

COMPLICATED CASE HISTORIES

Key Words: Bipolar Disorder; High Functioning Autism; Substance-Induced Mood Disorder

Drug Induced Mania in a Boy with High Functioning Autism

By *Mustafa Deniz Tutkunkardas,*
Nahit Motavalli Mukaddes

ABSTRACT ~ Drug induced mania is sometimes associated with drug that are primarily not used for central nervous system effects. Here we report a manic episode during the treatment of leukemia with various agents in an adolescent with diagnosis of high functioning autism. In this case, most likely candidates to induce a manic episode were dexamethazone, a corticosteroid used in the treatment of T-ALL, cyclophosphamide and cotrimoxazole. Although literature on mood disorders associated with corticosteroids exceeds that of cyclophosphamide and cotrimoxazole, an absolute causal drug cannot be stated. Psychopharmacology Bulletin. 2010;43(2):78-81.

INTRODUCTION

Manic symptoms are frequently reported with various drugs that cross the blood brain barrier. Drugs used primarily not for central nervous system effects that reportedly cause mania are: corticosteroids, androgenic steroids, thyroxine, chloroquine, baclofen, captopril, cotrimoxazole, clarithromycin.^{1,2} A literature review revealed a few reports of mania in patients treated with chemotherapeutics, namely ifosfamide^{3,4} and a combination of 5-fluorouracil, epirubicin and cyclophosphamide.⁵ Of these, one of the most well established are the corticosteroids, and literature review revealed a few steroid induced mania in adolescents.⁶

Here we report a manic episode during the treatment of leukemia with various agents in an adolescent with diagnosis of high functioning autism (HFA). The probable role of treatment and management program will be described.

Drs. Tutkunkardas, MD, Mukaddes, MD, Child, and Adolescent Psychiatry Department, Istanbul School of Medicine, Istanbul University, Istanbul, Turkey.

To whom correspondence should be addressed: Nahit Motavalli Mukaddes, Istanbul Üniversitesi, İstanbul Tıp Fakültesi Çocuk Psikiyatrisi Anabilim Dalı, 34093, Capa, İstanbul, Turkey. Phone/Fax: +902124142000, 31390; Email: nmotavalli@yahoo.com

CASE HISTORY

S.O., a 14 year old boy and a regular patient of our autism clinic with diagnosis of HFA (IQ: 92), was hospitalized in pediatric oncology clinic and received the diagnoses of T-cell acute lymphoblastic leukemia (T-ALL) and pneumonia. He had the additional diagnosis of attention deficit hyperactivity disorder at the age of 6. Because of his hyperactivity he had been given quetiapine, olanzapine, risperidone, methylphenidate and trazodone interchangeably. Due to the lack of efficacy and noncompliance all medications were ceased at the age of 9 and he was medication-free since then. His medical history was unremarkable until diagnosis of T-ALL. His family history revealed that his mother suffered from severe major depression, for which she was hospitalized a few times.

SYMPTOMATOLOGY

He had been given antimicrobial therapy that included cotrimoxazole, caspofungin, linezolid, netilmicin, a chemotherapy (CTx) regimen that consisted of dexamethasone, vincristine, cytarabine, methotrexate, cyclophosphamide, asparaginase and allopurinol. In the fifth day after the initiation of CTx his parents and doctors noticed some differences in his behavior. He started to talk too much, kept talking about football endlessly, didn't seem to care about his medical condition and started to stay awake during day and night. Therefore a psychiatric consultation was requested. His psychiatric evaluation revealed no disturbance in his orientation and perception. Mood elevation, irritability, pressured speech, flight of ideas and grandiose delusions were prominent. He claimed that he personally knew the prime minister of Turkey and was friends with the technical director of a football team.

DIAGNOSIS

According to his parents, his physician and other staff, all these symptoms appeared in the fifth day of treatment. In addition, a review of his records in our autism clinic revealed that he had no history of manic symptoms before admission to oncology service. Magnetic resonance imaging failed to show evidence of metastasis in his brain. Therefore, he got additional diagnosis of drug induced mood disorder, with manic features, with mood congruent psychotic features. And he got 41 points from Young Mania Rating Scale—Turkish Edition.

TREATMENT

His CTx regimen consisted of 7 day periods of drug therapy followed by a 2 week interval. As being a part of CTx regimen dexamethazone could not be stopped, he was prescribed risperidone 3 mg/day. His first CTx period ended 2 days after the initiation of risperidone but his mood disorder did not subside. So risperidone was titrated up to 5 mg/day. After 2 weeks and in the 8th day of 5 mg/day risperidone, his symptoms started to decline, he began to sleep at night, his speech slowed down, his grandiose delusions disappeared and his associations slowed down. Although not euthymic, his mood was not that elevated and he got 8 points from Young Mania Rating Scale—Turkish Edition. His second CTx period followed his stabilization, which produced some irritability but failed to flare up his previous symptoms. During this whole time none of his antimicrobial agents were stopped. As of writing this he is still hospitalized, and going on with his CTx and risperidone, and the outcome of both the T-ALL and the drug induced mood disorder are uncertain.

80*Tutkunkardas,
Mukaddes*

DISCUSSION

In the case presented above, there are some points that need to be discussed. First point is that absolute causal drug for mania cannot be easily established due to the polypharmacy the patient has been receiving. But most likely candidates were dexamethazone, a corticosteroid used in the treatment of T-ALL, cyclophosphamide and cotrimoxazole. Although literature on mood disorders associated with corticosteroids exceeds that of cyclophosphamide and cotrimoxazole, an absolute causal drug cannot be stated. Second important point is to establish other risk factors in subjects that suffer from HFA. Many studies detected a relationship between high functioning group of autism spectrum disorders (ASD) and bipolar disorder (BP).^{7,8} Although the reported range of bipolar disorder in clinical samples of ASD is wide (0.7% to 27%),⁹ majority of researchers agree that individuals with HFA are more vulnerable to develop both depression and BP. In this case, positive family history is another contributing factor for the development of a mood disorder.

Third important point that needs to be clarified is the management of mania in this case. Although in the case of emergence of a mood disorder during treatment, the established method of treatment is to stop the drug of interest, this method could not be applied in this instance both due to the polypharmacy he was receiving and the vitality of the

treatment of T-ALL. As the patient's symptoms subsided and didn't reemerge with the second period of CTx, this indicates that in cases which treatment is of vital importance and could not be stopped, careful management of manic symptoms could alleviate the problem.

Because drug induced mood disorders is not a well established entity in children, especially in children with ASD, there is no data about the need for long term mood stabilization, agents of choice in this specific subgroup, and long term occurrence of spontaneous manic episodes. Further studies investigating these debatable issues would shed light on our understanding and management of drug induced mood disorders in children and adolescents. ♣

ACKNOWLEDGEMENTS

Authors declare no competing interest.

REFERENCES

1. Peet M, Peters S. Drug-induced mania. *Drug Saf*. 1995;12:146–153.
2. Abouesh A, Stone C, Hobbs WR. Antimicrobial-induced mania (antibiomania): a review of spontaneous reports. *J Clin Psychopharmacol*. 2002;22:71–81.
3. Brieger P, Marneros A, Wolf HH, Schmoll HJ. Manic episode in an ifosfamide-treated patient. *Gen Hosp Psychiatry*. 2000;22:52–53.
4. Kerdudo C, Orbach D, Sarradet JL, Doz F. Ifosfamide neurotoxicity: an atypical presentation with psychiatric manifestations. *Pediatr Blood Cancer*. 2006;47:100–102.
5. Pacchiarotti I, Mazzarini L, Pellegrini P, Venturelli V, Sani G, Sánchez-Moreno J, Mancinelli I, Tatarelli R, Kotzalidis GD, Girardi P. A case of manic episode during treatment with 5-fluorouracil, epirubicin and cyclophosphamide for breast cancer. *Gen Hosp Psychiatry*. 2007;29:461–463.
6. Couturier J, Steele M, Hussey L, Pawliuk G. Steroid-induced mania in an adolescent: risk factors and management. *Can J Clin Pharmacol*. 2001;8:109–112.
7. DeLong R, Nohria C. Psychiatric family history and neurological disease in autistic spectrum disorders. *Dev Med Child Neurol*. 1994;36:441–448.
8. Munesue T, Ono Y, Mutoh K, Shimoda K, Nakatani H, Kikuchi M. High prevalence of bipolar disorder comorbidity in adolescents and young adults with high-functioning autism spectrum disorder: a preliminary study of 44 outpatients. *J Affect Disord*. 2008;111:170–175.
9. Mukaddes NM, Fateh R. High rates of psychiatric co-morbidity in individuals with Asperger's disorder. *World J Biol Psychiatry*. 2009;6:1–7.