

Methylphenidate Treatment for Severe ADHD in a Bone Marrow Transplant Child with DiGeorge's Anomaly(*)

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ABSTRACT:

Methylphenidate treatment for severe ADHD in a bone marrow transplant child with DiGeorge's anomaly

As the number of bone marrow transplantations (BMT) performed in the pediatric age group is on the rise, there is a growing need to expand our knowledge of psychopharmacological interventions in this special situation. We report a case who had undergone BMT for congenital immunodeficiency syndrome involving thymus aplasia. He was referred to the child psychiatry department with severe hyperactivity and mental retardation. Taking the necessary medical precautions, methylphenidate was started and continued for over a year. Marked improvement in the symptoms of attention deficit hyperactivity disorder (ADHD) and better adaptation to his educational setting were achieved. No adverse event occurred with regard to his vulnerable immune system.

Key words: methylphenidate, immune system, bone marrow transplantation, immunodeficiency, attention-deficit with hyperactivity disorder (ADHD)

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ABSTRACT:

Kemik iliği nakli yapılan DiGeorge anomalisi olan bir çocukta şiddetli DEHB'nun metilfenidatla tedavisi

Çocuk yaş grubunda gerçekleştirilen kemik iliği nakilleri artmakta olduğu için psikofarmakolojik girişimlerle ilgili bilgileri de geliştirme gereksinimi vardır. Bu konuya klinik bir katkı yapmak için timus yokluğunu da içeren doğumsal bağışıklık yetmezliği sendromu nedeniyle kemik iliği nakli yapılan bir olguyu bildiriyoruz. Olgunun çocuk psikiyatrisine getiriliş nedeni aşırı hareketlilik ve zeka geriliğiydi. Gerekli tıbbi önlemler alındıktan sonra metilfenidat başlandı ve bir yıldan uzun süre devam edildi. Tedaviyle, dikkat eksikliği hiperaktivite bozukluğu (DEHB) belirtilerinde belirgin azalma ve eğitim ortamına daha iyi uyum elde edildi. Hastanın duyarlı bağışıklık sistemini etkileyen hiçbir yan etki gözlemlenmedi.

Anahtar sözcükler: metilfenidat, bağışıklık sistemi, kemik iliği nakli, bağışıklık yetmezliği, dikkat eksikliği hiperaktivite bozukluğu (DEHB)

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INTRODUCTION

While behavioral aspects of secondary immunodeficiency syndromes receive considerable attention especially in cases with human immunodeficiency virus (HIV) infections, primary immunodeficiency syndromes are slow to evoke such interest probably due to their relatively low incidence and earlier presentation in life. It is already known that moderate to severe mental retardation is part of DiGeorge's anomaly (1) but no data regarding the behavioral features of primary immunodeficiency syndromes is available beyond this point. The medical treatments indicated in immunodeficient conditions bring out

new neuropsychiatric challenges which are complicated by developmental issues. Bone marrow transplantation (BMT), an accepted treatment modality in primary immunodeficient states, besides its being a stressful process for the child, requires important clinical considerations with regard to vulnerable immune and hematologic system. Although psychopharmacological recommendations after organ transplantation were described with a general perspective, there did not exist a specific focus for the pediatric age group (2). Therefore, to date, no published data available for psychopharmacological interventions in the child and adolescent transplant cases has left the issue of clinical practice in an uncertainty.

We hereby report the beneficial

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use of methylphenidate in a primary immunodeficient and eventually bone marrow transplant child for severe attention deficit hyperactivity disorder (ADHD) without adverse effects.

CASE REPORT

G was a six and a half-year-old boy presenting with the chief complaints of severe hyperactivity and uncontrollable behaviors. This family of Turkish origin was residing in Germany, and the psychiatric admission was made during the summer vacation in Turkey. His mother was a 32-year-old unemployed housewife and father, a 45-year-old real estate agent. He had a 10-year-old brother.

The onset of hyperactivity was very early in his life. Besides that, he had also marked developmental delays. Although his developmental retardation was first recognized by the age of three, limited educational intervention could be made as a consequence of his hyperactivity. The most important part of his history was that he had been diagnosed as having congenital immunodeficiency (DiGeorge's anomaly) which manifested itself with diarrhea and respiratory infections in his early life. Thymus was found to be absent. Subsequently he underwent BMT twice, the first one at the age of 8 months and the other one at the age of 24 months. Donor of the histocompatible bone marrow was his father. He was in complete remission since that time whilst monthly immunoglobulin injections were indicated.

In the clinical assessment, the presence of a persistence state of hyperactivity, short attention span, oppositional behavior, disordered verbal communication, and an apparent state of mental retardation were noted.

In the psychological testing, Ankara Developmental Screening Inventory (ADSI) (3) and Goodenough-Harris Test (4) were applied. Whilst he was 78 months old at the time of the assessment, ADSI revealed an overall developmental level of 45 months, verbal-cognitive, social skills-self care and fine motor development level of 42 months, and gross motor development level of 31 months. Goodenough-Harris Test showed an overall intelligence quotient of three and half years equivalent. The revised Conners Parent Rating Scale

(CPRS-R) (5, 6) revealed the scores which were suggestive of inattentiveness and hyperactivity, but not conduct problems: 11, 9, 4 and 7 on the hyperactivity, attention, oppositional and conduct problems subscales, respectively.

All these data led to the diagnoses of ADHD and moderate mental retardation (MR) based on the criteria of DSM-IV (7).

The priority was given to adapt him to the educational settings; therefore we aimed to control his hyperactivity. The risks and benefits of the planned psychopharmacological interventions were discussed with the parents and parental consent was obtained. After consulting his pediatrician and obtaining basic physical and laboratory data of hepatic, nephrologic, hematologic and thyroid functions, methylphenidate (Ritalin®) was started at 10 mg/daily (0.6 mg/kg) in divided doses in the morning and during lunch time. The drug was continued at the week-ends also. He responded very well to the medication and his hyperactivity remarkably diminished. Delay of sleep onset and reduced appetite were the only noticed side effects early in treatment which were mild and short-lived. Significant reductions were achieved on the CPRS-R subscales: 4, 3, 3 and 4 on the hyperactivity, attention, oppositional and conduct problems subscales, respectively. No sign of deterioration in his vulnerable immune system was observed for over a year. Monthly whole blood counts and immunoglobulin levels were all within normal limits. No incident of infection was noted. Dose adjustment was not needed except for occasional midafternoon doses indicated. He could readmit to the psychoeducational settings in Germany and adapt well. Significant improvement was noted in his abilities which were the primary focus of special education.

DISCUSSION

The question of whether there may be a psychiatric implication of aplasia of thymus, an organ where endocrine and immune functions meet, certainly remains. What we already know is that mental retardation is a common comorbidity in congenital syndromes. In contrast to ADHD, which is the most commonly diagnosed behavioral disturbance

affecting up to 4-12% of all schoolchildren (8), congenital immunodeficiency syndromes are rare. Therefore, it is unclear whether these two conditions are related or it is just a coincidence.

Psychostimulants are still the drug of first choice in ADHD with a well-established therapeutic efficacy. Despite clinical experience with methylphenidate is vast, little evidence is available to ease the practice in post transplant children. However, there's no reported contraindication in either immunodeficient or post transplant cases (9). For comorbid ADHD and MR, stimulant medication is recommended even at higher doses than usual doses (10). As pointed out above, methylphenidate treatment produced very positive effects in psychoeducational setting which would have not been achieved otherwise. The side effects observed early in treatment were short-lived and did not hamper further treatment. Among the most common side effects in the stimulant treatment are delay of sleep onset, reduced appetite, weight loss, tics, stomach-ache, headache, and jitteriness (9). The latest long-term effects of the drug will be monitored meanwhile.

Auci et al. (11) reported the transient suppression of T-helper/inducer cells and hypergammaglobulinemia in humans and mice as side effects of methylphenidate treatment which imply further studies. What he suggested is that if hyperactivity of the immune system is a side effect of methylphenidate treatment, then treatment with this drug may be risky for children who are HIV-positive, possibly because of triggered events that may facilitate the entry into the cells and replication of the virus. Recent reports of

amphetamine effects on T-cells seem to support this suggestion (12,13). On the contrary, methylphenidate treatment in HIV-positive cases is advocated (14). Moreover, in a case report, clonidine, which is an alternative drug in the treatment of ADHD, was described to be helpful in a 4-year-old child with HIV-1 infection who presented with hyperactivity, impulsivity and aggression (15). However, as can be obviously seen, these reports provide little help for the medication of the present case as the described syndromes are infectious in nature and BMT is never indicated in their treatment.

To our knowledge, this is the first report of the use of methylphenidate in a child with ADHD who had undergone BMT for immunodeficiency syndrome. The appropriateness of using methylphenidate in children who has undergone BMT for other indications should also be considered. Psychopharmacological interventions after solid organ transplantations, particularly the use of methylphenidate as in the present case, are also need to be done so. Although the case we report here is with positive outcome and no adverse effect, necessary precautions should always be taken in medicating similar cases with methylphenidate. Clinical guidelines, based on empirical evidence may then be developed to help the clinicians in their practice for this special group of patients.

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