

Adderall-Induced Psychosis in an Adolescent

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Of all possible childhood disorders, attention-deficit-hyperactivity disorder (ADHD) accounts for more than any mental health, special education, and behavioral referrals in pediatric medicine.¹ Behavioral modification techniques and stimulant medications are the mainstay of current ADHD therapy. Adderall, which is a mixture of 75% of the D-isomer of amphetamine and 25% of the L-isomer, is one of the stimulants approved by the Food and Drug Administration for such therapy. The efficacy of stimulant medication is well documented throughout medical literature.^{2,3} The induction of schizophrenic-like states in amphetamine abusers is equally well documented, though the onset of such states in children on prescribed doses of stimulant medication is observed far less often.⁴⁻⁶ We performed a search of MEDLINE and pre-MEDLINE (1966-2002; English language) using keywords including "Adderall," "amphetamine," "dextroamphetamine," and "psychosis." Abstracts and subsequent relevant articles were reviewed by one author (JG). To date, there have been no published reports of psychotic reactions to amphetamine (Adderall) in an adolescent patient.

Case Report

A morbidly obese adolescent (body mass index = 50 kg/m²) came to her physician complaining of symptoms of poor concentration and inattention at the age of 12 years, 9 months. Her mother brought her for an evaluation secondary to failing grades in mathematics. Upon in-depth evaluation by both her physician and a psychologist, the patient was found to have serious difficulties in organization, social interaction, and attentiveness. Further investigation showed that she had such difficulties for several years, but the symptoms had recently worsened in relation to increased life stressors (death of

a beloved grandmother, loss of her home after Hurricane Floyd, onset of menses, mother's pregnancy). Her medical history included obesity. The patient used no medications and had no known drug allergies. She was a full-term infant delivered by cesarean section for failure to progress and weighed 8 pounds 15 ounces at birth. She reached all developmental milestones within the expected time frame.

Her family history was notable for attention-deficit hyperactivity disorder (ADHD) but no other psychiatric illnesses. Other positive family history includes obesity and coronary artery disease. The patient lived in a trailer with both of her parents, who are married, and a new baby brother. Her mother was a homemaker and her father was a mathematics teacher. The patient denied alcohol, drug, or tobacco use, and denied intercourse. The mother smoked in the house.

School records were obtained and showed a wide discrepancy between her performance on standardized tests of reading and mathematics, suggesting a possible learning disability or lowered performance as a result of attentional factors. In addition, the parents and teachers completed the Conners' Rating Scale as a screening measure for attention and behavior problems. Elevated scores on the cognitive problems-inattention and ADHD index scales were highly consistent across parent and teacher ratings (average T-scores of 77 and 71, respectively). Hyperactivity subscale ratings were within the average range (T-score of 50). Attention-deficit with hyperactivity disorder-inattentive type was diagnosed after a diagnostic interview based on *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) criteria.⁷ The patient was then started on amphetamine, 10 mg daily.

One month after starting the amphetamine medication, the patient returned for a follow-up visit and reported that her difficulties with attention and concentration had abated. Her mother noted considerable improvement in her grades. The patient's mother distributed the medication as prescribed. The patient had not experienced any sleep disturbances, weight loss, appetite changes, or

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tics, but she noted that she had occasional mild headaches that occurred in the evening. Her mother denied any disturbance of mood or affect.

One week later she came to the Emergency Department after having an anxiety attack at school. Findings of a physical examination at this time were normal. She was released to follow up with her physician the next day. At that follow-up visit, her parents complained that she had not slept for 2 days secondary to agitation, would not eat or drink, displayed bizarre behavior, and would not groom herself. At this visit, the patient admitted that she was having visual hallucinations (bugs crawling on the walls). Her speech was slow and her thought was tangential. Even so, she was oriented to person, place, time, and situation, and neurologic findings were normal. The patient's amphetamine medication was discontinued, and she was started on clonazepam, 0.25 mg every 6 hours as needed for agitation.

The patient was seen again for follow-up 4 days later. At that visit, she was intermittently oriented to person, place, time, and situation. She had flight of ideas, tangential thought, a flat affect, psychomotor retardation, loss of short-term memory, and extremely poor hygiene. She also displayed magical thought, describing a personal acquaintance with characters from Greek mythology, and described visual hallucinations: disembowelment of her baby brother and bugs crawling on the walls. She had command auditory hallucinations instructing her to "stab holes in [her] brother," she had tactile hallucinations of bugs crawling under her skin, and she displayed waxy flexibility. When asked about suicidal ideation, the patient replied, "I want to scare myself to death, but I haven't been alive long enough to know how to do it without me knowing." Neurologically she was normal at this visit. The patient was admitted for further evaluation as a result of her worsening condition.

At the time of her admission, findings of a complete physical examination were normal. A computed tomogram of her head and chest radiographs were normal. Laboratory work-up included complete blood count with differential; comprehensive metabolic panel; toxicology screening for barbiturates, benzodiazepines, cocaine, opiates, and amphetamines; thyroid-stimulating hormone; vitamin B₁₂ level; urinalysis and urine culture; rapid plasma reagin; and pregnancy test. All laboratory studies were normal or negative except for a slightly

elevated white cell count of 11,100/ μ L (normal 4,500–11,000/ μ L) and an elevated vitamin B₁₂ level of 1,036 pg/mL (normal 199–732 pg/mL). Toxicology screening results were specifically negative for stimulants and benzodiazepines.

The patient was kept completely medication-free while hospitalized. Throughout the hospitalization, her psychotic symptoms improved, and she became progressively more lucid and conversational. After being off amphetamines for 7 days (approximately 5 half-lives), her emotional status and behavior returned to premorbid levels. She had no recollection of the events of her hospitalization, and replied to all questions appropriately. She no longer had hallucinations of any type and was consistently oriented to person, place, time, and situation. A reaction to amphetamine was documented, and the patient was released home.

Discussion

It is thought that the mechanism of amphetamine-induced psychosis, such as that of schizophrenia, is mediated by dopaminergic excess.⁸ Amphetamines inhibit norepinephrine uptake and directly release dopamine from newly synthesized pools. The psychotic states induced by amphetamine abusers are characterized by parasitotic delusions and a predominance of visual hallucinations.^{9,10} Several studies have described the induction of psychotic states by amphetamines. Controlled hospital studies in which small, hourly doses of amphetamines were given to patients for prolonged periods of time show that a progressive flattening of affect and anhedonia occurred in patients before the onset of a more psychotic-like state.^{11,12}

Some studies have shown that amphetamine effects can be short-lived. Others, however, indicate a more chronic nature of amphetamine-induced psychosis. In one study, amphetamine-induced psychosis lasted for 1 to 2 days in most of the study participants, and 6 days in 2 participants.¹³ Notably, psychotic symptoms continued intermittently for 26 days in 1 participant. Findings from animal model studies suggest that amphetamine-induced dopamine release in the striatum and nucleus accumbens areas of animal brains can have lasting effects.^{14,15} The animals, which had displayed psychotic reactions to chronic administration of amphetamine, relapsed into psychotic behaviors readily after readministration of a single dose of

amphetamine or after exposure to nonspecific stress conditions. Amphetamine abuse has also been shown to initiate and maintain chronic schizophrenia.¹⁶

Our patient displayed many of the characteristics of amphetamine-induced psychosis: visual hallucinations, parasitotic delusions, anorexia, flattening of affect, and insomnia. That our patient's symptoms cleared when taken off the stimulant medication suggests that her psychosis was indeed secondary to amphetamine. As described in this case, it appears that 7 days (approximately 5 half-lives) are necessary for resolution of psychotic symptoms. Our patient, however, also displayed some symptoms more characteristic of schizophrenia, such as command hallucinations and waxy flexibility. Whether her psychosis was an acute reaction to amphetamine or an early initiation of schizophrenia remains to be seen. She will require close observation for the recurrence of schizophrenic symptoms and the possible need for future neuroleptic medication.

More studies are necessary to determine which patients are at risk for stimulant-induced psychosis. Until these risk factors are elucidated, appropriate caution must be exercised when treating attention-deficit disorder and hyperactivity with stimulants. Careful screening for personal or family history of schizophrenia, and close surveillance of early behavioral changes are imperative.

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