Improvement in refractory psychosis after initiating management for underlying ADHD

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ABSTRACT

We report on a unique clinical case of psychosis precipitated by Attention Deficit Hyperactivity Disorder (ADHD) and explore its implications for clinical practice as well as our understanding of these conditions. We describe a clinical case of a 46-year-old male presenting with auditory, olfactory, tactile, and visual hallucinations. We reviewed the literature on reported cases in which psychotic symptoms were treated with stimulant medications for ADHD comorbidity. This case report reveals the potential for properly selected patients to benefit from a consideration of ADHD comorbidity and a trial of treatment with that focus. In addition, the literature reveals a pathophysiologic association between psychosis and ADHD supported by neurobiological data. However, far more research is required to fully understand these conditions and their relationship. We conclude that ADHD and psychosis have some related pathophysiologic mechanisms but their connection has not been adequately explored. This case adds support to literature suggesting that in refractory psychosis, clinicians should re-evaluate the diagnosis and one of the considerations should be ADHD. In certain cases, the presence of psychotic symptoms with ADHD should not exclude the use of stimulants.

BACKGROUND

Psychosis is a common presenting problem in emergency departments (ED). Such episodes may present with positive symptoms, which include delusions, thought disorder, disorganized thinking, and hallucinations. They may also present with negative symptoms, which include deficits in normal functioning such as flat affect, avolition, and anhedonia. Cognitive symptoms of psychosis are also well documented, including deficits in working memory, attention, and executive functioning.

The management of psychosis is dependent on the cause, and therefore establishing etiology may be the most significant step in caring for the psychotic patient. Several disorders associated with psychosis, including schizophrenia, are also associated with ADHD.^{1,5} However, there is a lack of available data examining the relationship between ADHD and psychosis. In addition, stimulants commonly prescribed for ADHD management are considered to be contraindicated during psychotic episodes as they have been shown to exacerbate or even trigger positive symptoms in some patients.⁶ These barriers have prevented a thorough examination of the connections between psychosis and ADHD, despite there being a theoretical relationship.^{2,3}

We describe a relatively unique case, in which the presentation of psychosis was managed successfully by treatment with stimulant medication even though criteria for adult ADHD was not met. The difficulty in meeting adult ADHD criteria in this case relates to the similarity of cognitive symptoms seen in psychosis with ADHD symptoms, which include poor attention and executive functioning, and to psychomotor effects of ongoing antipsychotic medication. Criteria for a history of childhood ADHD were likely met on retrospective review of the case.

CASE PRESENTATION

INITIAL VISIT

JP was a 46-year-old male seen for a consultation following an ED visit 6 months prior where he presented with depressive symptoms. At that time, he was started on psychotropic medication (including lithium and risperidone) for a possible mood disorder. At the time of consultation, his mood was stable. However, he also admitted to experiencing visual, auditory, olfactory, and tactile hallucinations, and paranoid delusions for several months.

JP's visit to the ED was his first encounter with psychiatric care. He did have a history of alcohol abuse though he stated he had successfully stopped consuming alcohol 12 years ago. He also described a history of marijuana use which ended 2 years ago. His past medical history was otherwise unremarkable.

Following his initial consult, JP was tried on various medications in attempts to address his psychotic symptoms. These included Invega Sustenna (paliperidone palmitate), Loxitane (loxapine), Risperdal (risperidone), and Zyprexa (olanzapine). He was also tried on lithium, Epival (divalproex sodium), and Prozac (fluoxetine) to continue managing his mood. Unfortunately, over the next 12 months he continued to have paranoid and persecutory delusions, with the occasional return of his visual, auditory, olfactory, and tactile hallucinations.

NEW MANAGEMENT

At 18 months from his initial ED presentation, JP revealed that his brother was also seeing the same psychiatrist. It was discovered that he was being treated successfully for ADHD with Dexedrine (dextroamphetamine), which is an amphetamine-based psychostimulant.

JP did not have any overt symptoms of ADHD that would have led to a clinical diagnosis of ADHD. However, given evidence of the genetic heritability of ADHD⁷ and the successful treatment of JP's brother, a trial of Dexedrine was decided upon.

JP's dose of Dexedrine was gradually increased from 5 mg to 10 mg. His psychotic symptoms decreased, and he was eventually taken off all of his antipsychotic medications. Currently, JP's medications include Dexedrine 10 mg twice daily, fluoxetine 40 mg once daily and temazepam 15 mg once daily. He experiences no more psychotic symptoms. His mood is stable and he is doing well. After being off work for at least 2 years, he has since returned and was promoted to a role as supervisor.

LITERATURE REVIEW

There are multiple studies suggesting a relationship between childhood ADHD and psychotic presentations later in life.^{2,8,9} However, there is limited evidence in the literature examining the use of stimulants in refractory psychosis in situations where a comorbid diagnosis of ADHD is suspected.

Huey and colleagues (1978) describe a patient with chronic paranoid schizophrenia with a childhood history of minimal brain dysfunction (minimal brain dysfunction was a past term used prior to ADHD becoming a diagnosis) who received methylphenidate and subsequently suffered from decreased anxiety and intensity of hallucinations.¹⁰ Bellak and colleagues (1987) describe a young man presenting with schizophrenic episodes with a poor response to phenothiazines subsequently having a good response to methylphenidate plus lithium.^{11,12} Pine and colleagues (1993) present 2 adults with ADHD and comorbid psychosis successfully treated with a combination of stimulants and antipsychotics. They were then tapered off of their antipsychotics and remained free of psychosis with methylphenidate treatment alone.¹³

More recently, Tossell and colleagues (2004) describe 5 cases where the use of stimulants was beneficial in patients diagnosed with childhood onset schizophrenia and ADHD once their psychotic symptoms were well controlled.¹⁴ A 2009 literature review and case report by Sambhi and Lepping describes 2 cases of patients suffering from psychosis benefiting from stimulant use.¹² Finally, Rittmannsberger and colleagues (2014) describe the case of a 21-year-old patient who presented with a substance-induced psychosis and a highly probable diagnosis of adult ADHD;¹⁵ there was no major improvement on antipsychotic medications, and symptoms only significantly improved with the addition of methylphenidate.

DISCUSSION

Although our literature search revealed several case studies showing the improvement of symptoms of psychosis with methylphenidate treatment, there is an important nuance to consider. Stimulant medications in general lead to an upregulation of neural catecholamines such as dopamine and norepinephrine. This mechanism of action is opposite of that typically used to treat psychotic presentations in other disorders which generally respond to blocking of catecholamines such as dopamine.

Indeed stimulant medications have been shown to induce psychosis in some patients, a phenomenon referred to as *hallucinosis* or *stimulant toxicosis*.¹⁶⁻²³ For this reason it is important to better understand the conditions that dictate whether stimulant use will lead to improvement or worsening of symptoms of psychosis.

In order to better understand the relationships that underlie

this decision, we must consider the pathogenesis of these 2 conditions. The prefrontal cortex acts as a gating mechanism that enhances goal-directed activities and inhibits irrelevant activations. In ADHD these prefrontal processes are impaired. This is thought to be related to underactivity in several areas. Brain imaging studies have shown patients with ADHD have reduced activity in the pre-motor cortex and superior prefrontal cortex, both areas that are important for executive function, attention, and working memory.²⁴⁻²⁶ Deficits in these specific regions appear to be associated with hypoactivity and dysregulation of dopamine, particularly the prefrontal D1 receptors, and norepinephrine. The decreased dopamine activity in the prefrontal cortex in ADHD is also seen in schizophrenia. This is thought to be related to the cognitive impairment (negative symptoms) associated with the disease.

One manifestation of cognitive impairment common to both ADHD and schizophrenia involves salience identification. In schizophrenia-associated psychosis, patients lose the ability to perceive their environment accurately and to pick up key information. The inability to filter this information contributes to an altered sensory experience marked by an inability to attend to important stimuli in a normal fashion.²⁷ Similarly, inattention is a significant symptom of ADHD due to above-described prefrontal cortex dysfunction. As a result, someone with ADHD may experience symptoms similar to those of psychosis via an inability to properly attend to salient information.

The link between ADHD and schizophrenia can be potentially explained by the idea that they share deficits in prefrontal functions such as salience identification, working memory, and response variability. In line with these common neurobiological dysfunctions, new research has revealed some genetic repertoires for ADHD that also overlap with those of schizophrenia.^{15,28}

In light of this information, it may be reasonable to consider an underlying diagnosis of ADHD in a patient such as JP with refractory psychosis and a strong family history of ADHD. As stimulant medications may be associated with psychotic symptoms themselves, the decision to use stimulant medication should be done only after multiple other avenues have been explored. As we continue to unravel the relationship between psychosis and ADHD, the use of stimulants for management in ADHD may become more clear.

CONCLUSION

ADHD and psychosis are both common psychiatric disorders and have related pathophysiologic mechanisms. However, there has been longstanding reluctance to consider stimulant treatment in psychotic patients, preventing its use from being adequately explored. This case adds support to previous case reports noted in the literature that suggest that in refractory psychosis, one should re-evaluate the diagnosis and consider ADHD. In certain cases, the presence of psychotic symptoms with ADHD should not exclude the use of stimulants.

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