was necessary to establish the connection between the structure and morphofunctional properties of the muscle on the one hand, and its functional potential on the other hand.

The evaluation of muscular fatigue can be made under intermittent electrical stimulation of the muscle. This stimulation is made with a TMG–S1 electrostimulator (Furlan & Co., Ltd.), using 5/5 cm Platinum-type electrodes. The stimulation is performed under increasing electrical current intensities, between 10–65 mA, the length of the stimulation being one millisecond. An isometric contraction is produced because of electrical stimulation. The detection of the muscular response to the electrical stimulus is performed with a G40, RLS Inc. sensor, perpendicular to the muscle surface, in the area in which the muscular geography is well displayed (this can be more precisely determined if the subject is requested to perform an isotonic contraction, if a muscle strength higher than 2 is possible). The sensor is placed at this level; it will exert a 0.7 N/mm² pressure on the contact surface.

**Signal recording**

The TMG signals are received by a Matlab Compiler Toolbox on a 1 kHz frequency. Two supra-maximal responses are stored and then the mean is calculated. The supra-maximal stimulation [14] is regarded as corresponding to a minimal stimulation and it determines maximal amplitude of muscular deformation, recorded as Dm.

TMG evaluation was performed in the muscle groups of the leg: anterior tibialis muscle (TM), twin medial muscle and twin lateral muscle.

For a complete evaluation, we proposed also the biomechanical gait evaluation was performed using a platform for force distribution and plantar pressure distribution Footscan Scientific Version planting, RSscan International, Olen, Belgium, able to perform measurements with a frequency of 500 Hz in 2D and record the complete action of both plants. The platform was used to record the pressure distribution values in the lower limb at ground contact. The plant applied on the platform measures local pressure at full contact with the ground at high frequency, the operational substrate is represented by the total impact force measured at the level of a sensor matrix on a known surface [19].

RSscan force platform performs the gait analysis in terms of ground reaction force, the pressure developed during gait and other dynamic parameters but also, important for our study, the limbs axis and subtalar angle, foot balance in antero-posterior and frontal planes, pressure center position [20].

Both plants were recorded during two gait cycles,
paying attention to alternative placement of the right/left lower limb.

In the present study, we grouped the eight stages of gait into three stages, namely: heel attack phase – the initial contact heel; midstance phase, in which the middle region of the plant is involved, and propulsion phase, in which the loading is higher in the metatarsals; this stage depends on the way the tibial-tarsal control is achieved.

Biomechanical aspects assessed were: heel rotation, foot balance, uploading metatarsian area and pressure distribution center.

This protocol was applied following the rules of the Ethics Committee of the Research Centre for the Study of Human Body Movement from University of Craiova, Romania, and is compliant with the Helsinki Declaration principles. In this respect, the investigated subject was informed about the proceedings of this study, based on informed consent.

Results

After clinical functional evaluation, we observed the existence of score 2 according to Hamilton score (absence of depression), an ADL score 8 falling within normal limits and a score of 2.5 – minimal disability according to Kurtzke scale. Clinically, there were not noted any significant changes. Also, there was reported the ability to travel and to work, the patient being classified in severe disability, grade II. In the same time, for neurological evaluation we recorded low muscle strength of the lower limbs, impaired static and dynamic balance, lack of pyramidal signs, the presence of paresthesias, diplopia, without hearing alteration.

Band and nodular demyelination at the semioval center and at the level of minor and major forceps have been observed on NMR.

Results of TMG neuromuscular assessment indicated the parameter values are given in Table 1.

Regarding biomechanical evaluation indicated the some specific changes of heel rotation – left heel (green) is in slight pronation up to 5° in midstance phase, outside the minimum risk area, and in the right heel (red) – it is noticed an emphasized pronation up to 10° during the contact phases and midstance phase with the foot outside the minimum risk area (Figure 1).

Another aspect is foot balance, which present a supination up to -53 in the left foot, totally exceeding the minimum risk area, and an emphasized supination in the right foot during the midstance and an emphasized pronation during the propulsion stage (Figure 2).

Loading in metatarsal region, graph shows instability of the left foot (green) during the propulsion phase, which means lack of neuromotor control; in right foot (red), we observed a loading in the low risk area where the foot is stable and corresponds to midstance phase, emphasizing foot instability during the propulsion phase (Figure 3).

In correlation with gait disorders distribution of the pressure center, left foot is performed in the metatarsians 2 and 5, and in the right foot only at the level of finger 1. Distribution of the pressure center in the right and left foot indicates that there is a tendency of the body anterior projection with left anterior lateral deviation (Figure 4).

Analyses of the foot angle and subtalar angle are shown in Table 2.

**Table 1 – Values of assessed TMG parameters**

<table>
<thead>
<tr>
<th></th>
<th>Tc [ms]</th>
<th>Normal Tc [ms]</th>
<th>Dm [mm]</th>
<th>Normal Dm [mm]</th>
<th>Td [ms]</th>
<th>Normal Td [ms]</th>
<th>Ts [ms]</th>
<th>Tr [ms]</th>
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<td>63.1</td>
<td>32.83±4.5</td>
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<td>40.6</td>
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<td>28.7</td>
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</table>

mTA – Tibialis anterior muscle; mGM – Medial gastrocnemius muscle; mGL – Lateral gastrocnemius muscle; Tc – Contraction time; Dm – Muscular displacement; Td – Delay time; Ts – Sustain time; Tr – Relax time.

![Figure 1 – Heel rotation.](image-url)
Discussion

The results of clinical and functional assessments indicated a minimal disability, which allows carrying out normal daily activities, a Kurtzke score of 2.5 means a limitation of the progressive character of the disease.

TMG assessment

Comparing left anterior tibialis muscle group with the right one we found much lower Tc values, which indicated a better maintenance of the integrity of fast muscle fibers in the right foot compared to the left foot. Regarding Dm, we found higher values in the right foot correlated with the values of the contraction time. Td registered higher values in the right foot, which indicated a delay in nerve influx, aspect that was correlated with Tr and had higher values in the right foot. Ts values were elevated in right anterior tibial muscle, which meant developing compensatory muscle fibers resistant to fatigue. In conclusion, these data analysis estimated the possibility of developing gait disorders even in the absence of evident clinical manifestations.

In the calf posterior muscles of the right foot, we noticed an increase of Tc in the lateral gastrocnemius (mGL) whose value was close to normal values, much
more evident in the left leg. This meant that there was a predominant development of type I fibers in the lateral twins, bilaterally as an adaptive postural recovery mechanism once the gait was initiated [18]. Regarding Dm, we noticed much higher values of mGL compared to medial gastrocnemius (mGM) in the right leg, while the left foot values were similar for the two muscles. The analysis of this parameter determined that there was an increased muscle tone in these muscle groups [16]. Td had higher values in the right mGM and comparative values in the twin muscles of the left leg. these values were significantly elevated and predicted the existence of a right–left asymmetry in correlation with the evolution of Tc. Tr was high in the right mGM and left mGL, the values were correlated with low values of Dm, which indicated a significant right–left value asymmetry. The same asymmetry, probably caused by the existence of muscle fatigue, was reflected in Ts values, which were increased in the right mGM as compared to the right mGL and to the twin muscles of the left leg. The explanation to these differences was given by the alteration of the structural configuration of the muscle in accordance with increased muscle tone in the right foot.

Biomechanical evaluation of data analysis experienced a symmetrical gait, abnormally explained by the difference in the right foot-left foot angle (Table 2) and subtalar angle that expressed the degree of coordination and control of foot gait initiation and execution [21]. In this context, there was an exorotation of both feet.

Regarding the foot balance, we noticed a supination during all three phases of gait. There was a predominance of left-right asymmetric instability specific to the propulsion phase [22].

Analyzing planter symmetry (center of pressure distribution), we observed an abnormal pressure distribution allowing estimation of future development in terms of the patient’s functional deficit.

Conclusions

Analysis of the results of this research about full assessment by following the protocol described above allow us to conclude that the patient had no clinical evidence of gait disturbance, muscle structure; however, as evidenced by TMG, indicated predominant development of type I fibers in the right foot. Presence of clinical balance disorders was explained by the development of intrinsic balance disorders of the foot, which were more obvious during propulsion; also, the lack of a neuro-motor control and instability that could be detected only by biomechanical assessment, allowing training and development of prophylactic mechanisms. These aspects can be corroborating with the results of neuro-muscular evaluation and with biomechanical results, allowed predicting the risk of development of normal gait patterns. Also, changes of the structural configuration of the calf muscle groups, determined by assessments and monitoring, enabled the development of a training protocol to have a recovery neuromuscular control and coordination in the foot, which would be a beneficial impact not only on walking but also on foot balance.

References

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