Key Words: psychosis, narcolepsy, first episode psychosis

First Episode Psychosis in a Teen with Narcolepsy and Cataplexy

By Trishna Sharma, Annette C. Kestner, Abhishek Reddy

ABSTRACT *~ Narcolepsy with cataplexy (NT1) is a sleep disorder very rarely associated with early-onset psychosis. The incidence of this association is unknown but appears to be more common in children and adolescents. This combination of diagnoses presents a diagnostic and therapeutic challenge. This case report discusses an adolescent female with first-episode psychosis who was being treated for NT1 and had no prior psychiatric history. After ruling out other possible medical causes, she was given an initial diagnosis of a brief psychotic episode and treated with Risperidone while continuing treatment for NT1 with Modafinil and Venlafaxine. Following partial response to Risperidone, her psychosis improved with Chlorpromazine, one of the first documented cases of successful use of this medication for first-episode psychosis with NT1.* Psychopharmacology Bulletin. *2025;55(1):80–88.*

Introduction

Narcolepsy is a rare sleep disorder that reflects a selective loss or dysfunction of orexin neurons of the lateral hypothalamus.[3] Low to absent levels of hypocretin is associated with narcolepsy with cataplexy phenotype and the genetic predisposition enlists HLA DQB1*0602 haplotype to be a sensitive marker for NT1.[9,19] Narcolepsy with cataplexy is also known as narcolepsy type 1 (NT1).[2,6] It is characterized by sleep-wake dysregulation, excessive daytime sleepiness, cataplexy, hallucinations, sleep paralysis, and disturbed sleep, along with motor, cognitive, psychiatric, metabolic, and autonomic disturbances.[2,6] Narcolepsy patients typically experience hallucinations when falling asleep (hypnogogic) or shortly after awakening (hypnopompic).[5] Narcolepsy is commonly treated with Modafinil, sodium oxybate, pitolisant, solriamfetol, or methylphenidate.[2] Venlafaxine has good evidence in the treatment of cataplexy symptoms.[2]

Sharma, MD, Child and Adolescent Psychiatry fellow- PGY-5, Department of Psychiatry, Virginia Tech Carilion School of Medicine, Roanoke, VA, United States. Kestner, LMSW, Licensed Master of Social Work and Mental health therapist, Department of Psychiatry, Virginia Tech Carilion School of Medicine, Roanoke, VA, United States. Abhishek Reddy, MD, Assistant Professor, Child and Adolescent Psychiatry, Sleep Medicine, Department of Psychiatry, Virginia Tech Carilion School of Medicine, Roanoke, VA, United States.

To whom correspondence should be addressed: Dr. Abhishek Reddy, MD, Assistant Professor, Child and Adolescent Psychiatry, Sleep Medicine, Department of Psychiatry, Virginia Tech Carilion School of Medicine, Roanoke, VA, United States. Phone: 540-527-4900; E-mail: abhishekreddy@carilionclinic.org.

Psychosis is defined by impairment in reality testing, often including hallucinations.[14] Epidemiological studies indicate that there is a connection between Narcolepsy and true psychosis in early-onset cases.[11] In a Taiwan nationwide study by Yeh et al. 2020,[21] they found that narcolepsy and psychotic disorders were commonly comorbid and not related to pharmacotherapy.[21] The frequency of NT1 and psychosis is unknown, but the body of research indicates that this comorbidity is more commonly found in children and adolescents.[6] Huang et al. 2014 reported that 10% of their NT1 patients developed Schizophrenia in adolescents.[12] The unique co-occurrence of narcolepsy with schizophrenia raises pathophysiological curiosity reported as either a chance finding or coexisting autoimmune diseases.[5] Other explanations could be related to hypocretin 1 which functions as an arousal regulator in the brain's sleep-wake circuity.[10] Hypocretin 1 has also been reported to influence the dopaminergic activity in the midbrain and prefrontal cortex.[7] This association may explain the possibility of a shared pathophysiology between narcolepsy and schizophrenia[7] Additionally, the younger age of NT1 diagnosis has been associated with an elevated risk of psychotic disorder suggesting mechanisms in the neurodevelopmental period to be contributory.[9]

We describe the case of a young woman with NT1 who presented to our hospital due to psychosis with religious persecutory overtones. Furthermore, we discussed how we used a multidisciplinary approach to treat her NT1 and psychiatric symptoms during her hospitalization. This case report adds to the growing literature on early-onset first-episode psychosis episodes in adolescent patients with NT1. We outline the patient's initial presentation, two psychiatric hospitalizations, and gradual improvement.

Case History

A 17-year-old female with a history of NT1 and no past psychiatric history presented to the hospital from the community due to a psychotic episode of unknown etiology. During this event, she was told by "the Lord" to cross the street, which consisted of a four-lane highway, with her eyes closed, and she did this five times before returning to her workplace. She was noted to be praying and talking to herself. Before this event, the patient had received high grades and was employed part-time. There was no reported history of substance use. The patient does not have a family history of psychiatric illness and does not have any concerns with meeting her developmental milestones.

Symptomatology

Her mother reported that Ms. B had been reading the bible for the last ten months, stating that "she was curious and just wanted to learn." Ms. B reported that she went to work after waking up around three that morning, which is unusual for her. She reported waking up due to hearing voices. She reported that it was the voice of "Jesus." She then went to work that day and started hearing more voices of "demons," which caused her to become confused between "voices of demons and holy spirits." Subsequently, she tried to clarify what they were and show her "loyalty" to them. To prove her "loyalty" to the "holy spirits," she walked into traffic with her eyes closed. She denied any visual hallucinations.

On initial presentation at the hospital, she continued to appear internally stimulated, screaming and crying. She was given olanzapine 10 mg intramuscular as she was, agitated, and refused labs for a workup. Her mother was at the bedside, and the patient was religiously preoccupied, saying that the devil was inside her mom and dad. The medication calmed her, and the medical team was able to proceed with an evaluation for altered mental status (AMS).

Diagnosis and Treatment

Labs were sent to rule out other causes of first-episode psychosis and to get a baseline for starting antipsychotic medication. Initial labs included complete blood count, comprehensive metabolic panel, serum folate, serum B12, vitamin D, thyroid stimulating hormone, urine analysis, urine drug screen, lipid profile, and hemoglobin A1c. All her blood tests returned within normal limits except for vitamin D and lipid profile. Her vitamin D was 22 ng/ml, and we started supplementation with 2,000 IU cholecalciferol. Her lipid profile showed elevated low-density lipoprotein and total cholesterol levels. Before admission, she was taking Modafinil 200 mg and Effexor 75 mg for NT1. However, she had recently restarted both medications a month before the presentation following a period of noncompliance for one and a half years due to her perceived financial concerns regarding the medication. Her narcolepsy medications were resumed during admission, but the dose of Modafinil was kept low at 100 mg instead of her outpatient dose of 200 mg due to concerns about psychosis precipitated by stimulants. We also continued the Venlafaxine at 75 mg for cataplexy.

Upon further evaluation, Ms. B was diagnosed with narcolepsy type 1 (NT1) in third grade. The first assessment was done at age seven, prompted by excessive sleepiness at school. Per chart review, she had multiple sleep latency tests (MLST) at age 7. MLST was 90 seconds and Polysomnography showed 4 rapid eye movement (REM) in 4 naps.

She was initially given low-dose methylphenidate, which was too stimulating for her and was later started on Modafinil 100 mg. Seven years later, she noted that if she laughed hard, she could not hold her head up, and her diagnosis was modified to Narcolepsy with cataplexy. Following this, Venlafaxine was added to Modafinil, which helped her with episodes of cataplexy.

During the inpatient stay, we initiated Risperidone 0.5 mg at bedtime; the patient gradually improved and no longer heard voices; she was also not religiously preoccupied. Her thought process was linear, logical, alert, and coherent. After her psychosis stabilized, her PHQ9 was 3 and the SCARED questionnaire showed elevation of anxiety across multiple domains with a total score of 41 (25 and above is clinically significant). After six days of inpatient management, Ms. B was discharged with Risperidone 0.5 mg to be taken at bedtime along with her narcolepsy medications. Her anxiety also improved around the time of discharge. Aftercare services were set up with the local community services board for the patient to begin psychiatry and therapy services following an intake.

After her discharge from her first psychiatric hospitalization, Ms. B was consistently taking her Modafinil, Effexor, and Risperidone as prescribed. She did well for a few days without major behavioral issues or concerns. She was, however, not eating well, and the mother attributed this to poor appetite from the COVID-19 infection she had been diagnosed with at the time of discharge from her first inpatient stay. On the eighth day after discharge, the mother observed that the patient was withdrawn, behaving oddly, not eating, talking about voices, and spending more time in the restroom. It was getting harder to redirect her to home, and she was observed praying excessively at odd places like the restroom. The patient's mother returned with her to the emergency department (ED) for assessment. In the emergency room, Risperidone was increased from 0.5 mg at bedtime to 1 mg Due to combativeness in the ED, she also received Olanzapine 10 mg intramuscular. On the second day in the ED, the Modafinil was held due to concerns that it may be causing psychosis. After partial stabilization in the ED, she was transferred to the inpatient psychiatry unit.

During her second admission, a plan was made to optimize Risperidone while doing further workup with Ms. B. The Risperidone was gradually titrated to 1 mg twice a day over the next five days. She responded partially to this regimen and endorsed breakthrough psychosis in the early morning and late evening. Her Risperidone was titrated to 1 mg three times a day and further work was done by getting magnetic resonance imaging (MRI), electroencephalogram (EEG), serum human immunoglobulin virus antibody (HIV), rapid

plasma reagin(RPR), and antinuclear antibody (ANA). Her MRI and EEG were unremarkable; HIV and RPR were non-reactive, and ANA tested positive for anti-scleroderma antibody (scl-70) antibodies with a titer of 1.4. Neurology suggested rheumatology follow-up if there is strong suspicion and clinical manifestation of connective tissue disease in this context.

The guardian also had concerns about Modafinil causing psychosis, so the dose of Modafinil was held for two days. Holding the medication worsened the patient's psychosis throughout the day. So, the decision was made to resume the initial dose of 200 mg of Modafinil after consulting with the patient's outpatient sleep doctor. Ms. B was more alert and participated in the group activities with a morning dose of 200 mg of Modafinil and 75 mg of Venlafaxine. Her psychosis improved with 1 mg three times per day of risperidone, but she still had breakthrough episodes in the evenings and early mornings. It was hard to redirect her during those episodes, and she would start praying in the unit and mostly skip meals as the voices wanted her to fast.

Neurology was consulted again regarding the possibility of anti-NMDA encephalitis. However, without clinical symptoms and consistent autonomic stability, an invasive procedure reflected risk outweighing benefits. Our investigations pointed us more in the direction of the beginning of a primary psychotic disorder, and we decided to switch from Risperidone to chlorpromazine. Chlorpromazine was introduced at 75 mg at bedtime, replacing Risperidone, and gradually titrated to 50 mg twice a day and 75 mg in the early evening. She was eventually stabilized on 175 mg total of Chlorpromazine. After her psychosis stabilized, her PHQ 9 was 4 and her SCARED questionnaire for anxiety was 26, (25 and above being clinically significant). There were more elevations in the social anxiety sub-group. She continued to hear voices, but her breakthrough psychotic symptoms stopped. She showed gradual improvement, evidenced by being more involved in daytime activities and groups and sleeping well at night. No napping during daytime was noted. She used coping skills she learned during her stay to challenge the voices she was still hearing. She participated in group and individual therapy during her admission. She was discharged with a diagnosis of first-episode psychosis, but early-onset psychosis due to Schizophrenia must still be ruled out. The patient has aftercare services set up in the outpatient setting for psychiatry and therapy.

Discussion

The relationship between Narcolepsy and mental illness has historically been difficult, as Narcolepsy can present with some hallucinations.[1,4,5]

Psychosis has seldom been reported in patients with NT1, but multiple studies, including a systematic review and a national Taiwanese study, show that there are occasions of comorbidity.[5,7,11,21] Here, we present comorbidity of NT1 with first-episode psychosis in an adolescent who responded partially to Risperidone and was switched to Chlorpromazine. This is the first case to our knowledge where Chlorpromazine has been used for managing first-episode psychosis in Narcolepsy with a favorable result. In previously reported cases, either Aripiprazole or Risperidone was mostly the choice of treatment for psychotic presentation in Narcolepsy with variable results.[5]

Chlorpromazine is the first antipsychotic drug, which is also listed as one of the "essential drugs" by the World Health Organization (WHO) in the category of antipsychotics.[17] It is known for its sedation properties, often making it useful for insomnia in Schizophrenia.[18] Our goal was to create a consistent wakeful period and restful sleep period to keep a balance between sleep disorder and psychotic disorder. When reviewing the literature, Chlorpromazine had promising results and showed significant improvement in the longest wake episode and other objective sleep variables in a cohort of patients with Schizophrenia.[18] Since our patient was dealing with a sleep disorder amidst new-onset psychosis and had only demonstrated a partial response to Risperidone, Chlorpromazine was chosen in favor of higher potency and sleep benefits.

While treatment modalities for Narcolepsy can play a role in triggering psychosis, Modafinil has a good safety profile and is the first-line treatment for Narcolepsy.[11] Narcolepsy does present sleep-related multisensory hallucinations; however, as with our patient, these can be differentiated from auditory hallucinations typical of Schizophrenia due to the behavioral alternations and delusional ideas.[16] The patient's worsening psychosis does appear to be independent of the NT1 diagnosis, as evidenced by the results of lab work, CT scan, MRI, and observation with and without medication. Consistent support from the body of research guided us against further hiatus from narcolepsy treatment. The consensus, therefore, is to treat Narcolepsy first when associated with psychosis.

Additionally, her ongoing belief that the hallucinations were the voices of demons, and the lord clarified that these were not her typical sleep-related hallucinations. Interestingly, multimodal hallucination was commonly described in dual cases of Narcolepsy and Schizophrenia. Multimodal hallucinations comprised the absence of formal thought disorder and the loosening of associations with a good grip on reality testing.[15] Our patient, during her first admission, also demonstrated a very linear thought process, a good insight into her illness, and a firm belief that the hallucinations are not real. However, during the

second admission, she would have episodes of disorganized behavior and delusions with religious preoccupations that interfered with her functioning. During initial admission, we listed a tentative diagnosis of brief psychotic disorder where the patient partially responded to Risperidone. The rebound admission helped us formulate a multidisciplinary cohesive management plan with further investigations and workup. During the second admission, the patient met the active phase symptom criteria for Schizophrenia as it had been over 30 days since her psychosis began.

Moreover, the literature supports early-onset cases where psychosis is comorbid with NT1.[9] Longitudinal follow-up of individual cases with a dual diagnosis of Narcolepsy and psychosis have been studied. These follow–ups demonstrated sustained improvement of associated psychosis after adherence to maintenance treatment of Narcolepsy.[15] Limitations to this case report include the inability to do psychological testing. Rorschach was considered, but due to her psychosis was not determined to be helpful at that time. However, validated scales including PHQ9 and SCARED were used on admission and repeated at close to discharge.

Additionally, we did not pursue cerebrospinal fluid (CSF) assessment to chase the possibility of anti-NMDA receptor antibodies. This is because our patient did not present with autonomic instability, elevated temperature, delirium, or seizures. Nonetheless, doing an invasive procedure with already anticipated low pre-test probability justified our approach. We also cannot rule in or rule out the possibility of COVID-induced psychosis due to the absence of studies or case reports that could identify what role COVID may have played in Narcolepsy presenting with the first episode of psychosis.

Conclusion

Given the growing literature of early onset psychosis with a diagnosis of NT1, it is reasonable to assume that the diagnosis of first episode psychosis while still needing to rule out Schizophrenia is appropriate. Patients with NT1 and psychosis have more neurocognitive impairments and require additional interventions like more severe psychotic symptoms and poorer response rates to antipsychotics. Our case report highlights the importance of optimal treatment of Narcolepsy and psychosis when presenting together. Due to limited reports of psychosis in children and adolescents with NT1, further research, including long-term follow-up or comparison groups with a larger sample size, is needed. ✤

Data Availability

Data sharing does not apply to this article, as no new data was created or analyzed in this study.

Informed Consent

Written informed consent was obtained from the legal guardian on the Carilion Clinic consent for case reports form. Assent obtained from the patient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this article.

Funding Statement

The authors report no financial relationships with commercial interests.

Acknowledgments

The authors would like to thank Kiran Khalid, MD Inpatient adolescent Psychiatry, Virginia Technological University School of Medicine for her review and suggestions along with Mandeep Rana, MD Chief of Pediatric Neurology, Virginia Technological University School of Medicine for her clinical care of this patient and for sharing her valuable expertise on the neurology portion of this manuscript.

A poster version of the manuscript was presented on April 9, 2024, at the Carilion research day.

References

1. BaHammam AS, Alnakshabandi K, Pandi-Perumal SR. Neuropsychiatric correlates of narcolepsy. *Curr Psychiatry Rep*. 2020;22(8):36.
2. Bassetti CLA, Adamantidis A, Burdakov D, et al. Narcolepsy—clinical spectrum, aetiopathophysiology, diagnosis and treatment. *Nat Rev Neurol*. 2019;15(9):519–539.
3. Barateau L, Pizza F, Plazzi G, Dauvilliers Y. Narcolepsy. *Journal of Sleep Research*. 2022;31(4):e13631.
4. Bond L, Killeen D, Hennessy B, et al. Comorbidities and COVID-19—A case study of an adolescent's tumultuous journey through psychosis. *Psychiatry Research Case Reports*. 2024;3(1):100200.
5. Canellas F, Lin L, Julià MR, et al. Dual cases of type 1 narcolepsy with schizophrenia and other psychotic disorders. *Journal of Clinical Sleep Medicine*. 2014;10(09):1011–1018.
6. Canellas-Dols F, Delgado C, Arango-Lopez C, Peraita-Adrados R. Narcolepsy-cataplexy and psychosis: a case study. *Rev Neurol*. 2017;65(2):70–74.
7. Cavalier Y, Kothare SV. The association of schizophrenia and narcolepsy in adolescents. *Pediatric Neurology*. 2018;83:56–57.

8. Chin WC, Liu FY, Huang YS, Hsiao IT, Wang CH, Chen YC. Different positron emission tomography findings in schizophrenia and narcolepsy type 1 in adolescents and young adults: a preliminary study. *Journal of Clinical Sleep Medicine*. 2021;17(4):739–748.
9. Feketeová E, Dragašek J, Klobučníková K, et al. Psychotic episode and schizophrenia in slovakian narcolepsy database. *Brain Sciences*. 2022;13(1):43.
10. Fernandez FX, Flygare J, Grandner MA. Narcolepsy and COVID-19: sleeping on an opportunity? *Journal of Clinical Sleep Medicine*. 2020;16(8):1415–1415.
11. Hanin C, Arnulf I, Maranci J, et al. Narcolepsy and psychosis: A systematic review. *Acta Psychiatr Scand*. 2021;144(1):28–41.
12. Huang YS, Guilleminault C, Chen CH, Lai PC, Hwang FM. Narcolepsy–cataplexy and schizophrenia in adolescents. *Sleep Medicine*. 2014;15(1):15–22.
13. Kallweit U, Bassetti CL. Pharmacological management of narcolepsy with and without cataplexy. *Expert Opinion on Pharmacotherapy*. 2017;18(8):809–817.
14. Kleiger JH, Khadivi A. Assessing Psychosis. 0 ed. Routledge; 2015.
15. Kishi Y, Konishi S, Koizumi S, Kudo Y, Kurosawa H, Kathol RG. Schizophrenia and narcolepsy: A review with a case report. *Psychiatry Clin Neurosci*. 2004;58(2):117–124.
16. Kıyak JM, Köse S, Bulut Demir MH, Özbaran B. Differential diagnosis of recurrent hypersomnia: a case report of primary narcolepsy and acute transient psychotic attack. *The Journal of Pediatric Research*. 2021;8(1):93–97.
17. Leucht S, Samara M, Heres S, Patel MX, Woods SW, Davis JM. Dose equivalents for second-generation antipsychotics: the minimum effective dose method. *Schizophrenia Bulletin*. 2014;40(2):314–326.
18. Meng Q, Li R, Hou F, Zhang Q. Effects of chlorpromazine on sleep quality, clinical and emotional measures among patients with schizophrenia. *Clinical Neurology and Neurosurgery*. 2018;165:134–138.
19. Mignot E, Hayduk R, Black J, Grumet FC, Guilleminault C. HLA DQB1*0602 is associated with cataplexy in 509 narcoleptic patients. *Sleep*. 1997;20(11):1012–1020.
20. Tsutsui K, Kanbayashi T, Tanaka K, et al. Anti-NMDA-receptor antibody detected in encephalitis, schizophrenia, and narcolepsy with psychotic features. *BMC Psychiatry*. 2012;12(1):37.
21. Yeh JY, Shyu YC, Lee SY, et al. Comorbidity of narcolepsy and psychotic disorders: a nationwide population-based study in taiwan. *Front Psychiatry*. 2020;11:205.