28-YEAR-OLD CAUCASIAN MALE WITH HISTORY OF SCHIZOPHRENIA AND SIGNIFICANT PROBLEMS WITH ATTENTION — Nicola Cascella, MD

BACKGROUND

Mr L is a 28-year-old Caucasian man with a history of chronic schizophrenia and a comorbid condition of trichotillomania. The patient’s family history is negative for schizophrenia but positive for a brother with cerebral palsy, mental retardation, and a seizure disorder. A maternal great aunt was hospitalized after her divorce for a “nervous breakdown.” Mr L was born at term, without complications. He repeated the eighth grade and had several behavioral problems in school, ultimately dropping out in the 11th grade. He had few friends, did not date, and seemed quiet and uninterested. He currently lives with his mother and works full time in a supermarket. He rarely drinks alcohol, does not smoke tobacco, and has no history of illicit drug use.

MEDICAL AND PSYCHIATRIC HISTORY

The patient’s medical history includes a heart murmur as an adolescent. His medications at the time of this case study presentation included aripiprazole 30 mg at bedtime, sertraline 250 mg daily, and guanfacine 1.5 mg daily. Mr L had behavioral problems in elementary school and developed increasing social withdrawal and poor concentration early in high school. His first psychiatric hospitalization occurred in 1998, during which he presented with delusions of persecution, auditory hallucinations, trouble concentrating, increased social withdrawal, and increased poverty of speech. During his stay in the Day Hospital, Mr L seemed distracted, his speech showed latency, and he often did not answer questions. He seemed to “zone out” briefly, and then he would ask the interviewer to repeat the question. The treatment team considered the possibility that he was experiencing absence seizures, but an electroencephalogram did not indicate the presence of seizure discharges. Mr L was finally discharged with improvement in his hallucinations after adjustments in the dose of olanzapine (which was eventually tapered and aripiprazole started), but he did not experience improvement in his concentration and distraction. He was then followed by the Community Psychiatry Program at Johns Hopkins Hospital, where the patient’s distraction was disruptive to the flow of conversations and interviews. Mr L was also unemployed because of lack of concentration and distraction, which he felt interfered with his capacity to follow directions.

A close review of the literature on pharmacologic treatment of “distractability” disclosed research demonstrating the efficacy of guanfacine, an α-2 agonist used for hypertension, in decreasing distractability in rhesus monkeys performing a delayed response task. Mr L agreed to a trial with guanfacine, which was started at a dose of 0.5 mg at bedtime because of the possibility of sedation and hypotension. Mr L appeared to tolerate guanfacine well, except for diarrhea that dissipated several days after starting therapy.

PHARMACOLOGIC REMEDIATION OF COGNITIVE SYMPTOMS

In the year 2000, Mr L was admitted to the Johns Hopkins Schizophrenia Day Hospital because of ongoing problems with distractability, in addition to “unclear thinking,” worsening auditory hallucinations, increased social withdrawal, and increased poverty of speech. During his stay in the Day Hospital, Mr L seemed distracted, his speech showed latency, and he often did not answer questions. He seemed to “zone out” briefly, and then he would ask the interviewer to repeat the question. The treatment team considered the possibility that he was experiencing absence seizures, but an electroencephalogram did not indicate the presence of seizure discharges. Mr L was finally discharged with improvement in his hallucinations after adjustments in the dose of olanzapine (which was eventually tapered and aripiprazole started), but he did not experience improvement in his concentration and distraction. He was then followed by the Community Psychiatry Program at Johns Hopkins Hospital, where the patient’s distraction was disruptive to the flow of conversations and interviews. Mr L was also unemployed because of lack of concentration and distraction, which he felt interfered with his capacity to follow directions.

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Because Mr L's problems with distraction continued, the guanfacine dose was slowly titrated over a month to 1.5 mg daily. After 1 week of receiving 1.5 mg, Mr L's symptoms dramatically improved, with near disappearance of "zone out" episodes and fluid, as opposed to strained, conversation. Mr L was encouraged to seek part-time employment, and he did attempt to attend General Education Diploma classes. Although he did not have trouble with his concentration, he was not able to complete the program because of problems with mathematics. He was successful in finding employment at a local supermarket that initially hired him as a part-time employee stocking goods and, subsequently, gave him full-time status with full benefits. Mr L has been on guanfacine 1.5 mg for the past 6 years without any related side effects. His concentration and attention have remained improved, with significant impact on his social functioning and sense of well-being.

**DISCUSSION**

As illustrated by the case of Mr L, cognitive impairments are common at the onset of schizophrenia and can frequently be identified in childhood, well before psychotic symptoms emerge. In contrast to psychotic symptoms which are typically episodic, cognitive impairment appears to be a stable feature of the illness and has become an important treatment target. An extensive literature, as documented by David J. Schretlen, PhD, ABPP, has demonstrated a consistent relationship between cognitive deficits measured in the laboratory and functional outcome in schizophrenia, including social outcome, vocational outcome, and success in rehabilitation programs. Antipsychotic medications, especially second-generation agents, may lead to some improvement in cognition, however, the overall effects are relatively weak (see article by Terry E. Goldberg, PhD). This treatment gap has inspired a search for co-treatments that can be added to an antipsychotic to improve cognition. Because at this time there is no US Food and Drug Administration approved cognitive-enhancing drug, clinicians must rely on agents, such as guanfacine, that are used for other indications but have limited cognition data.

**REFERENCES**