

Case report

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Brief psychosis induced by methylphenidate in a child with attention deficit disorder: a case report and literature review

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Abstract

Methylphenidate-induced psychosis has been scarcely studied due to bioethical and neurobiological issues regarding its research. Although some authors have hypothesized that there might be a vulnerability for the development of a major psychiatric disorder in the long term, there is no agreement about the predictive value of this type of psychosis in children and adolescents, and its origin is also uncertain. It has been suggested that higher dopamine levels in some cerebral regions and a family history of mental disorders might increase the risk of psychosis secondary to psychostimulants. We present the case of a nine-year-old child diagnosed with attention deficit disorder and oppositional defiant disorder, who exhibited visual and auditory hallucinations and delirious ideas about harm during methylphenidate treatment. The patient's symptoms regressed after drug removal. We discuss the key issues related to the origin, causality, management, and prognosis of psychostimulant-induced psychosis.

Introduction

Psychotic symptoms in children and adolescents as an adverse event associated to psychostimulants use have not been rigorously studied, and, for the most part, knowledge comes from isolated cases, because of the bioethical and neurobiological complexity of the phenomenon. Despite the several published cases, the majority of them come from Anglo-Saxon publications, and it is a poorly studied subject during the prescribers' training programs (i.e., general practitioners and specialists) in Latin America.

We hereby describe a clinical case of a child with methylphenidate-induced psychosis and appraise the available evidence about this topic as well.

Clinical case

A nine-year-old male patient with history of a father with attention deficit disorder subtype hyperactive and a personality of cluster B (with remarkable narcissistic and dissocial traits). From the age of six, the patient had shown psychomotor restlessness, distractibility and impulsivity, in

addition to an attitude of opposition and defiance to the rules in several contexts. He was treated during six months by a neuropsychiatrist who prescribed psychotherapy and aripiprazole 5 mg every 12 hours, showing a poor response.

He was brought to child psychiatric consultation by his mother. As a biographical milestone, a year before his medical appointment, his parents broke apart "abruptly" and in "bad terms," what worsened the behavioral disorder.

During the first interview with the child, sadness and anguish only appeared regarding parents' separation. No symptoms of hypomania or mixed phase were observed, discarding a mood disorder. The child psychiatrist diagnosed an attention deficit disorder combined subtype comorbid to an oppositional defiant disorder, according to DSM-5 criteria [1].

The physician prescribed behavioral management and rearrangement of family dynamics in terms of limits, direct supervision of homework and recommended a functional relationship between parents. However, due to the poor behavioral improvement and the persistence of an altered social and academic performance, *de novo* treatment with methylphenidate (retard effect) was prescribed. The suggested dose was 5 mg twice a day for a week in order to reach the target dose of 10 mg at breakfast and 10 mg at lunch (0.3 mg per kg per dose). Despite this correct dosage prescription, the child received 10 mg in the morning and in the afternoon from the first intake.

During the third day of treatment, the patient commented to his classmates that some dolls in his arms were "diabolical" and he should burn them, because they were evil goblins and they must die. He had no dolls in his arms. The patient talked to the discipline monitor about the presence of evil goblins. He also commented that this situation had happened with his father before and they had previously killed these creatures in the forest, opened their stomach to extract the organs, and to wash them with holy water in order to get rid of them.

The school psychologist indicated that the patient was "paranoid and confused, hyper-alert and hyper-vigilant with 'loss gaze' and facial expression of anguish and fear." The patient referred to himself as a wizard, capable to predict the future, which is why, according to his comments, he was the only human being able to observe and listen to the goblins and dolls. He commented his perception about objects changing their position, and a voice repeating words without affective concordance and without relation to delusional content. These symptoms persisted about an hour. After that, he asked for support to the psychologist because he felt frightened, confused, ignoring if he was sleeping and whether the things he perceived were real or not. The remission of hallucinatory phenomena and delirious ideas was achieved after two hours. His mother manifested that the previous day, she observed him weird, becoming isolated, introspective to his internal world, asking about the existence of goblins and monsters.

The patient received medical attention by a child psychiatrist the day after the episode. His temporospatial orientation was appropriate, without quantitative or qualitative consciousness compromise, nor psychomotricity alterations, thinking structure, psychotic symptoms or bizarre behaviors. He kept an adequate contact and was capable of properly judging the environment, showing astonishment, even though his memory was vague. His neurological exam was normal.

The diagnosis of attention deficit disorder combined subtype with defiant opposition and maladaptive mixed anguished and behavioral reactions remained, and the episode was defined as a brief psychotic reaction with a partial consciousness compromise secondary to psychostimulant use. Methylphenidate was discontinued and after two weeks, the treatment was slowly restarted, 5 mg AM and PM, for 10 days, in order to reach 10 mg twice a day. A good response was obtained in attention and impulsive areas and a mild improvement in the behavioral area. After six months of treatment, psychotic symptoms were not observed again.

Discussion

After Connell [2] described psychostimulant-induced psychosis in 1958, some authors have reported "hallucinatory" episodes related to the use of methylphenidate, using the concepts of toxicosis and hallucinosis to indistinctly refer to them [3].

In the reported case, we highlight as the most remarkable features: auditory and visual hallucinations, delirious ideas about harm, and incoherent thinking. These core features were preceded by a state of consciousness close to crepuscular consciousness and followed by perplexity. The central point was the delirious state with imbalance between objectivity (i.e., the relationship with the external world: sensation and perception) and subjectivity experiencing (i.e., internal world: feelings, thoughts, sensations and perceptions of internal events).

Previous articles have reported psychomotor agitation and formal alterations of thinking as lax associations and tangentiality [4], irritability, separation anxiety and manic-like symptoms such as euphoria, expansive mood and grandiosity [3],[5], emotional lability and motor tics [6], pseudohallucinations [5], haptic [6],[7] and auditory hallucinations [8] and delirious ideas about reference and harm [8].

Although psychostimulant-induced psychotic symptoms might indicate a greater vulnerability to a long-term psychosis [9],[10], there is no agreement on the predictive value of psychotic symptoms associated to methylphenidate use in children. Some researchers suggest that hallucinations are likely to show a good prognosis in this group, and their association to delusion would make the difference [11],[12], as it is the case of our patient. Despite it has been recognized from cohort studies that childhood hallucinations would imply higher risk for psychiatric disorders during the adulthood, it is unclear

whether psychotic symptoms caused by drugs have prognostic implications [13],[14],[15].

It has been estimated that 1/400 patients treated with psychostimulants will present psychotic symptoms [3], after the first dose or several months after the beginning of treatment [5],[16], both with high doses [17] and therapeutic range [18], with a transient duration among two and seven days and remission after discontinuation [3]. Nevertheless, the US Food and Drug Administration reported that 8% of patients with secondary hallucinosis to methylphenidate were, subsequently, diagnosed with bipolar or schizophrenic disorders [3],[19]. Although controversial, methylphenidate would induce psychotic symptoms in 40-60% of patients with schizophrenia [20], and, despite its idiosyncratic nature makes difficult predicting the occurrence of psychosis by methylphenidate, it has been verified that the history of attention deficit disorder in patients who suffer from schizophrenia or bipolar disorder is common.

At the same time, the estimated risk of suffering from schizophrenia in patients with attention deficit disorder is 4.3 times higher than the general population [21]. Moreover, the severity of attention deficit disorder symptoms is associated with an early development of psychosis in patients with schizophrenia and history of an attention deficit disorder in childhood [22]. On one hand, a hypothesis proposes that some stimulant medications contribute to bring forward the onset of psychosis in patients with attention deficit disorder that, ultimately, will develop it. Thus, in a case-control study, Moran *et al.* [23] found that psychostimulants use was associated with an earlier onset of psychosis in comparison to those who had not used psychostimulants. On the other hand, it has been suggested that the use of stimulants would not contribute to an earlier onset of psychotic symptoms by itself, but the prodromal executive dysfunction of certain types of psychosis could lead to wrongly diagnose an attention deficit disorder [24],[25].

Several studies about psychotic pictures demonstrate a greater dopamine availability in response to the psychostimulants administration, and, this greater availability would be positively associated with the severity of psychotic symptoms [26],[27]. This fact could support a possible explanation to the previously described phenomenon, since psychostimulant pharmacology is related to reuptake blockage and, therefore, an increase in the amount of dopamine at the synaptic cleft [28],[29].

Different aspects might influence the risk of the emergence of psychotic symptoms during psychostimulant treatment, namely, the family predisposition to develop mental disorders. In this case report, it is clinically remarkable that the patient's father suffered an attention deficit hyperactivity disorder comorbid to a personality disorder with narcissist and dissocial traits, as attention deficit disorder has an estimated heritability of 76% [30], and is common in an offspring of parents with severe mental illness with [31]. The evidence indicates an overlap among the genetic factors involved in stimulants-induced

psychosis and the genetics of schizophrenia [32], and stimulants would facilitate the onset of schizophrenia in people with family history [9], while other authors report that family history would not be helpful as a clinical predictor [3]. In this sense, MacKenzie *et al.* studied the association between psychostimulants usage and the onset of psychotic symptoms in 141 children and adolescents with one or both parents with major depressive disorder, bipolar disorder or schizophrenia. Psychotic symptoms appear in 62% among psychostimulants users (n=24), compared to 27% among those who do not (n=117). All the people that reported those symptoms were children with at least one parent with the above mentioned disorders. The association between use of medication and psychotic symptoms was significant and remained unchanged after controlling variables such as age, gender and parental diagnosis.

To dispel a possible association between attention deficit disorder and psychotic symptoms instead of being purely a secondary effect of the drug, it was verified that attention deficit disorder did not show a significant association with psychotic symptoms. These results suggest that psychotic symptoms may be relatively common adverse events in young people with family history of major psychiatric disorders. However, the authors point out that the great proportion of psychotic symptoms found in the study could be related to the active investigation of psychotic symptoms through measurement instruments in contrast to the spontaneous report of symptoms that it is described in the published literature [33]. Thus, the European Guidelines for hyperkinetic disorders state that the evidence of vulnerability to psychosis in terms of a positive family history or prior psychotic episodes may increase the risk of psychotic symptoms with the drugs prescribed for attention deficit disorder but with a weak evidence level [34].

In the described case, the therapeutic strategy was the withdrawal of the drug with a subsequent gradual restitution of it, which appears to be the most recommended approach [3],[5]. The use of antipsychotics and/or mood stabilizers is not recommended due to the frequent adverse events associated [3], although other reports suggest their use for short periods (especially in cases of persistent psychotic symptoms after withdrawal of psychostimulant), since adverse events are usually observed only in long therapies [5].

Conclusions

The psychosis associated with the use of a psychostimulant such as methylphenidate is a fact mainly known from the publication of anecdotal cases, meaning, it would be an idiosyncratic, unusual and unpredictable phenomenon. Since there is no strong evidence that methylphenidate-induced psychosis is associated with future schizophrenic or bipolar disorders, it should remain as the first-line psychotropic drug for the treatment of children over six years old with attention deficit disorder, keeping a close supervision.

By means of a case report, the main topics of discussion regarding hallucinosis by methylphenidate have been detailed, in order to warn the specialists and primary care professionals about its existence. It is strongly suggested to increase the basic and clinical investigation, since the underlying neurobiological processes are unknown, and, at the same time, the clinical features that would show a major risk of psychosis by psychostimulant usage are still ignored.

Notes

From the editor

The authors originally submitted this article in Spanish and subsequently translated it into English. The Journal has not copyedited this version.

Ethical aspects

The informed consent requested by Medwave has been signed by the patient's mother; A copy of this was sent to the editorial board of the magazine.

Conflicts of Interest

The authors have completed the ICMJE declaration of conflicts of interest form, and declare that they have not received funding for the report; Not having financial relationships with organizations that may have interests in the published article in the past three years; And not having other relationships or activities that could influence the published article. Forms can be requested by contacting the responsible author or the editorial board of the Journal.

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