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METHYLPHENIDATE FOR PSYCHOSIS AND AGGRESSION IN A PATIENT COMORBID WITH ADHD - A CASE REPORT

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INTRODUCTION

Attention-deficit/hyperactivity disorder (ADHD) may persist into adulthood in a substantial proportion of affected youth, with rates differing between 15 (persistence of full syndrome) and 65% (partial remission) (Faraone et al. 2005).

There is ample evidence that patients suffering from ADHD carry a heightened risk for other psychiatric disorders. Adults with ADHD show high rates of comorbidity with affective and anxiety disorders, antisocial personality disorder and substance abuse disorders (Barkley & Brown 2008, Kessler et al. 2006). Though these reports lack data on psychosis, this comorbidity was in fact reported independent of psychotic symptoms induced by treatment with stimulants. In children and youth with ADHD, comorbidity with psychosis was found in 5% (Stahlberg et al. 2004) and a retrospective study in adult patients with psychosis revealed a history of ADHD in childhood in 17% (Peralta et al. 2010).

Given such comorbidity the simultaneous treatment of both conditions is difficult, since the main therapeutic drugs for the two disorders – antipsychotics for psychosis and stimulants (amphetamines and methylphenidate) for ADHD – have opposing effects on the dopamine metabolism. Stimulants are known to frequently induce psychosis in recreational use (Darke et al. 2008) and were found to increase risk by an odds ratio of 11 (McKetin et al. 2006). Single doses of stimulants in experimental studies led to an increase of positive symptoms in 51% of symptomatic schizophrenic patients, 28% of remitted patients and 10% of healthy controls (McKetin et al. 2006). Stimulants serve as a model for psychosis in animal studies (Featherstone et al. 2007) and the reaction to a test dose of amphetamine has been used as predictor for schizophrenic relapse (Lieberman et al. 1987). During therapeutic use of stimulants in children psychotic states have occurred in 0.25% of patients (Ross 2006) or 1.48 cases per 100 patient-years (Mosholder et al. 2009).

Antipsychotics on the other hand block effects of stimulants and are used for treatment of amphetamine-induced psychosis (Shoptaw et al. 2009).

While caring for a patient with comorbidity of ADHS and psychosis we were not able to find guidelines or treatment recommendations issued by a major society concerning state of the art treatment of such a case.

CASE REPORT

A 21-year old male patient was committed to the psychiatric clinic because of aggressive behavior leading to damage of property and attacking intervening policemen. On admission he appeared agitated and could not explain what had happened. There were no signs of intoxication or withdrawal. Shortly after having been brought to the ward the patient armed himself with a piece of furniture he had ripped out of the bathroom and attacked the staff. It was not possible to quiet him verbally and finally a team of six policemen and the use of pepper spray were necessary to control him. He displayed extended periods of disordered thinking, auditory hallucinations and thoughts of persecution, considering himself in a fight with invisible enemies. Further explorations of the patient and his relatives revealed that he had been restless and aggressive since childhood, with poor performance in school and at work. Over the last few years he had been consuming cannabis heavily in order to calm himself down. There were no prior psychotic episodes. A diagnosis of a substance induced psychotic disorder (ICD-10, F12.5) was made and the patient's own accounts and those of his relatives made an additional diagnosis of adult ADHD highly probable. On the Wender Utah Rating Scale (Ward et al. 1993) he reached a score of 82 out of 100 possible points (maximum 100, cutoff for ADHD 46), strongly suggesting a childhood diagnosis of ADHD.

During inpatient stay there were three episodes of unprovoked assaultive behavior leading to destroyed furniture and requiring massive manpower to control the patient. Continuous medication first with Olanzapine 30mg, then with haloperidol 20mg, accompanied by prothipendyl 200mg, valproic acid 2000mg and lorazepam 10mg could not prevent these outbursts of psychotic aggression. During such assaults additional high doses of psychotropic drugs (haloperidol 10mg i.v., prothipendyl 360mg i.v., diazepam 80mg i.v.) were necessary to calm him down. Twenty days of this kind

of treatment brought no major improvement. The patient changed repeatedly between calm behaviors, even apologizing for his conduct, and agitated, disorganized and aggressive episodes. The lack of efficacy of treatment with antipsychotics, mood stabilizers and tranquilizers and the high probability of comorbidity with ADHD led us to propose to the patient a trial dose of methylphenidate (MPH). After obtaining informed consent the patient received 5mg of MPH in addition to the aforementioned medication. The small test dose of MPH seemed to calm the patient immediately and to improve the disordered thinking. Treatment was continued with 5mg bid and the patient improved continuously. Since starting MPH neither psychotic nor aggressive symptoms appeared any more. After 14 days the treatment with MPH was discontinued without causing any change to the patient's state. A treatment for ADHD with atomoxetine was proposed to the patient but not realized. He was dismissed on a regimen of risperidone 4mg and valproate 2000mg and was well at a follow-up investigation two months later.

DISCUSSION

The lack of knowledge concerning the comorbidity of ADHD with psychosis and its treatment has been termed an “enigma in clinical psychiatry” (Kraemer et al. 2010). If psychosis occurs as a side effect during stimulant treatment of ADHD, stopping this treatment and a trial of atomoxetine is recommended (National Institute for Health and Clinical Excellence (NICE) 2008). Our patient had psychosis comorbid with a hitherto untreated ADHD. The patient's poor response to antipsychotics, mood-stabilizers and benzodiazepines led us to search for alternative treatment options. In view of his prominent aggression, comorbidity with ADHD and the sometimes beneficial effect of stimulants on aggression in ADHD (Klein et al. 1997) we opted for a trial with MPH. Of course we considered other possibilities for treatment too, e.g. lithium or clozapine, and certainly would have proceeded to it if the test dose of MPH hadn't appeared so successful. So we were encouraged to continue the treatment with the smallest dose possible. Astonishingly not only aggression disappeared but also the psychotic symptoms resolved quickly.

Despite all the cited caveats concerning stimulants and psychosis there are reports in the literature indicating that in some instances stimulants are well tolerated or even helpful in psychosis. Thus, it has been shown that in schizophrenic patients stabilized on antipsychotics stimulants can be added without worsening the psychosis (Carnwath et al. 2002, Ross et al. 2003) while improving cognitive functioning (Barch & Carter 2005, Goldberg et al. 1991).

Concerning the comorbidity of ADHD and psychosis there are some reports showing that stimulants alone (Bellak et al. 1987, Huey et al. 1978, Pine et al. 1993) or in combination with antipsychotics (Blom & Kooij 2012, De Jong et al. 2010, Sambhi & Lepping 2009, Tossel et al. 2004) are beneficial, not for ADHD symptoms alone, but also for psychotic symptoms. Bellak (Bellak et al. 1987) even coined the term “ADHD psychosis” to stress the fact that psychoses in ADHD patients differ from schizophrenic psychosis, most of all in terms of poor response to antipsychotics and good results with stimulants. He also found that treatment with small doses of stimulants is often sufficient, as in our patient.

Our case report is not free from ambiguities. We cannot distinguish whether the improvement of our patient was really caused by methylphenidate or by the previous treatment finally showing an effect or by the disorder coming to end by itself. MPH was given only in a low dose (5mg bid) and for a short time (14 days) and was discontinued without obvious problems, which might be viewed as an indicator that treatment with MPH was of minor importance. Yet the time course of improvement seems to us a strong argument for methylphenidate's beneficial effect since the clinical impression was that change started with the very first dose of MPH.

The best explanation for this unexpected effect comes from the assumption that a frontal hypo-dopaminergic state, in ADHD as well as in psychosis, has been improved by MPH (Barch & Carter 2005, Opler et al. 2001). In frontal regions the excess in dopamine induced by MPH primarily acts on D1 receptors whereas in the mesolimbic system D2 receptors prevail. The concomitant medication with antipsychotics blocks D2 but not D1 receptors whereas frontal D1 receptors improve cognition by strengthening the signal-to-noise ratio (Barch & Carter 2005). What is remarkable in this case is that haloperidol and then risperidone were used, which both bind with high affinity to D2 receptors and such might have prevented a psychotic deterioration.

CONCLUSION

We reported on a patient comorbid with psychosis and ADHD in whom short-term treatment with low doses of MPH paradoxical proved beneficial for psychosis as well as for aggression. The problem how to treat patients with psychosis comorbid with ADHD is still unresolved and deserves much more investigation until firm recommendations can be given. Neither the pathophysiology of ADHD nor the mode of action of stimulants is fully understood. This case adds to some others in the literature showing that stimulants might be an option in such situations.

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