Case Report

Comorbidity of narcolepsy and schizophrenia in an adolescent patient

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Abstract

A 13-year-old boy suffered from hypersomnia, fragmented nighttime sleep, and cataplexy since age 10 years, and then developed prominent psychotic symptoms (i.e., auditory and visual hallucination, hallucinatory behavior, delusions of reference, and misidentification) that occurred persistently during the wakeful and consciously clear period when he was aged 12 years. The child underwent additional medical evaluation and testing, and comorbidity of narcolepsy and schizophrenia was diagnosed. The child’s psychotic symptoms and narcolepsy improved significantly upon treatment with methylphenidate 30 mg, olanzapine 25 mg, and haloperidol 10 mg. In this case, the child’s symptomology of narcolepsy and schizophrenia and the dilemma of the use of antipsychotics and psychostimulants are representative examples of the diagnostic and therapeutic challenges in adolescent psychiatry.

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1. Introduction

Narcolepsy is a chronic sleep disorder characterized by excessive daytime sleepiness, fragmented nighttime sleep, cataplexy, sleep paralysis, and hypnagogic hallucinations, with characteristic onset during childhood and adolescence.1 The prevalence of narcolepsy varies in different countries1 and is approximately 0.034% in the Chinese population.2 Symptoms of narcolepsy include problems in maintaining normal alertness and an abnormal intrusion of rapid eye movement (REM) sleep into periods of wakefulness. Specific laboratory findings include abnormally short mean sleep latency (≤8 minutes) and two or more sleep-onset REM (SOREM) periods in the multiple sleep latency test (MSLT), and lower hypocretin levels (<110 pg/mL) in cerebrospinal fluid analysis.3 Comprehensive therapies including both pharmacological and behavioral approaches have been suggested to treat narcolepsy and its pervasive effects on functioning in multiple capacities.

A number of patients with narcolepsy have experienced hypnagogic or hypnopompic hallucinations, which were possibly misdiagnosed as schizophrenia due to the similar symptomatology.4 However, the association between narcolepsy and schizophrenia remains inconclusive. A review article suggested that comorbidity of narcolepsy and schizophrenia is likely to be rare and sporadic.5 Our study presents such a rare case, in a patient suffering from comorbidity of childhood-onset narcolepsy and adolescent-onset schizophrenia.
milestones, including motor, language, learning, social
cognition, and interpersonal relationship, and denied any
previous physical or mental disorder. At age 10 years, he
began to experience excessive daytime sleepiness, recurrent
daytime naps, occasional cataplexy, and always fell asleep
in class. His family noticed that he would sometimes fall down
suddenly, on the road when walking or while sitting on
the chair, with a transient loss of motor tone, especially when
engaged in argument or excessive laughing. However, he
retained consciousness during this repetitive falling down.
Nonetheless, his parents did not take him for any medical
consultation and treatment. In early 2010 (age 12 years), he
developed auditory hallucination (AH), visual hallucination
(VH), and hallucinatory behaviors (self-talking and grasping
of the air) when he was wakeful and in a clear state of con-
sciousness. He was admitted to the pediatric ward to rule out
organic factors such as encephalitis. A series of physical
studies, laboratory examinations, and brain magnetic reso-
nance imaging was performed and no significant finding was
noted. There had been no previous seizure-like symptoms, and
electroencephalography revealed a diffused cortical dysfunc-
tion with no epileptiform discharge. He was then discharged
and had an irregular follow-up.

His parents refused to let him take any medication and
sought out a variety of religious-based treatments, although he
still suffered from excessive daytime sleep, persistent self-
talking, and AH. In February 2011, his AH and VH signifi-
cantly exacerbated with many bizarre verbal expressions (e.g.,
“I was not myself, someone possessed my body, someone
controlled me, the real me was in Russia”1), with prominent
delusions of reference and misidentification. He said that his
mother was an unfamiliar friend and that many people were
observing him. According to observations of his parents and
his own statements, the patient was in a clear state of con-
sciousness, with a fair level of concentration when he expe-
rienced the aforementioned psychotic symptoms. However,
the patient denied hypnagogic or hypnopompic hallucination.
Regarding the psychiatric family history, his aunt had been
diagnosed with schizophrenia.

With the tentative diagnosis of schizophrenia, the patient was
again admitted to the child and adolescent psychiatric ward. A
regimen of risperidone was started at 4 mg/day, and titrated up to
8 mg/day within 3 weeks because of the patient’s prominent
psychotic symptoms. During the treatment period, he slept for
over 16 hours daily. His psychotic symptoms and bizarre
behavior did not improve much during his wakeful time. The
patient’s risperidone regimen was shifted to olanzapine at 25 mg/
day, to address his severe psychotic symptoms and potentially
benefit from the antipsychotic efficacy of olanzapine.

After 2 weeks of olanzapine treatment with some measure of
improvement of psychotic symptoms, haloperidol 10 mg
was augmented for his persistent residual bizarre behavior and
delusions. Meanwhile, polysomnography (PSG) and MSLT
were performed after all psychiatric medications had been
temporarily discontinued for 3 days (half-life: olanzapine:
21–54 hours; haloperidol: 10–30 hours) to prevent the
pseudo-positive artifact that can be caused by drugs. PSG
findings revealed that total sleep time was 6 hours, REM sleep
comprised about 13.4% of total sleep time, REM latency was
201 minutes, apnea-hypopnea index was 0.2, and without
periodic leg movement. MSLT confirmed the diagnosis of
narcolepsy with a mean sleep latency of 1.4 minutes (<8
minutes), and three of five (>2) naps had SOREM periods.
The diagnosis of narcolepsy was made. However, due to
limited information about the hypocretin level and
HLADQB1, and to further improve diagnostic validity, PSG
and MSLT were again performed, with consistent findings.
Methylphenidate 15 mg twice daily was added and we closely
observed the changes in the patient’s narcoleptic and psychotic
symptoms because some evidence suggested that methylphe-
nidate may exacerbate the psychotic symptoms.

Two weeks later, the excessive daytime sleep, AH, VH, del-
usions of misidentification and reference, and bizarre behavior
subsided gradually. He was able to maintain clear consciousness
in the daytime, with more appropriate behavior; he also reported
fewer delusions and hallucinations. Furthermore, no adverse
effects such as extrapyramidal syndromes and decreased appe-
tite were noted. The patient was then discharged with the di-
agnoses of childhood-onset narcolepsy and adolescence-onset
schizophrenia. During the outpatient follow-up in the following
months, residual psychotic symptoms (i.e., AH, bizarre speech)
and intermittent hypersomnia were still noted. Methylphenidate
and the antipsychotics were maintained.

3. Discussion

Both psychotic symptoms and narcolepsy were noted in
this case. In reviewing the previous literature, three possible
differential diagnoses were found than could explain the
comorbidity.7–10 First, narcolepsy may co-occur by chance
with schizophrenia or other psychiatric disorders. Second,
some authors support the existence of a psychotic form of
narcolepsy, in which the psychotic symptoms exceeded the
common hypnagogic or hypnopompic hallucinations. Third,
psychotic symptoms developed sequentially after treatment
with central stimulants (i.e., methylphenidate and modafinil).
Although they might be difficult to differentiate, psychotic
symptoms differed between patients with narcolepsy and
schizophrenia.4,7,8,10 Previous studies demonstrated that
narcoleptic patients experience multisensory hallucinations
significantly to a significant extent, and not just the predomi-
nantly verbal—auditory hallucinations of schizophrenic pa-
tients.4,11 Delusions and associated delusional behavior are
rarely noted in patients with narcolepsy.4,11 The psychotic-like
symptoms of narcoleptic patients (sleep-associated hallucina-
tions) differ from the core symptoms of schizophrenia (AH,
delusions, disorganized behavior, and negative symptoms).4,11
However, diagnosis was more difficult with a small group of
narcoleptic patients who experienced typical hallucinations in
the half-asleep period or developed delusional thoughts in
response to hypnagogic or hypnopompic hallucinations.12
Consequently, it is essential for clinicians to take a thorough
patient history, including a focus on the longitudinal develop-
ment of the illness and the temporal sequence of the illness.
and medication. Additionally, a carefully scrutinized clinical assessment and a sleep test would help clinicians make a proper differential diagnosis.

Furthermore, considering the impact of antipsychotics on a patient's sleep architecture, Cohrs \cite{13} and Giménez et al \cite{14} suggested that olanzapine and first generation antipsychotics (i.e., haloperidol) increased the REM latency and total sleep time both in schizophrenic patients and in healthy volunteers. According to our patient's 3-year previous history with narcoleptic and persistent psychotic symptoms, and positive findings (i.e., ≤8 minutes mean sleep latency and ≥2 SOREM periods) of MSLT after discontinuation of antipsychotics, the comorbidity of narcolepsy and schizophrenia was diagnosed.

Finally, regarding the treatment in narcoleptic patients with prominent psychotic symptoms or those with dual diagnoses of narcolepsy and schizophrenia, such treatments remain a clinical dilemma because antipsychotics have sedative effects and psychostimulants may induce or exacerbate the psychotic symptoms. \cite{8,9,15,16} Current evidence reflects this treatment difficulty for patients with narcolepsy and comorbid schizophrenia, and those patients had the poor response to antipsychotic medication. \cite{9,17} Further studies are required to better elucidate potentially effective treatment for narcolepsy and comorbid schizophrenia, and clarify the possible underlying mechanism of this comorbid association.

Our patient experienced excessive daytime sleepiness since childhood and developed psychotic symptoms during wakefulness at age 12 years. Hallucinatory and delusional symptoms during the waking period persisted for over 1 year and impaired the patient's academic and social function. Childhood-onset narcolepsy and adolescence-onset schizophrenia were diagnosed and the combination of antipsychotics and a psychostimulant were therapeutically effective in our patient.

In conclusion, when practitioners encounter a narcoleptic patient presenting with psychotic symptoms, a differential diagnosis that distinguishes a co-occurrence of narcolepsy and schizophrenia from narcolepsy with psychotic symptoms is difficult, but of great importance to ensure the optimal treatment. A treatment regimen consisting of a combination of a psychostimulant and antipsychotics may be potentially beneficial, but would require further study.

References

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