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Misdiagnosis in three boys with predominantly hyperactive ADHD

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Attention deficit and hyperactivity disorder (ADHD) is a neurodevelopmental disorder present in early childhood (typically before the age of 6 years) whose core symptoms are an attention deficit and/or hyperactivity disorder with or without impulsivity [1]. This disorder, in its various clinical subtypes, has consequences both on academic learning and on the relational and social life of children, which can lead, in serious cases, to exclusion from the child's normal school career and/or serious risk-taking behavior. However, certain clinical profiles may suggest other diagnoses, leading us to neglect ADHD, which can have negative consequences on the child's psychological development. We will treat about three relatively atypical cases of ADHD followed in a medical-psychological center for children and adolescents in the Paris suburbs, where hyperactivity and impulsivity are the main symptoms.

Case 1

The first case concerns a 10-year-old boy, adopted, with a very difficult academic background linked to behavioral problems in addition to other difficulties in grammar (tendency to write in a "phonetic" way), and in arithmetic. His family history was not well known due to the adoption. From our first interview we noticed an unusual hyperactivity, with excessive logorrhea that led other hospital practitioners to interrupt their consultations when the child was in the waiting room. Dialogue with the child was impossible: he almost did not answer simple questions, either went from the rooster to the donkey or took a puppet with which he talked and then had the puppet answer for him ("answers the doctor, yes, I feel fine, thank you !"), then moved on to another game and then left the office, entered into other offices during, unexpectedly addressed the child in consultation, took his toys, went out and ran in the corridors to throw himself on the ground, slid, took new toys, stole little toys with which he filled his pockets and claimed to leave the center with them, etc. Given this symptomatology, we first thought that this child could meet the criteria for mania in the context of a bipolar disorder and disruptive mood dysregulation disorder (according to DSM-5). However there was neither mood fluctuations nor depressive phases, nor hallucinations or delusions: this led us to exclude these hypotheses and to retain the diagnosis of ADHD, with hyperactivity and impulsivity. Taking account the severity of the agitation, we decided to prescribe risperidone, which was gradually increased to 3 mg/day for this 41 kg child, without obtaining any therapeutic effect. After two weeks, we opted for a reduction and discontinuation of risperidone and a prescription of methylphenidate (MPH) sustained release form. We started with 10 mg, with good tolerance and no side effects, and gradually increased to 50 mg/day with an exceptional clinical response. The child became very calm, could sit still during the interview, play board games, write on the board and understand, when told, that he or she is making spelling or syntax mistakes, etc. He sleeps well at night, but he lost 4 kg due to appetite reduction. This led us to adjust the MPH dose at 40 mg/d. A brain magnetic resonance imaging (MRI) did not reveal any structural anomalies.

Case 2

The second case was a 12-year-old boy, 40 kg, followed at a children and adolescents center for behavioral disorders such as aggressiveness, very frequent fights (several times a week), attention difficulties and disruptive behavior in class. This behavior led

teachers to suspend him several times, which worsened his school results. Brain MRI and EEG did not reveal any obvious abnormalities. The clinical examination revealed no particularities: the contact was pleasant, and the dialogue was easy. However, he soon disclosed that before falling asleep, he heard a kind of humming. Later on he even said that he heard several voices. On one occasion, one of these voices told him to throw himself through the window, but he never considered doing so. Considering a diagnosis of psychosis, a treatment with risperidone 1 and then 2 mg was initiated with an improvement in auditory hallucinations. Behaviorally, he was much calmer, there was no more fights, yet he remained hyperactive: frequently he stood up during the class and tried to talk with his classmates. He also still had learning difficulties, was distracted and unable to concentrate. After twelve weeks of risperidone his grades were still declining. We thought again about the diagnosis of psychosis. Schizophrenia in childhood is rare the lack of relational alterations or behavioral strangeness, challenged this diagnosis. A clinical reappraisal revealed the nature of his hallucinations: it was in fact his own voice that he heard, inside his head, expressing his own thought. We thus considered the diagnosis of ADHD and then decided to start extended-release MPH at 10 and then 20 mg which clearly improved attention and hyperactivity without a resurgence of auditory hallucinations. Risperidone was reduced to 1 mg/day.

Case 3

The third case was a 10-year-old boy, 23 kg, with a history of quite extreme violent behavior since the age of 4 years, despite a normal development. On the first day of kindergarten he bits his teacher and hit other children. His father and three of his paternal uncles had a diagnosis of ADHD and his twin brother met criteria for attention deficit without hyperactivity. The patient underwent psychometric and medical check-ups at a university hospital at the age of 6 years to rule out an ADHD: he was diagnosed as "oppositional defiant disorder" (DSM-5). He continued to attend school normally, with good academic results and there was no significant attention deficit in classrooms. It should be noted that almost all impulsive episodes (biting, tapping, kicking and insulting) occurred during pause or canteen time. He also had a persistent nocturnal enuresis and frequent nightmares. The Wechsler scale (WPPSI-IV, 4th edition) informed us that he had a working memory with a "low average" index of 82 (12th percentile). Especially in the "image recognition" and "spatial memory" tests, the child had a tendency to rush to give the answer (information processing speed = 97; 42nd percentile). Throughout the test, he tended to be agitated. and the psychologist concluded to "oppositional disorder with provocation with psychomotor agitation episodes depending on the context. Because of hetero-aggressivity, risperidone 2 mg was prescribed, with a decrease in the frequency of nightmares and limited effects on aggressiveness. Valproic acid was prescribed up to a dose of 400 mg/day. But faced with the persistence of nightmares, and given the family history of ADHD, it was decided to prescribe MPH extended-release 10 mg in addition to the risperidone dose, with a very good tolerance of the product and without any increase in impulsivity. A gradual decrease and discontinuation of valproic acid could be performed without an increase in impulsivity.

Discussion

Hyperactivity in children has been described for more than a century. Currently, the DSM-5 describes three core symptoms to define ADHD: attention deficit, hyperactivity and impulsivity. Mixed forms are described as well as non-mixed forms, namely either pictures where what predominates is attention deficit without hyperactivity or impulsivity, or clinical pictures where what predominates is hyperactivity with or without impulsivity and where attention deficit is not in the foreground, although it may be present. It is possible that different regions of the brain are involved in each clinical subtype (motor cortex for hyperactivity, orbitofrontal cortex for impulsivity, dorsal anterior cingulate gyrus for selective attention [2], etc.). The clinical polymorphism of this disorder should lead us to contemplate the different functional components involved in ADHD. Although MPH is prescribed in ADHD, there are contraindications to it, including the presence of hallucinations. The three cases described above show us that we must be very attentive to the different clinical forms and carefully assess the patients.

For the first case presented, agitation and logorrhea were so important that the first diagnosis mentioned was that of hypomania. The fact that the symptoms have existed since early childhood (before the age of 6 years), made us to exclude this diagnostic hypothesis and focus on ADHD. As far as the "Disruptive mood dysregulation disorder" is concerned, we did not have the existence of outbursts or even "verbal rages". Antipsychotic treatment (risperidone up to 2 mg/day) was initiated with no effect on permanent agitation or logorrhea. The fact that the picture has been normalized through MPH should indicate that neurobiological processes different from those overactivated in bipolar disorder were at stake. In the second case, the severe attention deficit, hyperactivity and impulsivity clearly pointed us towards ADHD, but the presence of "auditory" hallucinations led us to make a diagnosis of "psychotic disorder" (for example, schizophrenia). With regard to the latter diagnosis, the lack of relational alterations or behavioral strangeness, as well as the absence of delusions, and finally a requalification of hallucinations as his own thought, made us to consider an ADHD diagnosis. Although hallucinations are not common in patients with ADHD (except as a side effect of MPH), when we have clear criteria for ADHD we should wonder whether this is not a consequence of attention deficit, namely a tendency to "dream" that could be described as highly animated and confused scenarios, by the child and interpreted by the child and the clinician as "voices": It should also be noted that this child, even at the age of 12, still use to play with small cars and soldiers to whom he lent his own voice. Furthermore, according to some authors [3, 4], ADHD and "psychotic disorder" could exist in the different moments of lifespan. The third case presented is undoubtedly the most typical and atypical at the same time: on the one hand, impulsivity and hyperactivity were obvious from early childhood but the assessment carried out at the university hospital did not conclude at the presence of an ADHD. But the presence of both an outstanding family history of ADHD and a nocturnal enuresis from birth directed us towards the diagnosis of ADHD. Indeed, enuresis is more prevalent in the pediatric population with a diagnosis of ADHD than in the general pediatric population [5]. Another question seemed to us relevant is the fact that episode of impulsivity occurred in the particular sensorial conditions (pause or canteen time): sensorial stimulation would be more difficult in ADHD children [6]. We hesitated before prescribing MPH but not only was it well tolerated without side effects but, moreover, it significantly improved its impulsivity. Again: the prescription of MPH could have caused behavioral problems or aggravated agitation, but we do not perceive such side effects.

Finally, let us also consider the co-prescription of anti-psychotics (risperidone) in two of the three cases described: although at first sight the prescriptions for MPH and antipsychotics may seem almost paradoxical (one increasing dopaminergic transmission and the other inhibiting it), it must be noted that these two drugs can act on two different regions of the CNS and, on the other hand, that dopaminergic receptor antagonism (particularly D2) can reduce the side effects of MPH, as has been reported by other authors[7]. Other authors have described the use of methylphenidate in combination with risperidone in ADHD children with conduct disorders symptoms [8].

Conclusion

ADHD is a neurodevelopmental disorder that has been present, in general, since early childhood. Mixed forms are common, as are those in which there is only one of the components present, giving very different clinical profiles: the child with attention deficit alone will be a rather calm, distracted child, who could be considered shy and with a tendency to isolate himself, while children with hyperactivity (and/or impulsivity), on the contrary, will tend to socialize, speak more than others, impose their will, etc. In the cases presented in this article, the severity and complexity of clinical pictures of very disruptive and aggressive behaviors led us not to consider the diagnosis of ADHD: first clinical impression in the first case seems to be an hypomania, the second case seems to be an early onset of schizophrenia and the third case seems to be an oppositional defiant disorder, while a more accurate clinical and psychiatric examination and the positive response to MPH leads us, on the contrary, to revise the initial diagnoses for a diagnosis of ADHD.

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