

Case report

# Neuromuscular rehabilitation interventions and COVID-19 management in a case of incomplete paraplegia with neurogenic bladder, post T3-T5 ependymoma

Mihai Băilă<sup>1,2</sup>, Aura Spînu<sup>1,2</sup>, Cristina Popescu<sup>1</sup>, Costică Zamfir<sup>1</sup>, Elena Constantin<sup>1</sup>, Elena Brumă<sup>1</sup>, Cristian Raducanu<sup>1</sup>, Ștefan Petre<sup>1</sup>, Gelu Onose<sup>1,2</sup>

<sup>1</sup> The Teaching Emergency Hospital "Bagdasar-Arseni" (TEHBA), Bucharest, Romania

<sup>2</sup> The University of Medicine and Pharmacy "Carol Davila" (UMPCD), Bucharest, Romania

Correspondence: Mihai Băilă, [mihai.baila@rez.umfcd.ro](mailto:mihai.baila@rez.umfcd.ro)

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**ABSTRACT: INTRODUCTION:** Spinal ependymomas are a group of mostly slow-growing tumors that can cause non-traumatic spinal cord injury with insidious clinical symptomatology ranging from neck or back pain to associated sensory-motor impairment. Due to their neurological and systemic frailty, patients with spinal cord injury might be especially vulnerable to the effects of SARS-CoV-2 infection and the resulting respiratory impairment. **CASE PRESENTATION:** We present the case of a 66 year old women admitted in our Neuromuscular Rehabilitation Clinic Division for severe incomplete paraplegia and neurogenic bladder. She was previously diagnosed in the Neurosurgical Ward with a thoracic grade II (classic) ependymoma and underwent a gross tumor resection. During the neurorehabilitation program the patient was diagnosed with COVID-19. The multi-drug related treatments were associated with supportive oxygen therapy and neuromuscular and respiratory rehabilitation techniques. **RESULTS:** Despite of the patient's favorable rehabilitation, consisting of walking abilities with support in a walking frame on short distances, her prognosis may be worsened by resting neurogenic bladder symptoms. COVID-19 has led to important acute respiratory morbidity in our patient, regardless of the mild course of the disease, and might further cause a post-infectious respiratory impairment. **ONCLUSION:** Spinal cord injury remains a life-long condition and emphasizes the necessity of supporting the affected patients on the long run.

**Keywords:** *students, balance, postural stability, physical exercise, progress, motor skills*

## 1. INTRODUCTION

Spinal cord injury (SCI) is a neurological/neurosurgical condition that often generates long-term, functional impairments, systemic comorbidities and psycho-social challenges which can persist over a lifetime. Ependymomas are a heterogeneous group of rare central nervous system (CNS) tumors, (1.8% of all primary CNS tumors) (1), classically believed to develop from ependymal cells, while recent molecular evidences point out to radial glial cells, a type of neural stem cells, as the primary site of growth/transformation (2). Positive prognostic factors for ependymomas are spinal location and older age (3). Spinal ependymomas reach the highest incidence after the fourth decade of life (4) and are the most common intramedullary tumors in adults (5). In most cases such tumors have a benign character and a good evolution. Usually the patients may develop insidious symptoms caused by the slow (6) and constant compression of close neural structures. Patients may present in a Neurological or Neurosurgical Unit with lasting neck or back pain and newly expressed or worsened sensory-motor impairment and sphincter or sexual

dysfunction, depending on the lesion's location (7). Long-standing non-traumatic SCI causes secondary complications such as diminished pulmonary function, respiratory infections, cardiovascular disease and immunosuppression (8). Respiratory complaints are often related to high spinal cord injury, especially with long-standing neurological deficits, and are an important morbidity (9) and mortality cause (10). COVID-19 is a novel viral infectious condition which is transmitted by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). SARS-CoV-2 primarily affects tissues that express high levels of angiotensin converting enzyme 2 receptors, such as lungs, heart, vascular endothelium, gastrointestinal tract (11). It was hypothesized that COVID-19 would begin as a simple viral infection in the upper respiratory tract or the gut and could develop towards a local and systemic immune and vascular disease (12,13). It has also been hypothesized that the SCI population would be severely affected by COVID-19 and additionally difficult to diagnose too, due to symptoms and signs which at least are partially overlapping with each other: reduced respiratory symptoms, impaired cough and diminished fever reactivity (14).

### CASE PRESENTATION

Reason for admission and evaluation. A 66 year old women with medical history of obesity, arterial hypertension was admitted in our hospital, in February 2021, for progressive upper and lower back pain with anterior irradiation towards the rib cage, decreased muscle strength and numbness in the lower limbs. She initially had difficulties in climbing/descending stairs and ultimately was unable to walk. Following admission in the Neurosurgical Unit the patient was diagnosed with AIS/Frankel D paraplegia with T2 neurological level. The magnetic resonance imaging (MRI) study with gadolinium-contrast enhancement revealed an expansive intramedullary lesion extending from T3 to T5 with homogeneous enhancement and hypo-intensity on T1-weighted and T2-weighted images. The lesion associated syringomyelia. The neurosurgical treatment was T2-T6 laminectomy and gross surgical excision of the tumor mass. The histological report confirmed the diagnosis of grade II (classic) spinal ependymoma.

The patient attended two successive rehabilitation admissions which lasted one month each. The AIS / (Frankel) scale (15) was used for the assessment of the spinal cord injury consequent neurofunctional impairment, according to the International Standards for Neurological Classification of SCI (16). Spinal Cord Independence Measure (SCIM) (17) and Functional Ambulation Categories (FAC) International Scale (18) were used in order to evaluate the patient's ambulation and motor functionality. The modified Ashworth scale (19) was used to describe the muscle tone status. The Quality of Life (QoL) was measured using a scale after Flanagan (20). In our Unit the patient presented with AIS/Frankel C paraplegia with T2 neurological level. She had hypoesthesia and neuropathic pain below the level of lesion. The patient needed an indwelling catheter for bladder voiding due to neurogenic bladder. Spasticity was discrete in the lower limbs (Ashworth 1/4). She had no muscle spasms. She could sit independently, but was not able to transfer into sitting position unaided. She was unable to maintain the upright position and could not walk.

Treatment plan and evolution. Treatment goals included the prevention of secondary complications caused by immobilization, the progressive mobilization in up-right position and initiation of walking, the management of neurogenic bladder and the overall improvement of quality of the patient's life. The pharmacological treatment included low molecular weight heparin, analgesics, non-steroidal anti-inflammatory drugs, gastric protector, urinary antiseptics, antihypertensive and anxiolytic drugs. The physiotherapy program included trunk and lower-extremity muscle strengthening, standing and balance exercises and walking re-training with assistive devices.

During the first admission the patient had a positive evolution. She could transfer from sitting to standing position with help from the physical therapist, maintained the orthostatic position for several minutes and exercised walking. Neurogenic bladder was approached initially through indwelling catheter and progressed through an intermittent

catheterization program. Spasticity remained unchanged. Following the second admission in our Unit the patient suddenly developed fever, chills, nasal congestion and dry cough. The laboratory tests for differential diagnosis included urine and blood cultures and a RT-PCR test for SARS-COV-2.

Table 1. Evaluation scores at admission and discharge.

Evaluation scale	Admission	Discharge
AIS / (Frankel) scale	C	D
AIS motor score	68/100	85/100
Spinal Cord Independence Measure (SCIM)	18/100	31/100
Functional Ambulation Categories (FAC)	1/5	2/5
Ashworth scale	1/4	1/4
Quality of Life after Flanagan (QoL).	105/112	109/112

#### COVID-19 episode

The patient was tested positive for SARS-COV-2 and had a positive urine culture for *Pseudomonas aeruginosa*. She was isolated and received together with the aforementioned pharmacologic treatment, a multidrug therapy including antiviral (remdesivir), corticosteroids (dexamethasone), antibiotic (for urinary tract infection) and respiratory support: low flow oxygen therapy in order to reach peripheral oxygen saturation (SpO<sub>2</sub>)=92-96%. The patient's symptoms and vital parameters were frequently monitored. The patient continued to benefit from physical therapy. Exercises included passive, active-passive, and active in-bed exercises combined with assisted transfers in sitting and standing position at the bedside if the patient could tolerate them. Respiratory rehabilitation techniques included diaphragmatic respiration with emphasis on expiration and cough assistance. During this period the patient also developed gastrointestinal symptoms including diarrhea. The clinical evolution was constantly stable and characterized by no cardiovascular or respiratory acute complications. Despite this favorable evolution the patient lost the previously obtained progress and reported ongoing fatigue and marked exertion when exercising. A chest CT was done 9 days after the initial diagnosis and showed a moderate lung illness (Figure 1).

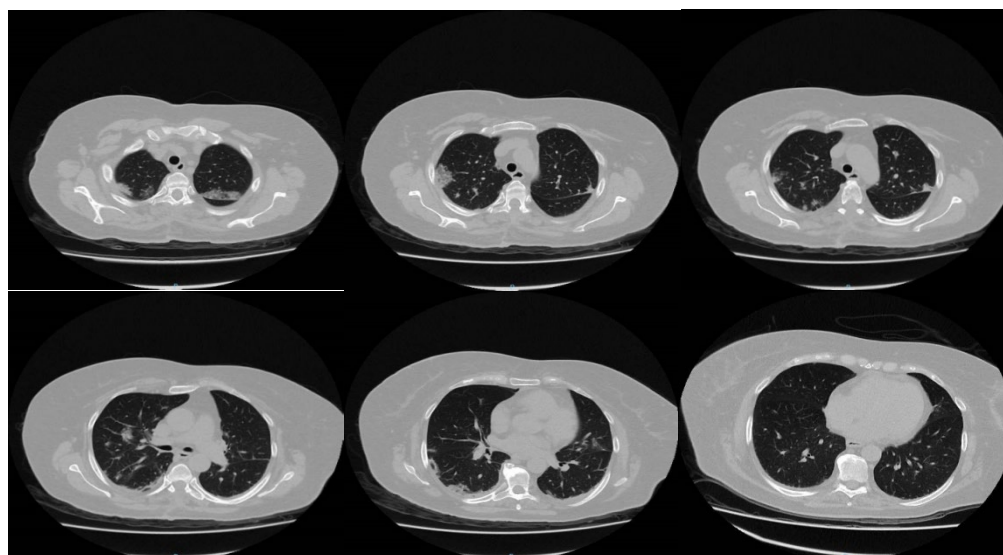


Figure 1. Chest CT performed 9 days after COVID-19 diagnosis reveals multilobar consolidations with positive air bronchograms, localized in the subpleural and central regions in both lungs, more frequently in the upper and lower pulmonary lobes.

Post-COVID-19 evolution. After having a negative RT-PCR test the patient re-attended the normal rehabilitation program, benefiting from exercises in the physiotherapy rehabilitation gym. The patient transfers and standing tolerance improved. She could maintain sitting and standing position for longer periods of time. She could endure walk on very

short distances (20 m) with support in wheeled frame and assistance from the physical therapist. The overall evaluation scores assessed at admission improved at discharge (Table 1). The intermittent catheterization program was interrupted in agreement with the patient's wish, due to her inability to perform it independently and an insufficient social support for this intervention. An indwelling catheter was mounted. The outcome of the control chest CT examination performed at discharge is represented in (Figure 2). Blood tests are shown in Table 2.

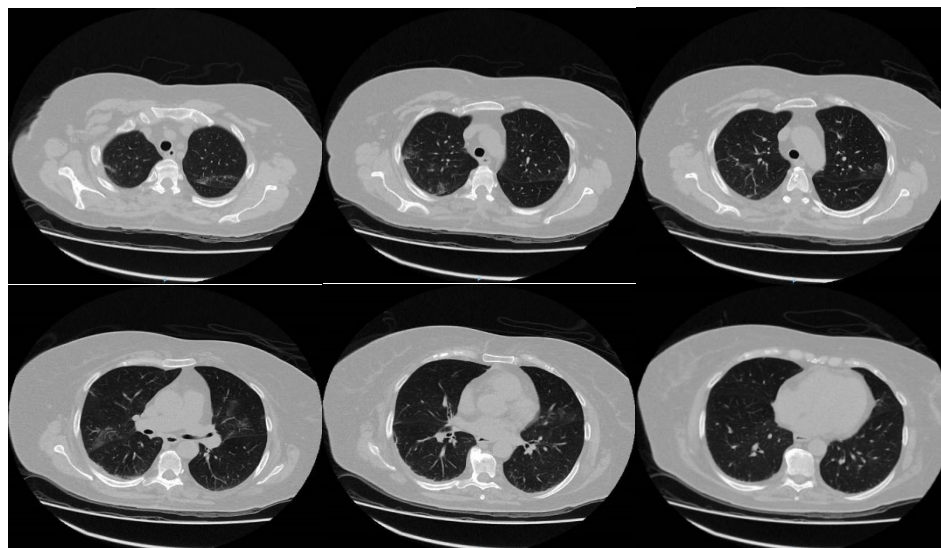


Figure 2. Chest CT performed at discharge (28 days after COVID-19 diagnosis) showing a gradual resolution of the multilobar pneumonia with remaining abnormalities (multiple ground glass opacities with predominant peripheral distribution, associating interlobular septal thickening and fine fibrotic bands).

Table 2. Biochemical parameters during a 28-day period from COVID-19 onset to discharge. Mild alterations included leucopenia, monocytosis, anemia, elevated erythrocyte sedimentation rates, single-time elevated ALT liver enzyme. WBC - white blood cells, PLT – platelet count, RBC – red blood cells, ESR - erythrocyte sedimentation rate.

	Positive SARS-COV-2 RT-PCR result (0 days)	Negative SARS-COV-2 RT-PCR result (+ 14 days)	Discharge (+28 days)	Measurement Unit	Reference range
<b>WBC</b>	3.1	5.8	3.6	* 103/uL	[4.8 - 10.8]
<b>RBC</b>	3.62	3.43	3.61	* 106/uL	[4.2 - 5.4]
<b>PLT</b>	191	272	180	* 103/dL	[130 - 400]
<b>Lymphocytes</b>	26.1	41.1	40.7	%	[20.5 - 45.5]
<b>Neutrophils</b>	61.2	45.3	40.6	%	[43 - 65]
<b>Monocytes</b>	12.1	12.4	11.9	%	[5.5 - 11.7]
<b>Eosinophils</b>	0.4	0.9	6.3	%	[0.9 - 2.9]
<b>Basophils</b>	0.2	0.3	0.5	%	[0 - 1]
<b>ESR</b>	13	20	10	mm/h	[3 - 11]
<b>Hemoglobin</b>	11.5	10.8	11.4	g/dL	[12 - 16]
<b>PT</b>	14.1	16	15	s	[11.8 - 15.1]
<b>APPT</b>	28.8	27.4	27.1	s	[24.3 - 35]
<b>INR</b>	1.03	1.2	1.1	-	[0.85 - 1.15]
<b>Fibrinogen</b>	492	352	416	mg/dL	[169-515]
<b>Glycemia</b>	93	72	80	mg/dL	[70-99]
<b>Amylase</b>	44	60	32	U/L	[25 - 125]
<b>LDH</b>	-	161	161	U/L	[125-220]
<b>ALT/GPT</b>	65	31	-	U/L	[0-55]
<b>AST/GOT</b>	33	15	22	U/L	[5-34]
<b>Serum Albumin</b>	3.6	3.3	3.0	g/dL	[3.5-5.2]
<b>Cholesterol</b>	202	179	208	mg/dL	[0-199]
<b>Creatinine</b>	0.61	0.69	0.65	g/dL	[0.57-1.11]
<b>Urea</b>	20	-	7	mg/dL	[19-43]

## DISCUSSION

The patient's pre-operative neurologic and functional status are important for optimal postoperative outcomes in the case of spinal ependymomas (1). The tumor location has been shown to contribute to surgical morbidity and weaker results were reported for thoracic ependymomas as compared to other location (5,21). In this case the patient benefited from a gross total resection (GTR) of the tumor mass. GTR has been shown to be the most consistent factor determining the vital prognosis and the progression-free survival (22) and particularly for spinal ependymomas it has a high rate of success. Post-surgical outcomes, such as motor function, gait performance and sphincter control were also shown to differ with the tumor's location. Thoracic and cervical ependymomas have shown poorer recovery results than lower spinal tumors (5,20,23). Although the patient had an operated thoracic ependymoma she progressed during the rehabilitation program from AIS/Frankel C to AIS/Frankel D paraplegia and showed improvements in functionality and activities of daily living (Table 2), with unfortunately remaining neurogenic bladder. A few observational studies that included patients with spinal cord injury and COVID-19 were reported to the present moment (24-28). In a systematic review analyzing the clinical characteristics of SCI patients with COVID-19 fever was the most important symptom (29). Interestingly, an important number of asymptomatic infections (20,69%) was reported too. A better understanding of COVID-19 infection in SCI patients could be updated by designing studies to include mild and asymptomatic illnesses. In our case report the COVID-19 onset symptoms were fever, dry cough and nasal congestion.

The 66 year old, hypertensive patient had a non-severe evolution during the acute phase of this infection. In two other studies similar results were reported (24,25). The enrolled patients had mean ages of 60 years<sup>25</sup> or > 60 years<sup>24</sup> and additional respiratory (tracheostomy (24), cardio-vascular or metabolic comorbidities (high blood pressure, dyslipidemia, obesity). No deaths or Intensive Care Unit admissions were registered. The studies took place in a hospital setting, therefore, following COVID-19 confirmation, the patients were promptly treated, including with supportive respiratory interventions. Yet, two other clinical studies have contradictory results. In a series of cases, Burns et al. (26) report a 2.4 times higher death rate in SCI US Veterans with COVID-19 as compared to non-SCI Veterans with COVID-19. The authors state that these results might be overestimated, due to overlooking the real number of community based COVID-19 cases among veterans with SCI (asymptomatic and mild cases) and also biased towards selecting the more severe cases with older ages and associated comorbidities. Galea et al.<sup>27</sup> also present a high case fatality rate (3 out of 7 patients registered deaths) in a similar population, SCI US Veterans with COVID-19. The death incidents were reported in patients suffering from life-threatening conditions such as multiple organ failure and septic shock. The authors conclude that pre-existing comorbidities are the most reliable predictors for severe COVID-19 in the SCI population and admit that early diagnosis might lead to better outcomes. An interesting aspect discussed is that a long-lasting condition with a spinal cord injury predisposes to secondary complications that would negatively impact COVID-19 evolution. This was not the case of our patient, who had a recently discovered non-traumatic SCI caused by a spinal ependymoma.

The question to be answered remains why no death incidents and non-severe acute complications of patients with SCI, advanced age, as well as comorbidities and COVID-19 were registered in our study as well as in other clinical studies (24, 25)? A prompt diagnosis and complex treatment administered early in the disease's evolution could provide one answer. Such interventions were shown to markedly reduce mortality in elderly with COVID-19 in nursing homes (30). Secondly, a newly emerged hypothesis on COVID-19 pathophysiology might offer additional arguments in that direction. COVID-19 may act as a type III immune mediated hypersensitive disease consisting of three phases that intertwine and overlap: viral replication, cytokine storm, and endothelial injury (12). In the first phase the viruses rapidly replicates and propagates. The aim of the other two phases,

immunological and hemo-vascular, is to efficiently produce a coordinated humoral response against these pathogens. If this fails, emerging micro-vascular damages and thrombosis develop. This then reverberates on the respiratory system and on the entire body through the affected blood vessels. Calvo E et al (31) quantified the proteomic profile of patients with SCI and COVID-19 and compared those to patients with SCI and without COVID-19. They described that individuals with SCI and COVID-19 had significantly lower levels of fibrinogen and other pro-thrombotic proteins than the control group, which would explain a non-severe evolution in this population. According to the authors, patients with SCI already receive prophylactic doses of anticoagulant therapy in order to avoid vascular complications caused by immobilization (usually 0,4 mg/24h) before developing COVID-19 and they receive therefore increased doses (up to 0,6-0,8mg/12h) after the infection is confirmed. The study results include correlations (without statistical significance) between the level of coagulation proteins in the two groups and the doses of anticoagulation therapy (heparin) administered. The different heparin regimes between the two groups, the SCI patients with COVID-19 and without COVID-19, could be an answer for the reduced quantity of coagulation proteins in the infected SCI group and could represent a very important protective factor. The strategy of adjusting anticoagulant therapy to higher doses (if not contraindicated) in SCI patients with COVID-19 was regarded to be a necessity in order to combat life-threatening vascular complications (29). Our patient received prophylactic low molecular weight heparin anticoagulation therapy (0,6 mg/day) until the COVID-19 onset, and afterwards increased doses (0,8-1,4 mg/day) for 12 days. The anticoagulation therapy has been reduced to the previous prophylactic doses after this 12 days period and in the next days the patient has been tested negative for SARS-COV-2. Our results are interestingly completed and contrasted by the results of multi-institutional autopsy cohort from Italy and New York City. In this study, A C. Borczuk et al. report the presence of frequent thrombi and vascular injuries in the pulmonary vessels, and less frequent thrombotic microangiopathy in other extrapulmonary organs. Out of all studied cases, 71% (48/68) received anticoagulant therapy (the authors do not provide additional information to the therapeutic regime) and still had large pulmonary thrombi (22/48) and/or microthrombi of the arterioles and capillaries (42/48) (32). This further underlines the importance of coagulation alterations in COVID-19 (coagulopathy, endotheliopathy, vasculitis) and underlines the need to analyze the death toll according to multiple factors such as: comorbidities, COVID-19 evolution and complications (systemic inflammation secondary to cytokine release, endothelial inflammation, acute respiratory distress syndrome), treatment setting, medication.

The acute respiratory dysfunction was manifested in our patient by hypoxemia, which required oxygen support and respiratory rehabilitation interventions, such as bronchial secretions drainage, respiratory muscle strengthening and improvement of lung capacity. The results of the study of Rodríguez-Cola M, et al. (24) point out to the need of all SCI patients with COVID-19 to benefit from bronchial drainage and hyperinflation techniques, which were initially required only for patients with SCI and tracheostomy. S.D'Andrea, et al. (25) report that low flow oxygen therapy was required by 60% of the patients with COVID-19 and SCI as compared to approximately 30% of the control group (general population with COVID-19). Regardless of a mild course of the disease, COVID-19 may still lead to important respiratory morbidity in patients with SCI. Reduced respiratory volumes and flow rates and the loss of innervation to the abdominal and/or intercostal muscles predispose patients with SCI to a chronic respiratory dysfunction (33). These functional changes are of restrictive type, similar to the COVID-19 pneumonia induced sequelae (34-36).

## CONCLUSION

Spinal ependymomas are regarded as benign tumors, but need to be further considered in terms of tumor grade, localization as well as clinical features at the time of diagnosis which are important therapeutical outcome predictors. Surgical treatment has a high rate



of success but is not completely without risks and complications. Spinal cord injury remains a life-long condition and emphasizes the necessity of supporting these patients on the long run<sup>11</sup>. COVID-19 is a potentially serious respiratory infection, especially for SCI patients who require additional respiratory interventions in the acute phase of the disease. The patient had a favorable neurological evolution, consisting of walking abilities with support in a walking frame on short distances. In addition to the persisting dysfunctional neurogenic bladder, post-COVID-19 residual respiratory impairments could develop due to parenchyma fibrosis and remodeling. These negative effects may worsen the patient's prognosis. The non-severe evolution during the acute phase of COVID-19 in our patient could be related to the prompt diagnosis followed by a multi-drug treatment, including higher doses of anticoagulation therapy (without contraindication), and additional respiratory interventions, consisting of oxygen support and rehabilitation techniques performed by physical therapists. More complex and large studies, with SCI patients and control groups, in patients having COVID-19, could provide more results that would lead to stronger based generalization.

**CONFLICT OF INTERESTS** The authors declare no conflict of interest.

**ETHICS** This case presentation received the THEBA Ethics Committee approval (Nr 24389/28.06.2021).

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