



Clinical short communication

Abnormal movements in hospitalized COVID-19 patients: A case series

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ABSTRACT

Background: Abnormal movements in Covid-19 patients have been reported with varying degree of frequency, prompting neurologic consultation and additional diagnostic evaluation. We sought to evaluate the frequency and etiology of abnormal movements among hospitalized Covid-19 patients undergoing neurologic consultation.

Methods: We retrospectively analyzed the first 50 consecutive patients with confirmed Covid-19 hospitalized at our tertiary medical care center who underwent acute inpatient neurology consultation from March 2020 through May 2020. Indication for neurologic consultation and diagnostic studies performed were identified by electronic medical record review.

Results: Of the 50 initial consultation requests, 11 (22.0%) patients were evaluated for abnormal movements (nine male and two female). Myoclonus was diagnosed in 6/11 (54.5%) patients. Additionally, two patients were diagnosed with seizures (confirmed on EEG in one), while two additional patients were diagnosed with tremor (physiologic and probable functional). A single case of serotonin syndrome was also identified.

Conclusion: Abnormal movements observed in hospitalized Covid-19 patients can have a wide range of etiologies and were a frequent initial indication for neurologic consultation. Myoclonus was the most frequent type of abnormal movement observed. Early clinical recognition and directed diagnostic work-up is essential for accurate diagnoses in these patients.

1. Introduction

Abnormal movements reported in COVID-19 patients have been attributed to seizure, myoclonus, serotonin syndrome, tremors, and functional movement disorders [1–4]. Limited studies in severe cases of COVID-19 have reported novel types of movement disorders, suggesting a unique neuropathological feature of SARS-CoV-2 [5,6]. Abnormal movements are often broadly recognized as complications of critical illness in the setting of toxic and metabolic triggers, such as hypoxia, electrolyte derangements, and medical sedation [7]. The etiology of these movements varies significantly, and further characterization is challenging in the context of comatose or uncooperative patients undergoing various medical treatments [8]. Neurologic consultation is often sought in this setting to assess for manifestations of the primary disease, or neurologic complications such as seizures or stroke.

The COVID-19 pandemic has vastly impacted health care systems around the world [9]. Limited personal protective equipment, strict infection control guidelines, and overstretched clinical teams have

negatively impacted the bedside assessment of patients. Restriction in bedside assessment raises the risk of failing to detect abnormal movements. Given the limited reports of abnormal movements in hospitalized COVID-19 patients, and increased recognition of neurologic manifestations of COVID-19 [10–12], we sought to examine the frequency and etiology of this finding as an indication of neurologic consultation.

2. Methods

We retrospectively analyzed the first 50 consecutive patients hospitalized for symptoms of COVID-19 at Northwestern Memorial Hospital, Chicago, IL who underwent evaluation by our acute inpatient neurologic consultation services from March 17, 2020 through May 18, 2020. SARS-CoV-2 infection was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) assay by nasopharyngeal swab or bronchoalveolar lavage. All patients underwent bedside evaluation by at least one board-certified neurologist. All laboratory and radiologic assessments were performed as part of standard clinical care. This study

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Demographic, medical comorbidity, laboratory, imaging, and hospital course data were extracted from the electronic medical record. Indication for neurologic consultation and concern for abnormal movements were identified and characterized by review of clinical documentation and diagnoses.

3. Results

A total of eleven patients (22.0%) were identified with having an abnormal movement as the primary indication for acute neurologic service consultation. Nine patients were male and two were female, and ranged in age from 36 to 78 years (Table 1). Common medical comorbidities on admission were obesity (BMI > 30, six patients), hypertension (six patients), diabetes mellitus (three patients), chronic kidney disease (three patients), and coronary artery disease (two patients).

COVID-19 was diagnosed based on positive RT-PCR in each patient, six by nasopharyngeal swab, four by nasopharyngeal swab and bronchoalveolar lavage (BAL), and one by BAL alone. Ten patients presented with respiratory symptoms, five with gastrointestinal symptoms, three with headache, and two with anosmia. One patient presented with altered mental status in the absence of any of the above symptoms. All eleven patients were admitted to the intensive care unit (ICU) within seven days of admission to the hospital meeting criteria for severe COVID-19 [11]. At first neurological consultation, Glasgow Coma Scale (GCS) scores ranged from 3 T to 15, and Richmond Agitation-Sedation Scale (RASS) scores ranged from -5 to 1. All except one patient experienced encephalopathy or agitation during admission. Three patients were discharged home, three were discharged to acute inpatient rehabilitation, two were discharged to a long-term acute care facility, two patients died, and one left against medical advice. The broad range of abnormal movements identified were categorized based on diagnoses, and included myoclonus, seizure, tremor, and serotonin syndrome. Further details regarding patients identified by diagnosis are described below.

3.1. Myoclonus

Six patients were diagnosed with myoclonus (generalized and focal). In three cases, high-intensity sedation was implicated as a potential cause, while three cases were attributed to toxic-metabolic disturbances.

Location and affected regions of the body varied. Myoclonus was noted throughout the torso and extremities in two cases (Supplemental Video 1), while myoclonus was limited to the extremities in another two cases. One case involved myoclonus of the chest and neck and another solely involved myoclonus in the diaphragm. Evaluation consisted of computed tomography (CT) of the brain in five patients, and additional brain magnetic resonance imaging (MRI) in two patients, without evidence of any clear structural abnormality. Four patients underwent EEG evaluation without evidence of seizures or epileptiform discharges.

Treatments administered included benzodiazepines (two patients), levetiracetam (two patients), weaning of sedation and PEEP (one patient) and renal replacement therapy (one patient).

Three patients were eventually discharged home, one patient discharged to long-term acute care hospital (LTACH), while two patients died during hospitalization. Myoclonus had resolved in all four of the living patients at time of discharge.

3.2. Seizure

Two patients' atypical movements were attributed to focal seizures occurring in the setting of encephalopathy (waxing/waning), and both manifested as focal facial twitching. Radiographic studies did not demonstrate any evidence of focal structural abnormality, however one patient demonstrated symmetric dural enhancement, even in setting of

normal CSF studies, which has been reported with COVID-19 [13]. EEG was obtained for one patient, confirming seizure activity.

Treatment consisted of benzodiazepines in both patients, with one patient also receiving levetiracetam and lacosamide. Treatment was effective in aborting seizures in both cases, resulting in sustained resolution.

One patient was ultimately discharged to acute inpatient rehabilitation and the other was discharged to a LTACH.

3.3. Tremor

Two patients were evaluated for a tremors. One patient presented with increased upper extremity tone and bilateral upper extremity tremor and recent falls, and was found to have acute subdural hemorrhage on CT. Management strategies were not directed specifically at resolving the tremor but rather addressing the patient's need for sedation and ventilator support.

The second patient was evaluated for concern for right upper extremity weakness, blurry vision in the right eye, and diffuse tremor shortly after extubation. Brain MRI demonstrated no evidence of ischemic stroke or any other structural abnormality, and the patient improved during the hospital course. Probable functional tremor was diagnosed based on pattern, frequency, and resolution of movements observed.

The first patient was ultimately discharged to acute inpatient rehabilitation with interval improvement in tremor diagnosed as exacerbation of physiologic tremor in setting of critical illness.

The second patient received physical and occupational therapy during the hospitalization and was eventually discharged home.

3.4. Serotonin syndrome

One patient was diagnosed with serotonin syndrome when noted to have abnormal high-amplitude non-rhythmic movements of the lower extremities (Supplemental Video 2) exacerbated by stimulation with accompanying ocular clonus, hypertension and fever after seven days of mechanical ventilation. The patient was receiving high-doses of fentanyl for ventilator synchrony, and the movements resolved after cessation of fentanyl. No additional work-up or treatment was sought by the treatment team based on examination and resolution with fentanyl cessation.

The patient was ultimately discharged to acute inpatient rehabilitation.

4. Discussion

Of the first 50 acute neurologic consultations in hospitalized COVID-19 patients, we present eleven cases (22.0%) in which abnormal movements were the chief neurologic complaint prompting initial consultation. Among patients with complex neurologic manifestations of severe COVID-19, abnormal movements may occur frequently and range in etiology. We identified cases of myoclonus, seizure, tremor, and serotonin syndrome in this series, all of which should be considered in the management of critically ill COVID-19 patients. Appropriate neurologic evaluation and diagnostic studies were essential to implement directed treatments in eight of the eleven patients with abnormal movements.

Bedside consultation is an essential component of the neurologic evaluation, and is critical in recognizing abnormal findings requiring urgent intervention in the absence of extensive diagnostic studies. All patients in this series were admitted to the ICU during their initial hospitalization, reflecting the severity of COVID-19 disease in this series. This presents a challenging environment for clinicians to assess the etiology of abnormal movements with limited patient participation and confounding sedation required for mechanical ventilation [14]. A heightened awareness of abnormal eye movements, or subtle facial tremoring, may be the first steps in recognizing potentially dangerous

Table 1

Clinical characteristics of COVID-19 Patients with Neurologic Consultation for Abnormal Movements.

Case #	Age	Sex	BMI	Comorbidities	COVID-19 Symptoms on Admission	Admit PaO2 (mm Hg)	BUN (mg/dL)	Crea. (mg/dL)	GCS	RASS	CT Brain	MRI Brain	EEG	Diagnosis	Treatment	Disposition at Discharge
1	51	M	30.2	CAD	Respiratory, GI, Headache	74	40	1.0	8 T	1	No acute findings	N/A	Generalized slowing consistent with encephalopathy	Myoclonus	Midazolam	Home
2	77	M	30.7	HTN, CKD, PVD	Respiratory, GI	104	30	1.64	8	−4	Acute Subdural Hemorrhage	N/A	N/A	Probable Physiologic Tremor	None	Acute Inpatient Rehabilitation Home (AMA)
3	68	M	29.9	HTN, CKD	Respiratory, Syncope	94	16	0.8	3 T	−4	Chronic Microvascular Disease	Incomplete sulcal FLAIR suppression, no acute stroke	Generalized R > L slowing consistent with encephalopathy	Myoclonus	Levetiracetam	Home (AMA)
4	41	M	34.7	None	Respiratory, GI, Anosmia, Headache	89	8	0.68	3 T	−5	No acute Findings	Subtle cortical FLAIR signal, no acute stroke	N/A	Myoclonus	Weaning of ventilator	Home
5	54	M	36.9	HTN	Respiratory	60	13	1.25	3 T	−5	No acute findings	N/A	Generalized slowing consistent with encephalopathy	Myoclonus	Levetiracetam	LTACH
6	36	F	55.2	None	Respiratory, GI, Anosmia, Dizziness	93	18	0.61	15	0	N/A	No acute findings	N/A	Functional Tremor	Physical and Occupational therapy	Home
7	68	F	29.9	HTN, DMII, CKD	Encephalopathy	67	69	4.82	7 T	−3	Chronic Microvascular Disease	N/A	Generalized slowing consistent with encephalopathy	Myoclonus	Renal replacement therapy	Deceased
8	42	M	41.4	None	Respiratory, GI, Headache	89	49	2.41	3 T	−4	N/A	N/A	N/A	Myoclonus	None	Deceased
9	66	M	23.8	HTN, DMII	Respiratory	97	17	0.92	14	0	No acute findings	Symmetrical dural enhancement	Seizure	Focal Seizures	Lorazepam, Levetiracetam, Lacosamide	Acute Inpatient Rehabilitation
10	78	M	22.4	Cancer	Respiratory	81	39	1.46	10 T	−1	N/A	N/A	N/A	Serotonin Syndrome	Discontinuation of fentanyl	Acute Inpatient Rehabilitation
11	78	M	24.8	HTN, DMII, CAD, Stroke	Respiratory	129	75	3.5	9 T	0	Diffuse atrophy, no acute findings	N/A	N/A	Focal Seizures	Lorazepam	LTACH

Key: M = Male, F = Female, BMI = Body Mass Index, BUN = Blood Urea Nitrogen, Crea = Creatinine, CAD = Coronary Artery Disease, HTN = Hypertension, CKD = Chronic Kidney Disease, PVD = Peripheral Vascular Disease, DMII = Diabetes Mellitus Type II, GI = Gastrointestinal, GCS = Glasgow Coma Scale, RASS = Richmond Agitation-Sedation Scale, AMA = Against Medical Advice, LTACH = Long-term Acute Care Hospital.

neurologic manifestations. Prompt treatment can prevent further neurologic injury and complications.

Restrictions in place during a pandemic can adversely affect recognition and treatment of these neurologic manifestations. The relatively small cohort evaluated, and lack of comprehensive neurologic diagnostic work-up in each patient, is a limitation of our study. Infection control protocols early in the pandemic limited availability of MRI for critically ill COVID-19 patients. Ischemic stroke, such as small vessel infarcts or embolic events in setting of hypercoagulability, may have contributed to the presentation of myoclonus in a few of our cases that may not have been appreciated on brain CT. A detailed series of critically ill patients with COVID-19, including patients with myoclonus, were found to have small ischemic lesions or abnormal contrast enhancement of the cerebral vessel walls [15]. Additionally, mechanisms of para-infectious myoclonus remain poorly understood, but also appear to be reported in COVID-19 [16,17].

As we gain further experience with the treatment and management of COVID-19, detailed characterization of neurologic symptoms and findings will be essential to understand the neuropathogenesis of SARS-CoV-2 [18]. Emphasis on bedside neurologic examination remains of critical importance in this patient population for recognition of traditional neurologic diagnoses that can readily be treated. Clinicians caring for severe COVID-19 patients should be well-versed in recognizing abnormal movements and seeking appropriate neurologic consultation when indicated.

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