New-onset Psychosis and Catatonia as the initial presenting symptom of Autism in an adolescent female with global developmental delay: A Case Report

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We report an adolescent girl with perinatal hypoxic ischemic encephalopathy, left hemiplegic cerebral palsy, global developmental delay with moderate intellectual disability, who presented with acute onset psychosis, echopraxia and posturing, and dysautonomia. As these symptoms resolved with a lorazepam challenge, she was subsequently evaluated by a child psychiatrist in the outpatient setting and diagnosed with autism spectrum disorder (ASD) with associated catatonic disorder.

The case

A 14-year-old female with global developmental delay and moderate intellectual disability since birth presented with an acute mental status change. Family reported uncharacteristic reservedness, visual hallucinations, insomnia, and easy startle response. Upon examination, she demonstrated posturing, echopraxia, and symptoms of dysautonomia, which included drooling, lacrimation, and hypertension. She was treated with a lorazepam challenge and experienced improvement of insomnia within the first twenty-four hours and resolution of behavioral and motor symptoms by the third day of hospitilization, supporting the suspected diagnosis of catatonia. Workup was inconclusive of organic etiologies of catatonia. She was discharged with a 2 week course of oral lorazepam and outpatient follow up with child psychiatry, during which she was diagnosed with autism spectrum disorder (ASD) with associated catatonic disorder.

Conclusion: As suggested in the literature, there is an association between catatonia, ASD, and psychosis. Because these conditions share overlapping symptoms, diagnosis and treatment can be difficult. This case further underscores the diagnostic challenges of catatonia and importance of timely management as catatonia is associated with risks of high mortality.

J.W. is a 14-year-old girl with perinatal hypoxic ischemic encephalopathy, left hemiplegic cerebral palsy, and global developmental delay with moderate intellectual disability, who presented to the hospital due to several days of headache, insomnia, and confusion. Mom reports that the headache started first and that the patient also had tearing of her eyes and pointed at her right jaw persistently. The following day, the patient reported seeing people and things that weren't there. She also would step gingerly, fixate on her hands and at the wall, and startle easily at noises such as the door closing or a cell phone ringing. Her speech appeared acutely more slurred than baseline. Her caretaker also expressed that she was having difficulty sleeping and endorsed poor appetite, constipation for 4 days, and new urinary incontinence. History revealed no current medications or access to medications, recreational drugs, or alcohol. She is fully vaccinated and had no new exposures to sick contacts. She had not been sick nor had recent fever or sick symptoms. No prior episodes. At baseline, JW is a very engaged, energetic young female. She has a 2nd-grade level fund of knowledge and slightly slurred speech that family members can understand. She requires minimal assistance with functional activities of daily living, sleeps well, walks with a mild limp, and has normal and regular urinary and bowel activities. No issues with growth. Family history was negative for neurologic and psychiatric illnesses.

On initial examination, the patient was well-appearing but appeared easily distracted and required prompting. She was able to follow most commands during the interview and was oriented to her name but

not location. The patient had paucity of speech and additionally, her few responses were slowed and slurred compared to her baseline. She had a flat affect but would smile when asked. Her neurological exam was significant for hypertonia in the bilateral lower extremities and left upper extremity and mild weakness in all 4 extremities. Cranial nerves 2-12 were intact and deep tendon reflexes of the upper and lower extremities were normal. She was distracted during the nose-to-finger test. She demonstrated grasp reflex. She would walk gingivally. Her pupils were equal and reactive to light with extraocular motions intact and no eye tearing or conjunctival injection noted. Her ear-nose-throat exam was unremarkable. She had full range of motion of the neck and no temporomandibular joint tenderness. Her thyroid was not palpable. There was no evidence of trauma. Her skin, cardiac, pulmonary and abdominal exams were benign.

In the emergency department, lumbar puncture was performed and cerebral spinal fluid was unremarkable. A meningitis PCR panel (E.coli, H. influenzae, L. monocytogenes, N. meningitidis, S. agalactiae, S. pneumoniae, CMV, Enterovirus, HSV1, HSV2, HSV6, Human parechovirus, VZV, Cryptococcus neoformans/gattii) and culture and CSF encephalopathy panel (AMPA-R Ab CBA, Amphiphysin Ab, AGNA-1, ANNA-1, ANNA-2, ANNA-3, CASPR2 IgG, CRMP-5-IgG, DPPX AB IFA, GABA-B-R AB CBA, GAD65 Ab, GFAP IFA, LGI1 IgG, mGluR1 Ab IFA, NMDA-R Ab CBA, PCA-Tr, PCA-1, PCA-2, IGLON5 IFA, NIF IFA) were negative. Urine drug screen was negative. Complete blood count was significant for mild leukopenia with neutrophilic predominance and mild microcytic anemia. TSH, free T4, TPO and thyroglobulin antibodies, antiphospholipid antibodies, ANA, dsDNA antibodies, ASO, DNAse B antibodies were unremarkable. Urinalysis showed ketones, but otherwise unremarkable. COVID-19 was negative. Neurology was consulted and routine EEG was normal. Given concerns for acute process with progression in symptoms, she was admitted for sedated MRI of the brain, which was non-diagnostic. While inpatient, she was seen by dentistry due to persistent headache and jaw pain and dental X-rays were negative. Due to food pocketing on exam, she was also seen by speech therapy who noted oropharyngeal dysphagia with weak and disorganized oral motor movements and incomplete oral clearance and was thus made NPO. Her exam on hospital day one was also notable for echopraxia, which increased suspicion for catatonia and psychiatry was thus consulted.

Our patient was suspected to be in a catatonic state due to paucity of speech, delayed response, prompting, decreased motor activity, dysautonomias (oropharyngeal dysphagia, drooling, urinary incontinence, constipation, elevated blood pressures), insomnia, and decreased interest in eating. The patient started IV lorazepam 2 mg at night. After three doses, she experienced resolution of mutism, improvement in rigidity and immobility, and return of normal appetite and ability to sleep. Serum and CSF encephalopathy panel, thyroglobulin and anti-thyroid peroxidase antibodies, phospholipid antibody, ANA, ASO, double stranded DNA antibody, deoxyribonuclease antibody and DNAse B antibody were unremarkable. She was discharged with daily oral lorazepam 2 mg for 2 weeks and outpatient psychiatry follow up where she did a taper for 4 weeks.

At her follow-up appointment, her caretaker reported sustained resolution of symptoms after the inpatient lorazepam challenge. Further evaluation revealed a lifelong history of difficulty with social interactions with peers. Based on her recent presentation of psychosis and catatonic state, she was ultimately diagnosed with ASD with catatonia by child psychiatry**.** Due to resolution of symptoms, her oral lorazepam was tapered over several weeks. During a follow-up telephone call four months later, her caretaker reported that the patient was doing well at home without remission of symptoms.

Discussion/Conclusion

Catatonia is a syndrome that is characterized by motor, speech, and behavioral changes and when severe, presents with autonomic dysfunction. The DSM-V defines catatonia as the presence of three or more of the following: Catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, mannerisms,

stereotypies, grimacing, echolalia, and echopraxia (2). Hallucinations are not categorized as a typical manifestation of catatonia. It is postulated that catatonia manifests when there is an imbalance of inhibitory and excitatory neurotransmitters; hypoactivity and hyperactivity of GABA, glutamate, dopamine, serotonin, and cholinergic neurotransmitters on their receptors are hypothesized to be a part of the disease process (5). Of clinical importance, catatonia is a symptom of an underlying medical and/or neuropsychiatric condition. One should consider infectious and autoimmune encephalitis, genetic and metabolic disorders, hypoventilation, thromboembolic events, trauma, intoxication, medication withdrawal, neurodevelopmental disorders, and neuropsychiatric disorders such as ASD.

A detailed history and physical exam can rule out conditions that can also cause acute mental status changes with motor, speech, and autonomic dysfunctions (such as delirium, neuroleptic malignant syndrome, toxic serotonin syndrome, and seizures). The Bush-Francis Catatonia Rating Scale was developed to help facilitate the diagnosis of catatonia. Screening questions include non-purposeful hyperactivity, immobility/stupor, mutism, staring, posturing/catalepsy, grimacing, echopraxia/echolalia, stereotypy (non goal oriented movement), mannerisms, verbigeration, rigidity (maintenance of a rigid position despite efforts to be moved; to be excluded if cog-wheeling or tremor present), negativism (motiveless resistance to instructions/movement), waxy flexibility (initial resistance before allowing themselves to be repositioned), withdrawal (refusal to eat, drink, make eye contact). If two categories are met, there is a high pre-test probility of catatonia and further questions include evaluation for symptoms of severe catatonia, which include impulsivity, automatic obedience, mitgehen (arm raising in response to light pressure of finger, despite instruction to the contrary), gegenhalten (resistance to passive movement), Ambitendency (appearing stuck in indecisive, hesitant movement), grasp reflex, perseveration, combativeness, and autonomic abnormality. Our patient's score was high risk for greater severity of catatonia.

Medical work-up should be guided by the history and exam and often includes blood work with basic hematologic and metabolic measures, comprehensive drug testing, and lumbar puncture to investigate autoimmune and infectious encephalitis. MRI of the brain and EEG may be helpful for ruling out other diagnoses, but there are no diagnostic findings on imaging that are associated with catatonia (5).

When catatonia is suspected, a trial of lorazepam can assist with diagnosis and treat the symptoms. Rapid resolution of symptoms with lorazepam strongly supports a diagnosis of catatonia. Interestingly, regardless of the etiology of catatonia, benzodiazepines appear to be an effective form of treatment. The therapeutic mechanism is thought to be due to benzodiazepine's enhancement of the GABA hypoactivity seen in catatonia (5). There are no established clinical guidelines for dosing but clinicians often start with 1-2 mg of lorazepam every 4-12 hours (5). If there is no response or a suboptimal response to these dosages, the dose is increased by 1 mg every 3-5 days (5). However, in our benzodiazepine-naive patient, immediate relief of catatonic symptoms was achieved with an initial dose of 2 mg/day.

It is important to note that even in the presence of psychotic symptoms, anti-psychotics, particularly first generation antipsychotics with higher D2-receptor blockade, are contraindicated when catatonia is suspected as they have been reported to increase the risk of developing neuroleptic malignant syndrome (NMS) and can lead to lethal catatonia. In a retrospective study, 3 of 82 patients (3.6%) developed NMS after having received antipsychotics during a catatonic state (4). The use of second generation antipsychotics is ambiguous; several studies reported beneficial effects (ie: clozapine, olanzapine, risperidone, quetiapine) which is important given that some patients can present with both delirium and catatonia (3). There is no consensus about treatment regarding these patients as administration of antipsychotics and withholding benzodiazepines can worsen catatonia.

Catatonia in the pediatric population is more common than once believed and it may be the initial presenting symptom of an underlying disorder such as in J.W.'s case. The medical team did not find an organic medical etiology for her catatonia and thus it was postulated that catatonia may have been a presenting symptom of previously undiagnosed ASD. The prevalence of catatonia has been suggested to be approximately 12-18% of adolescents and young adults with ASD (1). Autistic catatonia may present as mild, moderate, or severe and is defined by effect on functional status. The diagnosis of severe autistic catatonia is given when the autonomic system is affected, which can lead to dysregulation of body temperature, heart rate, blood pressure, and metabolism and affect their ability to swallow, breathe, urinate, and defecate. In our patient's case, J.W. had signs of new onset bulbar dysfunction that was concerning for progression to severe catatonia. Individuals with catatonia are at risk for acute decompensation and necessitate hospitalization. Thus, clinicians should remain vigilant and consider catatonia in their differential especially for a patient with neurological insult, developmental delay, and intellectual disabilities who is presenting with acute motor, speech, behavioral and autonomic dysregulation.

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