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Research Article

Profound Muscle Atrophy in a Patient with Chronic Disorders of Consciousness for 13 Years: Case Presentation

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Abstract

Chronic disorders of consciousness (CDC) are conditions that typically develop in patients after a coma and are characterized by wakefulness with a complete or almost complete absence of signs of purposeful behavior. This lack of purposeful behavior indicates a lack of awareness of one's own personality or the surrounding reality, and the disorder of consciousness must have persisted for at least 28 days. CDC includes two main categories: vegetative state or unresponsive wakefulness syndrome (VS/UWS) and minimally conscious state (MCS). It is important to note that with proper care and prevention of complications, patients with CDC can live for a long time at home or in palliative care centers, but they will be completely dependent on others. Additionally, most patients with CDC experience varying degrees of polyneuropathy and myopathy (known as myopathy of critical illness), which can impact their functional recovery. In this article, we present the skeletal muscle biopsy specimens of a patient who had been in a VS/UWS for 13 years. The patient, who was 45 years old at the time, suffered a hemorrhagic stroke in 2010, resulting in an intracerebral hematoma. Since then, the patient has remained in a vegetative state/areactive wakefulness syndrome and has been hospitalized in our center once a year for routine examinations and assessments of their level of consciousness.

Keywords: myopathy; skeletal muscles; chronic disturbance of consciousness; unresponsive wakefulness syndrome; clinical case

Abbreviations

CDC: Chronic Disorders of Consciousness; **VS:** Vegetative State; **PVS:** Persistent Vegetative State; **UWS:** Unresponsive Wakefulness Syndrome; **MCS:** Minimally Conscious State; **EEG:** Electroencephalography; **IHC:** Immunohistochemical

Introduction

Polyneuropathy and myopathy (myopathy of critical illness) are common complications in patients with severe brain damage and chronic disorders of consciousness (CDC). During the acute phase of brain damage, when the patient is in the intensive care unit, the diagnosis of polyneuromyopathy is based on clinical examination criteria and neurophysiological data. According to various studies, more than 50% of patients experience acquired nerve and muscle damage during their stay in the intensive care unit, which can last from several hours to several days [1-2].

The term "persistent vegetative state" (PVS) was first introduced by Jennett and Plum in 1972 [3]. However, since some patients may exhibit clinical signs of non-responsiveness (such as no reaction to commands) while still being awake (i.e. opening their eyes), Laureys S. et al proposed a more neutral and descriptive term, unresponsive wakefulness syndrome (UWS) [4]. In 2002, the Aspen Neurobehavioral Conference Working Group introduced a new clinical term, "minimally conscious state" (MCS), to describe patients who have recovered from a vegetative state. This means

that these patients exhibit more than just reflexive motor behavior, but they are still unable to demonstrate functional communication or use objects [5]. When studying the effectiveness of treatments for patients with impaired consciousness, it is important to clearly differentiate between UWS and MCS and to use treatment methods appropriate for each type of impairment [6].

Currently, there is a separate scientific focus on studying skeletal muscle changes in patients with CDC. In this case, muscle weakness is not a result of true critical illness polyneuromyopathy, but rather a possible subsequent state in the progression of the disease. Structural changes in skeletal muscles are an integral part of these syndromes [7].

Material and methods

The patient is a 59-year-old individual who has been experiencing chronic cerebrovascular accident for 13 years. According to the medical history, on September 8, 2010, the patient suffered a hemorrhagic stroke in the right hemisphere of the brain due to high blood pressure. This resulted in the formation of an intracerebral hematoma in the deep sections of the right hemisphere. On the first day after the hemorrhage, the patient underwent decompression trepanation in the right frontal-parietal-temporal region, during which the intracerebral hematoma was removed. However, this procedure did not have a significant effect on the patient's level of consciousness. From December 2010 to March 2011, the patient was admitted to the intensive care unit of the Polenov Neurosurgical Institute - Branch of Almazov National Medical Research Centre. During this time, botulinum toxin type A (Xeomin 200 U) was injected into the adductor muscles, but it did not have a clear effect due to muscle degeneration and contracture formation. The patient was hospitalized multiple times at the Polenov Neurosurgical Institute and other hospitals in St. Petersburg, where he received complex conservative therapy, transcranial micropolarization, and transtympanic chemical vestibular dereception. According to the discharge summary, the patient experienced episodes of consciousness activation (followed simple commands) during these hospitalizations. The patient also underwent several cerebrospinal fluid shunting interventions. In 2019, a session of electropulse therapy with the ESTER device was performed at the Polenov Neurosurgical Institute under EEG control. The patient has been at home for an extended period and his condition has remained stable. According to his wife, he occasionally pulls his left leg away when experiencing pain or tickling, and he also periodically turns his gaze towards her.

During his most recent hospitalization at the Polenov Neurosurgical Institute, his level of consciousness was assessed as HC/SAB, using the Coma Recovery Scale (CRS), which yielded a score of 5 points (1-1-1-0-0-2). The patient also exhibited tetraparesis, with decreased deep reflexes and skeletal muscle atrophy (see Figure 1).

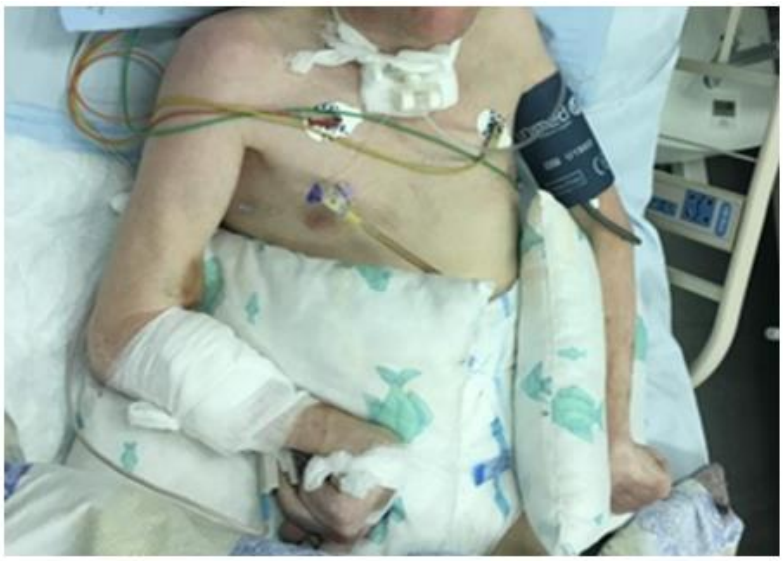


Figure 1: Patient's appearance in the VS/ UWS for 13 years, 59-year-old (Intensive Care Unit).

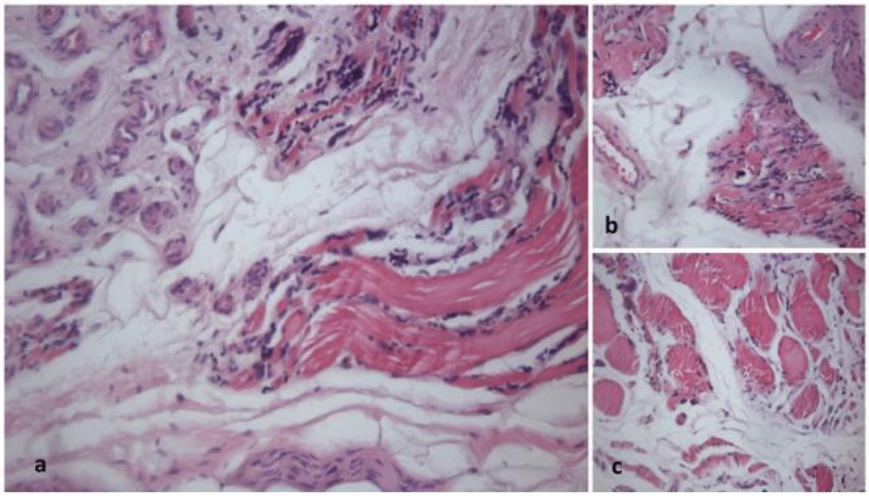
During the patient's current hospital stay, samples of the deltoid and soleus muscles were collected from both sides using aseptic techniques and local anesthesia. As a precaution, the patient was given standard antibacterial medication (cephalosporin) during the procedure. The biopsy specimens were fixed in a buffered 10% neutral formalin solution, embedded in alcohol, and then embedded in paraffin for histological examination. Thin sections (3-5 μm) were obtained using a rotary microtome. The sections were then stained with hematoxylin and eosin, as well as picric acid and fuchsin using the Van Gieson method to study the connective tissue structure. Additionally, silver impregnation was performed using the Foote method to analyze the level of vascularization.

Immunohistochemical (IHC) reactions were performed on paraffin sections according to the standard protocol, with antigen retrieval in a water bath. Primary antibodies to dystrophin (ab85302; 1:150), myosin (Fast, Mob207; 1:150), desmin (Mob060; 1:50), and anti-CD-31 (Dako IR 610) were used. The DBS imaging system was utilized for analysis.

The study was approved by the local Ethics Committee of the Almazov National Medical Research Center of the Ministry of Health of the Russian Federation (No. 1411-20, extract from the minutes of the meeting No. 11-20 dated November 16, 2020) and complies with the Helsinki Declaration adopted in 1964 and its amendments. Informed consent for the study was obtained from the patient's relative, who acted as their guardian.

Results

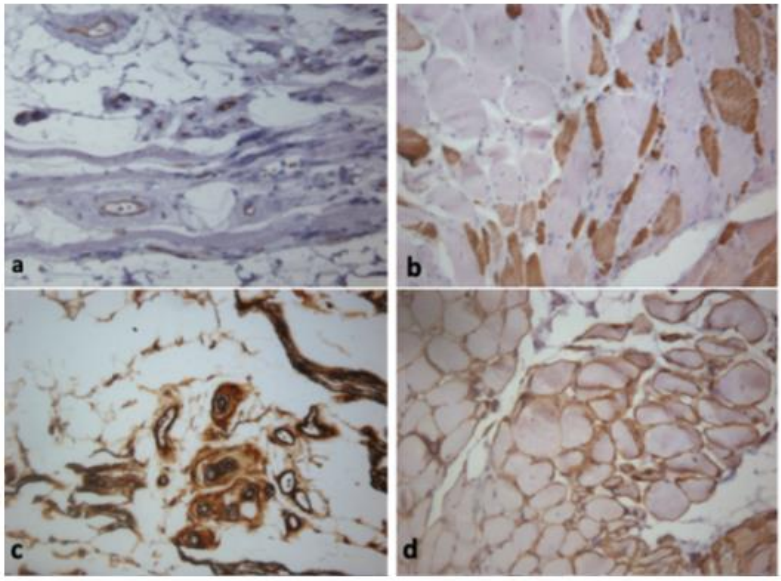
Histological examination of upper limb muscle biopsies showed moderate atrophy of muscle fibers, their thinning and foci with diffuse sclerosis (Figure 2). Transverse striation is predominantly preserved. Perinuclear lipofuscinosis was detected. Inflammatory cells were not detected. The predominance of preservation of the upper limb muscles over the lower limb muscles, as well as a high degree of vascularization in the deltoid muscles of the patient under study, were noteworthy.



a – pronounced fatty degeneration with local preserved areas of atrophic muscle fibers in m. soleus; **b** – pronounced fatty degeneration with local preserved areas of atrophic muscle fibers in m. deltoideus, **c** – degree of preservation of individual muscle fibers in m. deltoideus.

Figure 2: Results of histological examination of muscle biopsy. H&E stain, ×200.

Histochemical and immunohistochemical studies using desmin antibodies revealed areas of staining loss, uneven staining, and individual fibers with no staining. Cytoplasmic staining for myosin protein indicated the presence of transitional hybrid fibers, as well as clearly defined fast and slow fibers (Figure 3b). Furthermore, a decrease and increase in the size of muscle fibers, which is typical in patients with CDC, was observed. In all examined samples, a disruption of the structural integrity of the dystrophin layer of muscle fibers was found, including ruptures and thinning. The areas of staining loss in the upper and lower extremities reached up to 50% (Figure 3d). Fatty replacement of muscle tissue was also detected, with large collecting vessels remaining intact (Figure 3a). Smaller vessels were either single or located close to each other (Figure 3c).



a – preservation of large vessels among atrophied muscle fibers was observed through the use of IHC with antibodies to CD31, **b** – the individual muscle fibers showed varying sizes and an increased number of fast fibers, which were identified through IHC with antibodies to fast fiber myosin, **c** – in the area of fatty degeneration and loss of skeletal muscles, closely spaced vessels were found through Foot's silver impregnation, **d** – the muscle fiber membrane showed varying degrees of dystrophin expression, with focal loss in some individual fibers, as seen through IHC with antibodies to dystrophin.

Figure 3: Results of histochemical and immunohistochemical study of muscle biopsy, ×200.

Discussion and Conclusions

Structural changes in the skeletal muscles of a patient with a long-term CDC disorder have been found to have a non-specific degenerative-atrophic nature [7]. The severity of these changes appears to be more pronounced in the soleus muscle, possibly due to the body's biological needs. Muscle collapse has been observed, indicating a loss of cytoplasmic content caused by the destruction of the sarcolemma. It is believed that this atrophic mechanism is a result of autophagy processes [8]. Additionally, fatty degeneration of the muscles in both the upper and lower extremities was detected. Upon visual examination of the histological preparations, a notable difference was observed in this patient, with a greater preservation of the muscles in the upper extremities compared to those in the lower extremities. Furthermore,

a high degree of vascularization was noted in the deltoid muscles of the patient.

Conflict of interest. The author declares no conflict of interest.

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