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Rehabilitation course and functional outcome of acute disseminated encephalomyelitis related to SARS-CoV-2 infection

Jia Min Yen[1], MBBS, MMed, Matthew Rong Jie Tay[1], MBBS, FRCP, Karen Sui Geok Chua[1], MBBS, FRCP

[1]Department of Rehabilitation Medicine, Tan Tock Seng Hospital Rehabilitation Centre, Singapore

Correspondence: Dr Matthew Rong Jie Tay, Rehabilitation Physician, Tan Tock Seng Hospital Rehabilitation Centre, 17 Ang Mo Kio Ave 9, Singapore 569766. Matthew_rj_tay@ttsh.com.sg

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CASE DESCRIPTION

Acute hospitalisation

A 59-year-old Asian male migrant worker was diagnosed with acute disseminated encephalomyelitis (ADEM) 43 days after presentation with severe COVID-19, based on the combination of encephalopathy, generalised motor weakness and multifocal magnetic resonance (MR) imaging findings.[1] His acute neurological presentation had been described in a case series of COVID-19 patients with encephalitis.[2] He received four interval courses of intravenous immunoglobulin on Day 43, 67, 95 and 146 of illness, and his hospitalisation was further complicated by septic shock requiring inotropic support, acute kidney injury requiring haemodialysis, deranged liver function, provoked segmental pulmonary embolism and polyarticular gout flare. He had a history of polyarticular gout for ten years.

The patient was transferred out of intensive care on Day 50 of illness, with minimal neurological recovery and a Glasgow Coma Scale (GCS) score of E4VTM1. There was no consistent visual pursuit, vocalisations or functional communication. His encephalopathy gradually improved over time, and he scored 9/23 on the Coma Recovery Scale-Revised (CRS-R) on Day 70. He was able to follow instructions inconsistently on Day 72 of illness, and his CRS-R score improved to 10/23 on Day 83 of illness. In view of his generalised profound weakness, a nerve conduction study performed on Day 89 of the illness showed axonal sensorimotor polyneuropathy suggestive of critical illness polyneuropathy. Figs. 1 and 2 show the patient's rehabilitation and neurocognitive progress across different care facilities.

Rehabilitation course

The patient was transferred to inpatient rehabilitation facility on Day 186 of illness with a GCS of E4V4M6. A physiatrist-led transdisciplinary rehabilitation programme was commenced with three

hours per day of rehabilitation therapies, 5.5 days per week consisting of physiotherapy, occupational therapy, speech therapy, psychology reviews and fortnightly dietician reviews. Weekly multidisciplinary conferences were conducted for functional goal setting. Functional Independence Measure (FIM) was the primary instrument used to document improvements. The patient continued to make slow but considerable functional gains during his rehabilitative course. His rehabilitation problems are described below.

Cognitive and behavioural impairments

In this patient, global and severe cognitive deficits were noted upon his emergence from a minimally conscious state. On admission to rehabilitation, he showed sustained attention for 10–15 minutes each time, and was disoriented, with slow information processing speed. He was able to follow one-step commands only. Immediate information recall was impaired, and the Abbreviated Mental Test (AMT) score was 1/10. Participation was limited owing to attentional deficits, slow processing speed and impaired short-term memory. To address attention deficits, therapy was conducted in a quiet and visually bland environment to reduce distractions, and coaxing was frequently required to engage the patient in therapy sessions. In view of reduced information processing speed, cognitive demands were reduced through task simplification and increased time for information processing during therapy sessions. Occasional episodes of irritability and agitation, related to fatigue, pain or giddiness experienced during therapy, were de-escalated through time-out-on-the-spot techniques and redirection. The patient was unable to use cognitive remediation strategies such as errorless learning, repetition, visual memory aids or schedule reminders. Additionally, daily reality orientation, flexibility of therapy timings and sleep wake regulation were employed. His AMT improved to 3/10 on Day 258 of illness. Mini-Mental State Examination or Montreal Cognitive Assessment could not be performed throughout the stay due to the patient's limited attention span and fatigue.[3] The rehabilitation staff

maintained a consistent, encouraging and empathetic stance, and the patient's motivation and cooperation improved slowly, aided by regular supportive counselling and mobile digital media tools.

Quadriparesis

Motor examination revealed disproportionate spastic weakness in the patient's lower limbs with a Medical Research Council (MRC) grade 2/5 (left) and 1/5 (right), compared to his upper limbs (MRC scale 3/5), corresponding to the location of his periventricular lesions visualised on MR imaging. This improved from his initial complete quadriparesis during his intensive care unit (ICU) stay.[(2)] In addition, his motor recovery was complicated by the concomitant diagnosis of critical illness polyneuropathy (CIP) and steroid myopathy. Functionally, the patient had dependent in bed mobility with poor sitting balance and required maximum assistance for activities of daily living (ADLs). Physical therapy focused on training his sitting balance, sitting tolerance and verticalisation via a tilt table. Task-specific training for ADLs was carried out by occupational therapists using mirror visual feedback during grooming tasks.

Orthostatic hypotension

During therapy, the patient experienced symptomatic postural hypotension related to severe deconditioning owing to prolonged immobilisation. His blood pressure dropped from 135/92 mmHg in the supine position to 112/87 mmHg on inclination to 50° on tilt table standing. He was scheduled to receive 2–2.5 L of fluids per day, with fluid boluses administered before therapy, and bilateral thigh-length elastic compression stockings with abdominal binders were used to passively increase venous return. On Day 266 of illness, the patient tolerated sitting at the edge of the bed and was mobilised in a tilt-in-space wheelchair for 60 minutes without postural hypotension.

Swallowing and communication

The patient suffered from mild oropharyngeal dysphagia, which was thought to be related to prolonged intubation and tracheostomy. Upon cessation of feeding through the nasogastric tube on Day 142 of illness, he tolerated a blended diet. Video fluoroscopic swallowing study on Day 189 of illness showed no aspiration with regular diet consistency and thin fluids with controlled cup drinking, after which the patient resumed a normal diet. In terms of communication, he had functional communicative ability for both expressive and receptive speech.

Nutritional/metabolic parameters

Eight months into admission, the patient lost 14.4 kg (body mass index [BMI] 21.6 kg/m^2) from a premorbid weight of 84 kg (BMI 26.5 kg/m^2). Nadir albumin level of 24 g/L on Day 108 of illness improved to 30 g/L during rehabilitation. A high caloric diet of 2,000 Kcal per day with 70 g of protein was encouraged, with oral nutritional supplements mandated whenever oral intake was poor. In addition, the nadir anaemia of 6.3 mg/L improved to 10.2 mg/L during rehabilitation. Initial mild immobilisation-related hypercalcemia, at the highest level of 2.78 mmol/L on Day 53 of illness, normalised during rehabilitation.

Decubitus ulceration

Owing to severe immobility and prolonged recumbency, the patient unfortunately developed a 6-cm × 4-cm Grade 3 sacral ulcer on Day 133 of illness. This significantly limited adjunctive mobilisation efforts to a sitting position, such as electromechanical training using automated body weight-supported treadmills (e.g. Lokomat®), which were contraindicated owing to the presence of the decubitus ulcer under the pelvis straps. After strict 2–3 hourly bed-turning, pressure relief mattresses, pressure

offloading during tilt table exercises, and progressive increases in sitting duration over days with meticulous skin dressing and wound checks, wound healing was achieved on Day 258 of illness.

Urinary incontinence

In view of the patient's decubitus ulcer, an indwelling urinary catheter was required for skin hygiene. Upon catheter removal after decubitus healing, he regained spontaneous voiding but remained dependent on diapers owing to his high level of dependency.

Recurrent nosocomial infections

Therapy was hampered by three episodes of catheter-associated urinary tract infections and *Clostridium difficile* diarrhoea, all of which responded to appropriate antibiotics.

Recurrent polyarticular gout flares

Recurrent gout flares of the left hip, both knees and ankles, and the first metatarsal phalangeal joints hindered rehabilitation. Right knee and left hip aspiration performed on Days 46 and 174 of illness, respectively, yielded turbid straw-coloured fluid and confirmatory negatively birefringent crystals. There was no evidence of septic arthritis on cell counts and fluid cultures. The patient was treated with a tapering course of oral prednisolone and uric acid-lowering therapy with febuxostat in view of renal impairment. His serum uric acid levels decreased from a peak of 903 μM/L to 483 μM/L. The affected joints were mobilised gently during gout flares.

Acute and chronic lower body pain

The rehabilitation course of the patient was significantly interrupted by intermittent lower limb and back pain. The exact history, pain reporting and elucidation of the nature of pain were difficult to

delineate owing to the patient's impaired sensory discrimination and severe cognitive deficits. We postulate that the pain was multifactorial, with acute pain flares on a background of chronic pain. Possible sources of acute pain flares included polyarticular gout flares and his decubitus ulcer, which later healed. Chronic pain could have resulted from joint stiffness from prolonged ICU immobilisation, axonal sensorimotor polyneuropathy (CIP), the primary neurological insult (ADEM) and central neuropathic pain, accounted for by widespread lesions visualised within the brain and spinal cord at C1, T9-T11 and conus medullaris, causing dysfunction of spinal-thalamic-cortical pathways.[4,5] Additionally, bilateral adductor spasticity (Grade 2 on the Modified Ashworth Scale[6]) with restricted hip abduction and flexion (passive range of motion of hip abduction was reduced to 20° and left hip flexion to 90°) may have likely contributed.[6] Pain was managed by simple analgesia (acetaminophen, NSAIDS) as well as gabapentin. Physical modalities such as superficial heat or electrical stimulation were contraindicated owing to the presence of insensate skin and cognitive impairment.

The patient's FIM data and that at admission are shown in Table I, reflective of low FIM efficiency, slow progress and high dependency.

Table I. Summary of total and subset Functional Independence Measure (FIM) scores during inpatient rehabilitation course.

FIM domain	Illness		
	Day 186 (26 Oct 2020)	**Day 223 (2 Dec 2020)**	**Day 277 (25 Jan 2021)**
Total FIM	26	29	34
Motor-FIM			
Motor sub-score/91	16	17	19
Self-care	9	10	12
Sphincter control	2	2	2
Locomotion	2	2	2
Transfers	3	3	3
Cognitive-FIM			
Cognitive sub-score/35	10	12	15
Communication	7	7	8
Social cognition	3	5	7

DISCUSSION

This case report illustrates the dilemmas and challenges faced during the rehabilitation of a patient with ADEM in critical COVID-19.

Diagnostic delays

Diagnostic delays have been described during severe COVID-19 encephalopathy.[2,7,8] In the current case, computed tomography imaging of the brain was normal on Day 16, and radiological evidence of brain pathology was only detected on diagnostic MR imaging, which could only be obtained upon safe de-isolation on Day 34.

Rehabilitation in ADEM related to SARS-CoV-2 infection

The complex interplay between multiple medical complications and treatments received for COVID-19 related ADEM resulted in several rehabilitation challenges. Initiating early rehabilitation often needs to take into consideration the medical stability of patients and existing infection control protocols. In particular, decubitus ulcerations secondary to motor weakness, dependency and steroid-induced skin atrophy substantially limited initial rehabilitation efforts and prolonged the length of stay in hospital. Thus, meticulous preventive nursing care and nutrition are vital care components even after the critical phase of severe COVID-19.

Furthermore, this case demonstrates that neurocognitive sequelae of COVID-19 persist beyond acute care. This is in accordance with emerging evidence showing persistent fatigue, anxiety and depression even after acute COVID-19.[9] In overstretched healthcare systems battling with pandemic surges, prolonged inpatient rehabilitation stays may not be feasible. However, remarkable, albeit slow, functional gains were evident at more than eight months after the initial presentation, implying the presence of delayed yet sustained neuroplastic mechanisms in the brain and spinal cord.

Indeterminate prognosis of COVID-19-related ADEM

Case series of post-viral ADEM have reported variable functional outcomes, with paediatric patients having better outcomes compared to adults.[10] Previous reports also highlighted persistent chronic impairments, especially in cognitive domains, and hampered societal participation with consequential vocational cessation.[11]

Specific therapeutics for recovery from COVID-19-related ADEM

Carda et al reported on the role of initial stratification of rehabilitation needs and recommendations for rehabilitation in COVID-19 survivors, which was well illustrated in our case.[3] However, amantadine, which is deemed beneficial for recovery of conscious awareness following traumatic disorders of consciousness, could not be used acutely owing to severe orthostatic hypotension from severe deconditioning.[12,13] An empirical impairment-based approach with close clinical monitoring thus appears appropriate in view of the lack of evidence for specific therapies for disorders of consciousness in ADEM.

COVID-19 rehabilitation care and psychosocial challenges

Currently, recommendations for COVID-19 rehabilitation are still evolving; the general consensus argues against a specific COVID-19 rehabilitation service, which would increase service fragmentation and further stress healthcare systems.[14] Rather, emphasis should be placed on early detailed functional assessment with family engagement to decide on a suitable rehabilitation plan to maximise recovery and improve quality of life.[15] In our patient, the physical engagement of his immediate family who lived in a neighbouring country was not possible owing to prolonged pandemic-related cross-border

restrictions. Videoconferencing and digital communication were essential to facilitate interactions between the patient, family and rehabilitation professionals.

Rehabilitation challenges of COVID-19 survivors may arise owing to the interactions of multiple organ dysfunction. In addition, we found that the combination of chronic pain, cognitive impairment and irritability impeded rehabilitation efforts, emphasising the need to incorporate psychological interventions as part of a holistic rehabilitation approach.

CONCLUSION

In conclusion, this report describes the neuro-medical course and rehabilitation challenges of a patient with severe ADEM after COVID-19. The rehabilitation and medical needs of these patients are highly dynamic and formidable, long after the initial neurological insult. This results in significant long-term morbidity, physical and cognitive disability, and long-term healthcare-related costs, compounding the socioeconomic burden of patients with neurologic and other long-term complications following infection with SARS-CoV-2, including long COVID-19.

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FIGURES

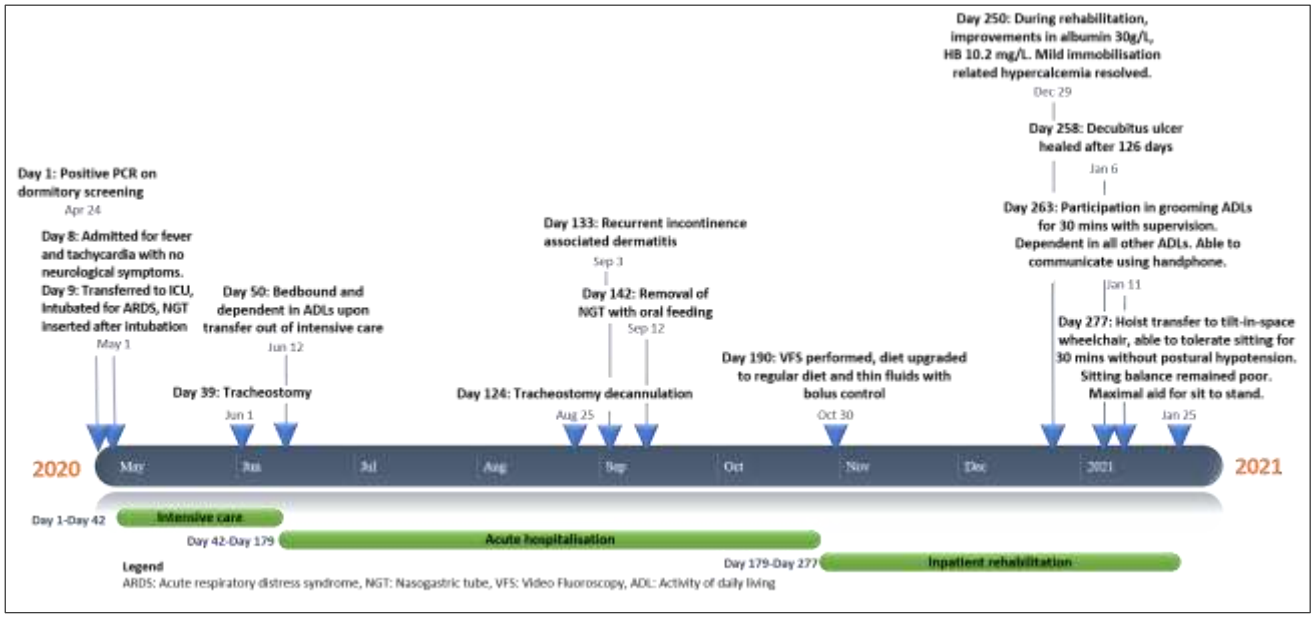

Fig. 1 Diagram shows the medical and functional course throughout the care continuum.

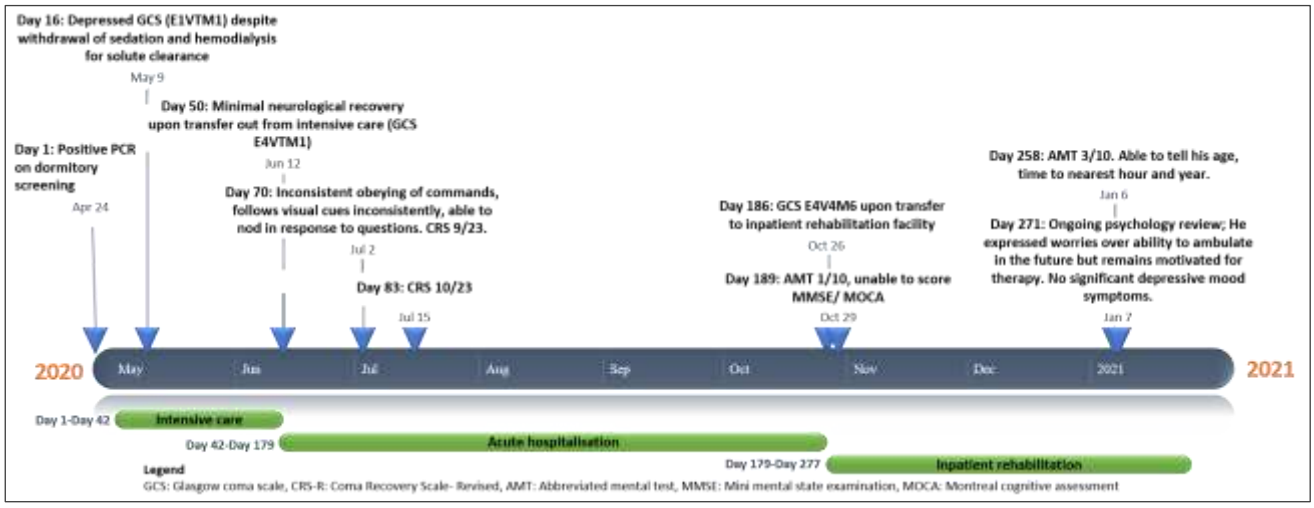

Fig. 2 Diagram shows the neurocognitive course throughout the care continuum.