Pediatric Catatonia and COVID-19

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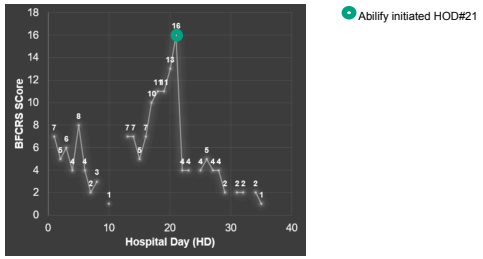
INTRODUCTION

- Catatonia is underdiagnosed in the pediatric population compared to adults, which predisposes them to significant morbidity and mortality [(1)]. There have been an increasing number of reports of catatonia in patients with COVID-19 infection and there are currently no reports elaborating the management of such patients in pediatric age group. The objective of this two-cases series is to discuss clinical courses, treatment and the neurobiological and psychosocial impacts of COVID-19 that may have played a role in the development of their symptoms. Given the widespread shortage of child and adolescent psychiatrists, consultation-liaison (C-L) psychiatrists are often called to evaluate and guide treatments for these pediatric patients[1].

CASE 1

BC is a 16-year-old White female with a past psychiatric history of depression and anxiety, no significant medical history, no vaccination against COVID-19, who presented to the Cooper Emergency Department (ED) on December 24, 2021, with a 3-week history of lethargy and behavioral change in form of pacing, hyperactivity, fearfulness, confusion about who she is, insomnia, and inability to focus. She tested positive for COVID-19 swab PCR, 2-weeks prior to admission. Mother noticed that she could follow simple commands but had "zombie-like" movements, abnormal gait, low mood, staring spells, and reduced speech. Psychiatry C-L team noted her to have a flat affect, blank staring, and mutism with a Bush Francis Catatonia Rating Scale (BFCRS) scores of 7. Vital signs were within normal limits and her labs and imaging studies were unremarkable, including complete blood count, basic metabolic panel, liver function tests, thyroid studies, C-reactive protein, antinuclear antibodies, creatine kinase, urine drug screen (UDS), and brain MRI. The next day on hospital day (HD) 2, the psychiatry team started a lorazepam challenge of 1.5 mg IV which reduced her BFCRS scores to 1 (mild posturing). Throughout her hospital stay of 35-days, she had two episodes of urinary incontinence. On HD 7, fluoxetine 10 mg oral daily was started to address underlying anxiety, but was discontinued after one week at the family's request, due to minimal improvement. On HD 14, methylphenidate was started but was then discontinued after two days due to minimal response. On HD 20, the team noted evidence of near remission with lorazepam 2 mg IV 6 times daily. On HD 21, lorazepam was changed to 3.75 mg IV three times daily, then to 4 mg IV three times daily. Aripiprazole 2 mg daily was also added. Over approximately the next two weeks, lorazepam was gradually transitioned from IV to oral. Aripiprazole was also uptitrated to 4 mg oral daily.
At the time of discharge, the patient showed an improved BFCRS score of 2. She was able to tolerate a normal diet and resume activities of daily living (ADL) including walking and intermittently speaking. She was discharged with outpatient psychiatry follow up and a pharmacologic regimen of lorazepam 4 mg oral three times daily and aripiprazole 4 mg oral daily. She stayed at CUH for 35 days total.

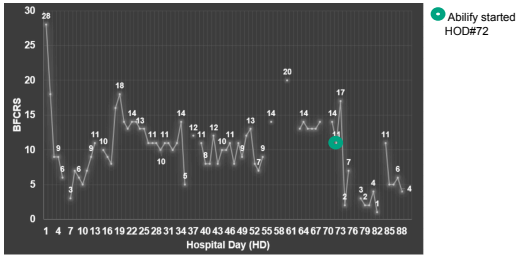
Case 1 Clinical course



CASE 2

Patient ES is a 15-year-old Hispanic female with no past medical history who presented to Cooper ED in March of 2021 with a 6-week history behavioral disturbances and personality change. Symptoms consisted of decline in school performance, poor self-hygiene, and inappropriate laughter. ES had negative work-up of EEG, MRI, and LP but tested positive for COVID-19. On physical exam by Psychiatry C-L team, patient appears altered, and there was concern for underlying psychosis. Risperidone 0.25mg QHS was initiated and her mental status slightly improved. She was discharged on this regimen and was given referrals for inpatient partial programs.
About 6 months later, ES presented to Cooper ED with a 3-day history of similar behavioral disturbances and refusal to eat, speak or move. On physical exam, she was found repeatedly shaking with stiffening of her upper extremities. At this time, her creatine kinase levels were elevated, likely secondary to rhabdomyolysis in the setting of muscle stiffness. She was admitted to the pediatric medical floor at this time with a working diagnosis of catatonia.
During evaluation by Psychiatry C-L team, she was selectively mute and minimally moving. Her BFCRS score was 28 pre-lorazepam challenge. She had a positive lorazepam challenge at this visit, confirming the diagnosis of catatonia. She was placed on lorazepam IV 2mg 3 times daily. increased to 3mg 3 times daily on HD 5, 3 mg 4 times daily on HD 9, 4 mg 4 times daily on HD 12, 5 mg 4 times daily on HD 19, 6 mg 4 times daily on HD 30, 5 mg 4 times daily on HD 35, 4 mg 4 times daily on HD 37, and 4.5 mg 4 times daily on HD 56. Patient was started on Methylphenidate 5 mg twice daily for augmentation of lorazepam on HD 15, increased to 10mg daily on HD 19, but discontinued on HD 23. Amantadine was started on HD 23, but discontinued on HD 27. IV Thorazine was started on HD 27 but was later transitioned to ziprasidone due to adverse effects to the thorazine, including increased balance disturbances, decrease in movements, and urinating involuntarily. Although the ziprasidone was titrated up to 40 mg daily, the patient did not respond to the medication and it was discontinued at this time.
During the hospital course, the patient had poor oral intake and refusal to eat by herself, requiring IV fluids on HD 13, and she was unable to tolerate NG tube placement. A PICC line was placed on HD 26 for total parenteral nutrition (TPN), which she remained on until HD 60, without any complications. She continued to take some nutrition orally throughout her hospitalization, even while on TPN. TPN was discontinued on HD 60 and the patient was able to tolerate food orally without difficulty.
Aripiprazole 4mg daily was added to the regimen on HD 67 resulting in improvement of symptoms significantly, with no further incontinence and improved extremity rigidity. Her IV lorazepam was weaned to 4mg 3 times daily on HD 79, and was gradually tapered to oral lorazepam on 2/1 4mg 3 times daily to prepare for discharge. Her Aripiprazole was increased to 5 mg daily on 2/2. Risperidone 1 mg daily was added to the psychiatry medication regimen on 2/2 as well.
Prior to initiation of aripiprazole, Neuropsychiatry evaluated the patient as a potential electroconvulsive therapy (ECT)candidate. After the patient's significant improvement on her medication regimen with the addition of aripiprazole and risperidone, the psychiatry team determined that the patient no longer required ECT treatment. Although she never returned to her baseline, the only residual catatonic symptoms include intermittent mutism (which may be culturally related due to no-English speaking) and mild muscle rigidity, thus, she was no longer considered a high-risk candidate for inadequate nutritional intake. With the improvement of catatonia, her psychosis became more prominent including increased inappropriate laughter. At this time, the patient was scheduled for discharge on lorazepam 4 mg 3 times daily orally, aripiprazole 5mg daily, and risperdal 1mg daily. This patient was subsequently to be followed closely outpatient with Cooper Psychiatry.

Case 2 Clinical Course



DISCUSSION

The origins of catatonia have been attributed to both medical and psychiatric causes, and within proposed psychiatric etiologies, it has been postulated to be both its own unique condition as well as a syndrome of underlying alternative psychiatric pathology. The symptoms of catatonia as delineated in the DSM or in the Bush-Francis Catatonia Rating Scale are not specific to any particular cause of the state, and can be seen in patients with mood disorders, psychotic disorders, developmental disorders, general medical disorders and dementias with no clear pathophysiology in how it arises[2,3].
The categorization of the causes of catatonia is imperative to its treatment. Patients who become catatonic in the setting of severe major depressive disorder would likely see only partial remission in symptoms if given intravenous lorazepam without any pharmacotherapy for their depression. This becomes particularly challenging in the setting of treating catatonia in the setting of a psychotic illness, as the treatment of the catatonic patient's underlying psychosis with antipsychotics without careful titration may worsen their symptoms of catatonia[1].
In both cases of catatonia explored in this review, the patients experienced a dramatic improvement in symptoms with the introduction of aripiprazole to their medication regimens. The use of typical antipsychotics is typically recommended against due to their higher affinity for dopamine receptors and subsequently higher likelihood of inducing neuroleptic malignant syndrome (NMS) in comparison to the use of atypical antipsychotics[4]. That said, case reports have demonstrated dramatic improvements in symptoms with the use of aripiprazole in the treatment of catatonia[5]. Unlike other atypical antipsychotics, aripiprazole is unique in its mechanism of action as a high-affinity D2-receptor partial agonist. Notably, studies have linked the use of aripiprazole to be associated with neuroprotective effects in various medical conditions. This may be attributable to the role that D2-receptors have in reducing the neuroinflammatory response by microglia in neurologic insults[6,7].
From this, it is postulated that the mechanism of aripiprazole makes it such that it can act as a D2-agonist in hypodopaminergic states and a D2-antagonist in hyperdopaminergic states[5].
The role of aripiprazole in the treatment of the patients in our review was essential to their recovery in spite of the variability in their presentations. This may be attributable to the use of aripiprazole both as an atypical antipsychotic (as seen in Case 2, where the patient had catatonia in the setting of hebephrenic schizophrenia) and an adjuvant medication for depression not adequately treated by antidepressants only (as seen in Case 1, where the patient had a depressive catatonia.)
For all patients seen by a consulting psychiatry service, appropriate communication and psychoeducation is of the utmost importance, and this is especially true in the case of catatonia. With data showing that catatonia is underdiagnosed in pediatric populations in comparison to adult populations, and that patients with adolescent-onset catatonia are predisposed to higher morbidity and mortality rates than their adult counterparts, it is likely that this will need special attention for pediatric primary teams who may not see this condition as often purely based on age demographics[1,8]. This is further complicated by how certain symptoms of catatonia can easily appear similar to those of other neuropsychiatric conditions[2].
Although catatonia may have more dramatic presentations, many patients who experience catatonia have a more subtle clinical picture[9]. Specific to the pediatric population, patients with catatonia are more likely to experience urinary incontinence and behavioral agitation than their adult counterparts, and these symptoms may be confused for other medical concerns or general altered mental status[10].
Given that patients experiencing episodes of agitation in the hospital may be given agitation medications that are more likely to precipitate neuroleptic malignant syndrome in patients with catatonia, ruling out this condition may be essential to their safety and prognosis[10].
Finally, due to linguistic barriers, communicating the nature and treatment of catatonia was challenging for patient families. Allying with the families and consistent use of phone and live interpreters were essential in the treatment of these patients, not only for their acute care in the hospital, but in demystifying psychiatry for the families so they may continue to follow-up outpatient with more ease.

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