

# Evaluation of a Complex Case: The Value of a Drug Washout Period

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### CASE PRESENTATION (Dr. Patel)

Mr. A is a 50-year-old single man with a 38-year history of psychiatric difficulties, presently a patient on our Research and Evaluation Unit, whose case has stimulated active (and at times angry) debate among those caring for him regarding his diagnosis and most appropriate treatment. His case is presented to elucidate how a drug washout period can help establish a diagnosis, which for him has vacillated between psychosis (schizophrenia or bipolar disorder) and antisocial personality disorder.

### Brief Psychiatric History

Over the years, there have been two problems facing clinicians dealing with Mr. A as they have tried to assess his diagnosis. First, information about him (including hospitalization records) from before the age of 37 is quite sketchy; and, second, his behavior has stimulated fear and even antipathy in some members of the treatment team. Regarding his early history, this much is known: The youngest of two children, Mr. A was born to a 44-year-old mother who was reported to have had a "difficult pregnancy and a forced delivery." He had a mild cerebral palsy, which left him with an odd gait. He was late in achieving developmental milestones; he had trouble nursing from a bottle and had problems in walking. He was

reported to have temper tantrums as a youngster and was a behavior problem at home and in school; he was also noted to have "terrible jealousy" and to break things frequently. Last, he had a learning disability, and beginning at age 15 he received "special education" in a "residential facility for emotionally disturbed children."

His family lived in a western state during his adolescence, and he was first hospitalized at age 17, when he was noted to have an "acute schizoid episode" according to available records. Over the next 15 years, he had multiple hospitalizations in this western state—each time, apparently, with a diagnosis of psychosis and personality disorder. When he was not in the hospital, he had a few jobs, mostly under careful supervision. There were conflicts with supervisors.

When Mr. A was 31 years old, his father died, and he and his mother moved to our area. Evaluated in an outpatient clinic at that time, he was described as "slovenly, unshaven, smelly, exceedingly nervous and distracted." He gave a vague history but was not noted to be overtly psychotic. He was placed in a vocational rehabilitation program but did not actively participate. His medication treatment during the next 6 years included mainly haloperidol. He spent most of his time at his mother's house smoking cigarettes.

At age 38, Mr. A became suspicious of his mother and physically assaulted her; then he assaulted a police officer when he was brought to an emergency room. He was noted to be unkempt, smelly, and dirty and was described as "responding to internal stimuli, vigilant, and with illogical speech." He was admitted to the hospital, and haloperidol was restarted. Because his mother refused to take him home, he was placed in a community psychiatric residence, where he set fire to a mattress when a female staff member tried to set limits to his behavior. Criminal charges were continued by the court, and he was rehospitalized. Once again, during a period of some frustration, he set a fire and ended up in a hospital for forensic psychiatric patients. His mother died while he was in this facility.

During the next year, he was transferred back to the local hospital and promptly pro-

ceeded to set off a fire alarm. This caused him to be sent back to the forensic facility, where an evaluation did not detect any psychosis. The treatment team at the local hospital had also failed to link psychosis to the fire setting or the false fire alarm. Rather, they viewed him as an angry, remorseless man with feelings of entitlement who had episodic psychosis and displayed manipulative behavior.

Over the next 6 years (from age 40 to 46) Mr. A spent much of the time in an inpatient facility at the local hospital, where he was closely monitored for fire setting. Very gradually his privileges on the inpatient unit increased as his behavior improved. He was maintained on 5 mg/day of haloperidol. Notes from this admission suggest that he became pleasant to talk to and was doing well in a sheltered work program. Eventually, the staff decided to attempt a gradual transition out of the inpatient setting. At first Mr. A did rather well; although his hygiene was poor, he was elected president of the outpatient social club. However, during this period, his dose of haloperidol was also decreased (in part because he missed scheduled doses), and as it reached about 2 mg/day, he began to miss appointments and his self-care deteriorated. He brought a knife to a therapy session and was readmitted to an inpatient setting, where his haloperidol was restarted at 5 mg/day. Gradually, he was able to be transferred to a highly staffed community residence.

At age 47, Mr. A again had a number of admissions to local hospitals because of threatening behavior in the community. Treatment at that time included haloperidol, 5 mg/day, and lithium, 900 mg/day (with a blood level of 0.8 meq/ml), to attempt to manage his behavior. In his day program, he would "hustle" other patients and got into conflicts over money. Setting limits would provoke him; he threatened a female staff member with a knife because she "tried to set a limit." Charges were pressed against him. He assaulted a female patient and was arrested and sent again to a forensic facility. There was no evidence of psychosis during the assaults. Following discharge from the forensic facility, he was readmitted to a local private hospital be-

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The authors thank the staff of the Continuing Care Service of the Massachusetts Mental Health Center (particularly Eileen Wong, M.D., and Kathleen Puckett, B.S.N.) and the staff of the Commonwealth Research and Evaluation Unit of the Massachusetts Mental Health Center for their assistance in the preparation of this report.

cause of threatening behavior in the community and because he had worn out his welcome at his residence. In the hospital, once again, there was an active debate about whether he actually had a psychotic illness. Some staff members even felt that he did not have a psychiatric disorder at all and would best be handled within the legal system. A clinical conference at that time concluded that "his antisocial personality is currently the driving force behind his behavior." However, to resolve the question of diagnosis, and especially the role of an underlying psychosis, a recommendation was made to withdraw his medications and observe him clinically. Since this was not possible at the local hospital (because of concerns about length of stay), he was accepted as a patient in our Research and Evaluation Unit for a full clinical evaluation and a medication trial.

### *Admission to the Research and Evaluation Unit*

On admission, Mr. A was slovenly dressed, with stooped posture, a decreased arm swing while walking, and an anxious and guarded facial expression. He paced the room and exhibited odd, stereotypical mannerisms; he would touch his forehead and run his hand through his hair in a repetitive manner. He was vague in his answers to questions and provided little history of value. He did, however, deny any history of alcohol or drug use. He appeared sad but could occasionally laugh, at times inappropriately. There seemed to be very mild loosening of associations, but his speech was mostly goal-directed. He denied hallucinations or delusions, although he appeared somewhat suspicious. He was mildly argumentative and seemed sensitive to even slight criticism. There were no vegetative symptoms, and he denied homicidal or suicidal thoughts. He was alert and oriented but seemed to have trouble with concentration. His proverb interpretations were idiosyncratic but not concrete.

A diagnostic conference held after Mr. A's entry into the Research and Evaluation Unit concluded from the available history that he most likely had a schizophrenic disorder. On the basis of this conclusion, a decision was made to observe the patient on his current medication regimen before attempting the drug washout period.

### *Course of Illness on the Research and Evaluation Unit*

On the unit, Mr. A continued initially with haloperidol, 5 mg/day. A behavior plan was put in place (with his agreement) to deal with potential disruptive behavior on the unit. Although, in general, he seemed to respond well to this behavior plan, he was noted at times to be agitated, suspicious, and anxious. In addition, he would occasionally appear mildly hypomanic. Brief trials of mesoridazine,  $\beta$  blockers, and valproic acid did not result in obvious changes in his

condition. Nonetheless, as his comfort on the unit clearly increased, he began to talk to the staff about his previous violent outbursts. He described his violence toward others as a kind of "resentment" that would increase over time, until "the last straw" would precipitate an assault. He would become increasingly agitated and anxious before the assault.

Gradually, despite the behavior plan, Mr. A became more agitated, irritable, and argumentative on the unit. The staff actively debated how much the medication trials were helping. Even though he seemed to have few obvious psychotic symptoms, his behavior was unpredictable. The old question (that had been addressed so frequently by others) about the role of psychosis in his history was again raised. Once more, some members of the unit staff questioned how much a psychotic disorder contributed to his behavior problems; others, the majority, felt that he most likely had a psychotic disorder. Some wondered if he might do better with clozapine. At this point, the decision was made to begin a neuroleptic-free period to resolve the question of diagnosis and to begin clozapine if psychotic symptoms emerged.

Mr. A agreed to this plan. His haloperidol was tapered over a period of 2 weeks. At first, his mood improved and there were no florid psychotic symptoms. After 5 weeks without haloperidol, he became somewhat irritable, but he slept well and was thought to be doing well overall. The drug-free period was extended. After 6 weeks of the drug-free period, he started to change dramatically. He became somewhat restless and developed bizarre delusions (his wristwatch could send messages to the corner of the room), and he began to talk openly about the Nazis and his need for guns. His speech at times became illogical, and when he was coherent he spoke freely about his "jealousy" toward his father and other family members. He smiled and mumbled to himself. There were no mood symptoms. He occasionally appeared confused, but even during the worst phase of his psychotic symptoms, he was not assaultive or disruptive on the unit. An EEG performed during the drug-free period, while he was quite psychotic, was reported to be normal. A magnetic resonance imaging (MRI) scan done before the drug-free period was also read as normal. Results of routine laboratory tests during this time were unremarkable.

For the unit staff, the emergence of florid psychosis during the drug-free period settled the diagnostic issue. Mr. A began a clozapine regimen, which he tolerated well following a slow increase in dosage. After 20 days of clozapine treatment, he seemed calm and cooperative, had good eye contact, was talking spontaneously, and was giving goal-directed answers to questions. The pacing and mannerisms seen while he was taking other antipsychotic medications were nearly absent. The issue of his long-term treatment plan began to be addressed, as he began to seem substantially less psy-

chotic and more socially available, with a clear sense of humor.

### *Alcohol/Drug Use History*

Throughout his hospitalizations, the patient consistently denied alcohol or drug use.

### *Neuropsychological Testing (Dr. Kalinowski)*

Neuropsychological testing done when Mr. A was 42 years old and again when he was 44 revealed moderate impairments in executive functions and difficulties with sustained attention and mental control. He seemed stimulus-bound (i.e., he had difficulty removing himself from the particulars of his immediate situation). He also demonstrated difficulties in mental flexibility, another aspect of attention. His immediate recall of simple visual designs was impaired. Despite this impairment, however, he was able to retain the material he had encoded. He had difficulties in various manual tests that may in part have been due to his minimal cerebral palsy. His overall intellectual functioning was at the low end of the average range. His memory for text was generally intact, while his memory for less explicitly organized verbal material was impaired. He refused projective testing.

### *Psychiatric Interview (performed by Dr. Tsuang)*

The patient was well groomed but somewhat sloppily dressed. He was calm, appeared comfortable, and did not seem to be in any distress. There were no obvious abnormal movements. His mood was good, his affect was appropriate, and his speech was spontaneous and goal-directed. He was cooperative with the interviewer. He denied hallucinations and Schneider's first-rank symptoms of schizophrenia. There was no clear thought disorder. He said that at times in the past he would "get paranoid," but he could not elaborate further on this. He was asked about his past assaults. He said they were unjustified, but it was clear that he did not feel responsible for the assaults. As this part of the interview continued, the patient became quite vague in his answers. Although he said that he wanted to leave the hospital and be transferred back to a community setting, he seemed to have formed no plans for activities outside the unit.

### DISCUSSION

*Dr. Tsuang:* This is a very interesting case, one that stimulated great controversy, over many years, among persons trying to care for the patient. In a case such as this, the diagnostic formulation is not merely an academic exercise; rather, it clearly has great implications for treatment and case management.

I am struck by the controversy re-

garding whether Mr. A has a psychotic disorder. Perhaps it is an example of how our frustration at not being able to control a patient's behavior blinds us to the underlying problem. From the age of adolescence, this man has been in and out of psychiatric or forensic facilities. Of course, if you interview him now, when he is taking clozapine, within an inpatient setting, you do not see frank psychosis. But there has been a sense of psychosis throughout his history. What is most striking, however, is that during the drug washout period, he became floridly psychotic, with bizarre delusions but without the destructive behavior that has been seen when he is less psychotic. My own feeling is that the diagnosis of schizophrenia given when he first came to the unit was correct. The increase in psychotic symptoms during the drug-free period simply tells us that he had responded to his previous treatment with neuroleptics. However, just because he meets the diagnostic criteria for schizophrenia, we cannot conclude that his violence and history of assaults is secondary to psychosis per se. In fact, as we noted, the increase in psychosis during the drug-free period was not associated with destructive behavior. In addition, multiple evaluations after his assaults (or fire setting) did not reveal a frank psychosis. Yet, given what we see now, I do not believe that his primary location for care should be a forensic facility. He is a psychiatric patient.

I would like to ask Dr. Green to comment on the patient's response to the drug washout period and the trial with clozapine.

*Dr. Green:* This is one case in which an ongoing clinical controversy regarding patient management was resolved by a prolonged period of observation during a drug washout period. The problem the staff faced, over many years, was that during neuroleptic treatment, the patient was generally not psychotic, but he had to be hospitalized for disruptive behavior in the community. As Dr. Tsuang notes, in retrospect, his treatment with neuroleptics probably was controlling his psychotic symptoms. Yet, when working with him, clinicians were often not convinced that there was a psychosis underneath his difficult behavior. This uncertainty about his diagnosis perhaps led to even more controversy as his reputation as a "bad actor" made him persona non grata in community settings. Even on the Research and Evaluation Unit, where he had been given the diagnosis of schizophrenia at

entry, this debate continued. The modest and transient response of his unpredictable behavior to various medication trials and behavior programs had frustrated the staff and once again raised the issue of "willful behavior."

I suppose someone might ask, Are we sure that the increase in psychosis during the drug-free period was not a withdrawal psychosis, as some (1, 2) have described? I doubt it, mainly because the dose of only 5 mg/day of haloperidol was tapered gradually over a 2-week period. Moreover, a striking aspect of the case is his apparent response to clozapine. He is clearly better on a clozapine regimen than he was with the previous treatments; he is calmer, more talkative, with a sense of humor, and, of course, not psychotic. Further, the apparent akinesia seen when he was taking the other antipsychotic medication has disappeared. By now, we are all used to dramatic responses to this atypical neuroleptic drug (3–5). And the response to clozapine is not only in positive symptoms (5, 6). Many patients seem to be "more real." Our data and those of some other groups (7, 8) suggest that clozapine may improve certain aspects of neuropsychological functioning, particularly attention. It might be worthwhile repeating Mr. A's neuropsychological testing at some time. Another point to raise involves the apparent ability of clozapine to decrease violence. A number of investigators have mentioned it (9–11), and Meltzer and Okayli (12) have reported that clozapine may also be associated with a decrease in suicidal behavior. For this patient, will the drug not only control his psychosis better than haloperidol did but also lessen his risk of violence? That is the key question for his future care.

*Dr. Tsuang:* I would like to ask Dr. Kalinowski to comment on the neuropsychological test results. Are they consistent with schizophrenia, and do they give us any clue to Mr. A's propensity for violence?

*Dr. Kalinowski:* We know from the patient's history that there were developmental delays, even some evidence of cerebral palsy, and that he had clear behavior problems as a child. On testing now, we find mainly attentional deficits that are generally consistent with schizophrenia. The normal MRI scan is also consistent with the apparently good response to neuroleptics (in terms of psychosis) and an even better response to clozapine. I suspect that his impulsivity can be best understood in the terms in which he de-

scribed it: he feels criticized, begins to fret about it, gets more anxious, and then strikes out. Does he become delusional regarding the criticism? Perhaps, and then he needs to strike out to protect himself. I will be interested to see whether his tendency to violence decreases with clozapine.

*Dr. Tsuang:* As Dr. Kalinowski notes, this patient is unusual in that there is evidence of cerebral palsy and early cognitive deficit, but the MRI scan that was done quite recently is normal. Cognitively, he probably becomes "flooded" in stressful situations and may then become confused, perhaps more delusional, and impulsive. Yet, as we know, patients with "normal" brain structure are more likely than those with "abnormal" brain structure to have a good response to neuroleptic medication. Thus, his psychosis was relatively well controlled by typical neuroleptics and may be even better controlled by clozapine.

The question of Mr. A's potential for violence in the future is also important. Although his violent outbursts were not directly associated with florid psychosis, as Dr. Kalinowski suggests, could the near-obsessive quality of his anger (as he described it to me) be a kind of psychosis? Moreover, could clozapine's antipsychotic effect or its ability to improve some cognitive functions be helpful in preventing his impulsivity? Put another way, will his apparent "antisocial personality" be undetectable as long as he takes clozapine? I doubt it, but I am interested to see. However, given the studies that Dr. Green described which suggest that clozapine provides a primary "antiviolence" effect, as well as a better antipsychotic effect than other medications, perhaps he will be able to keep himself more in control when he feels criticized as long as he takes this drug.

Assaultive and fire-setting patients generate intense feeling on the part of clinicians—with good reason. Moreover, they stimulate controversy regarding how best to treat them. In this case, the drug washout period allowed the controversy about whether the patient is psychotic to be laid to rest. It should be understood, however, that I am not predicting that there will not be continued behavior problems. Moreover, I suspect that even with clozapine, Mr. A may need a tightly structured program (perhaps a highly staffed community residence) for a permanent placement. The case reminds me, however, that apparently manipulative and destructive behavior is not always will-

ful, and that a good clinical workup, including, where appropriate, a drug-free period in a controlled setting, can clarify diagnostic confusion and lead to optimal long-term treatment.

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