

# Neuroleptic Malignant Syndrome due to Atypical Antipsychotics in a COVID-19-positive Pregnant Woman

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Presentation of COVID-19 patients to intensive care unit (ICU) is typically with respiratory deterioration and mechanical ventilation. COVID-19 patients frequently develop agitation and delirium during weaning of ventilation and sedation, which is managed with antipsychotics. We report a case of a pregnant COVID-19-positive woman who developed neuroleptic malignant syndrome (NMS) due to atypical antipsychotic.

A 29-year-old, 21-week-pregnant woman presented to hospital with acute respiratory distress syndrome (ARDS) due to COVID-19 and was intubated and ventilated. She received dexamethasone and prone ventilation along with usual care which rapidly improved oxygenation but extubation was delayed for 3 days as she was agitated and delirious. She was extubated and discharged on the 13th day to ward with atypical antipsychotic: quetiapine. In the ward, the dose of quetiapine was doubled. On the 3rd day in the ward, she developed Glasgow Coma Scale (GCS) of 3 with high fever, rigidity in upper limbs, hypertension, and the right lower lobe pneumonic patch with preserved oxygenation. Her white cell count was  $10 \times 10^9/L$ , and creatinine kinase (CK) was 352 U/L, and creatinine was normal with borderline oliguria. Quetiapine was discontinued on suspicion of NMS. She was reventilated, started on bromocriptine (2.5 mg twice daily) with diazepam (10 mg three times daily) along with analgo-sedation and paralysis. Her temperature of 39.7°C was managed with cold saline gastric lavage, antipyretic, and meningitic doses of meropenem that was discontinued after a normal result of cerebrospinal fluid (CSF) analysis. For persistent fever above 39°C, the dose of bromocriptine was increased to 10 mg 8 hourly. Improving trend of CK and creatinine was noted. On the 3rd day, her temperature was normalized, and neuromuscular blockade was discontinued. Physiotherapy was started and diazepam was stopped. She was extubated on the 4th day. Fetal well-being was constantly monitored and confirmed.

Because of fever, tachycardia, and hypertension, the following differentials were considered and ruled out: serotonin syndrome (no hyperreflexia, diarrhea, clonus, or use of linezolid), meningitis (normal CSF), cerebral sinus thrombosis (presence of pregnancy but no headache, visual impairment, obesity, and previous thrombosis), and posterior reversible encephalopathy syndrome (PRES) (presence of altered mental status, hypertension, pregnancy but no headache, seizure, visual impairment, and vasogenic edema in posterior cerebral hemispheres). NMS was confirmed by Levenson's criteria of three major and two minor factors—the presence of fever, lead pipe rigidity, high CK, and low GCS with hypertension.<sup>1</sup>

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Of the recognized risk factors for NMS, few are common with COVID-19 spectra like dehydration, agitation, and exhaustion.<sup>2</sup> In ventilated COVID-19 patients, the incidence of agitation has been reported to be around 40 to 60% after reduction of sedation,<sup>3</sup> necessitating the use of antipsychotics. Although NMS is rare with quetiapine, it can occur due to inhibition of noradrenaline reuptake, histamine antagonism, and serotonin toxicity.<sup>4</sup> NMS has a reported mortality of around 10%.<sup>2</sup> Management is by discontinuation of culprit drug and supportive care which includes temperature control by pharmacologic and physical means. Of the pharmacologic options, bromocriptine has a better safety profile than dantrolene in pregnancy and was preferred.<sup>5</sup> Adequate hydration and prevention along with supportive care for renal derangement, arrhythmias, rhabdomyolysis, and coagulation abnormalities are essential.

With increasing numbers of COVID-19 patients, common symptoms of prolonged fever, restlessness while weaning the sedation leading to frequent use of antipsychotics, a high index of suspicion for NMS is needed. Early recognition and timely management can improve the outcome significantly.

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