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Neuroleptic Malignant Syndrome Following COVID-19 Vaccination

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We have read the article by Soh et al. reporting two cases of neuroleptic malignant syndrome (NMS) with CoronaVirus 2019 (COVID-19) [1] and we have identified another case by Kajani et al. [2] and the three cases represent NMS with COVID-19, as a part of its neurological complications that was attributed to injury of skeletal muscles and Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) utilizing central nervous system ACE2 receptors. Also, autopsy studies of COVID-19 patients have shown evidence of neuronal degeneration and hyperemic and edematous brain tissue [3].

Since the pandemic started late in 2019 and the hunt for COVID-19 vaccine started and recently many vaccines received emergency use authorization (EUA) including BNT162b2 mRNA COVID-19 Vaccine and in the clinical trial four cases of Bell's palsy were reported [4] as the main neurological complication of this vaccine besides many reported cases of anaphylaxis after waxes [5]

Herein we report the first case of NMS following COVID-19 vaccination which highlights possible complications and alert emergency medicine physicians to uncommon presentations following COVID-19 vaccine.

A 74-year-old female with medical history significant only for dementia and bipolar disorder on maintenance therapy with memantine, Donepezil and quetiapine presented to Emergency Room (ER) after she sustained a fall and facial injury.

Her family members noticed that she had abnormal posture three days prior to admission and was confused so family members increased quetiapine dose and when she remained confused for two more days which ended by a ground level fall and head injury, they brought her to hospital ER, they reported she got COVID-19 vaccine 16 days prior to this event.

In the ER she was vitally stable but febrile at 38.5 C with delirium and on and off agitation, she had bilateral periorbital swelling and ecchymosis, she had generalized muscular rigidity including neck rigidity and hyperreflexia.

In the ER her initial labs were reported (Table 1) and she had negative CT of the brain followed by a spinal tap and COVID-19 RT PCR Swab.

Given negative cerebrospinal fluid analysis and elevated CPK she was diagnosed with NMS and started urgently in ER with intravenous dantrolene and transferred to ICU where amantadine and cyproheptadine were added to IV fluids with subsequent improvement in body temperature and rigidity and within two days she was out of bed to chair and after eight days she was discharged from hospital and followed up in clinic five days later after returning to her baseline mental status and ability to ambulate.

This case presents a grave complication of COVID-19 vaccine requiring ICU admission, there is a possibility that the condition was aggravated by increasing the dose of quetiapine, but family members reported worsening mental status even before increasing the dose. Her inflammatory markers were negative, and her cultures returned with no growth which rules out infection as precipitating factor for NMS.

Our patient here had acellular CSF which made encephalitis less likely and was tested for COVID-19 and her nasopharyngeal RT PCR was negative. COVID-19 is known to have many neurological complications ranging from anosmia to encephalomyelitis, seizures, and stroke [6] Although mRNA vaccines were found generally safe in clinical trials [5] apart from anaphylaxis and the few cases of Bell's palsy but the immune activation associated with such vaccines could have huge impact on the elderly.

Our case should raise awareness to NMS as a potential complication of COVID-19 vaccine and ER physicians should get vaccination history to properly diagnose such problem and any other possible future side effects of this novel vaccine.

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Variable	Reference Range	Admission Results
C- Reactive Protein (mg/liter)	<5.0	4
Procalcitonin (ng/mL)	<0.5	0.06
D-dimer (ng/ml)	<400	890
Sodium (mmol/liter)	136–145	146
Potassium (mmol/liter)	3.5–5.1	3.8
Blood Urea Nitrogen (mg/dl)	9–23	9.3
Creatinine (mg/dl)	0.7–1.3	0.68
Glucose (mg/dl)	80–140	95
Calcium (mg/dl)	8.7–10.4	9.18
Total Proteins (g/dl)	5.7–8.2	6.5
Albumin (g/dl)	3.2–4.8	3.8
AST (U/liter)	10–40	39
ALT (U/liter)	10–49	25
CPK (U/L)	26 – 192	2538
Total Bilirubin (mg/dl)	0.3–1.2	0.89
Alkaline Phosphatase (U/liter)	46–116	63
Lactate Dehydrogenase (U/liter)	120–246	250
White Cell Count (per mm ³)	5300–11,000	5600
Hemoglobin (g/dl)	13.2–17.0	10.1
Hematocrit (%)	39.0–50.0	31,3
Platelets (per mm ³)	150,000–400,000	115, 000
Absolute neutrophil count (per mm ³)	1900–7400	4200
Absolute lymphocyte count (per mm ³)	1100–3900	1100
Erythrocyte sedimentation rate (mm/hr)	1–20	9
CSF cell count (cells/ μ l)	<5	0
CSF total Proteins (mg/100ml)	15-60	50.3
CSF Glucose	50-80	55
CSF Lactic Acid (mmol/L)	<3	1.85
CSF Culture		No growth
Urine Culture		No growth
Blood Culture		No growth

Results of admission laboratory results.

Table 1. Clinical Laboratory Results