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Using of methylphenidate and risperidone in a case with Joubert's syndrome with comorbid disruptive behavior disorders

Yıkıcı davranım bozukluklarının eşlik ettiği Joubert sendromlu bir olguda metilfenidat ve risperidon kullanımı

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Abstract
Joubert sendromu molar diş görünümü ile karakterize nadir bir orta beyin-beyin malformasyonu bozukluğudur. Posterior interpedinküler fossa derinliğinde artma, süperior serebellar pedinküllerde kalınlaşma ve vermis hipoplazisi bu sendromda görülen bulgulardır.
Serebeller bozukluklar şiozfreni, bipolar bozukluk, depresyon, anksiyete, dikkat eksikliği hiperaktivite bozukluğu (DEHB) gibi birçok psikiyatrik bozukluğa neden olabilmektedir. Bir çok çalışmada DEHB'nda serebellumda değişiklikler gösterilmiştir. DEHB ile serbellum ve posterior fossa volumleri arasında ilişki gösteren çalışmalar da mevcuttur.
Bu olguda Joubert sendromunda DEHB, davranım bozukluğu ve mental retardasyon etyolojik mekanizmaları ve tedavileri açısından tartışılması amaçlanmıştır.

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Keywords: Joubert sendromu, DEHB, mental retardasyon, davranış bozukluğu, tedavi.

Özet
Joubert syndrome (JS) is a rare disorder characterized by a peculiar mid-brain-cerebral malformation and is known molar tooth sign (MTS)) Posterior interpedincular fossa's depth increases, superior cerebellar peduncles thicken and vermis is hipoplastic in this syndrome.
Cerebellar disorders; can cause many psychiatric disorders, including schizophrenia, bipolar disorder, depression, anxiety and attention deficit hyperactivity disorders. Many studies have shown that changes in the cerebellum in ADHD. In fact, some studies report that there is a relationship between ADHD severity with cerebellum volume and posterior fossa.
ın this case report we aimed to discuss etiological mechanisms and treatment of mental retardation, ADHD and conduct disorder in joubert sydrome.

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Anahtar sözcükler: Joubert syndrome, ADHD, mental retardation, conduct disorder, treatment.

Introduction

Joubert's syndrome (JS) is a rare disorder characterized by a strange midbrain-brain malformation known as molar tooth image (MTS) [1]. There is an increase in the depth of posterior interpeduncles fossa, thickened superior cerebellar peduncles and vermis hypoplasia [2]. In addition, Joubert syndrome is a versatile syndrome with neuroanatomical, physical components as well as neurobehavioral components [3]. Joubert syndrome with autosomal recessive inheritance can be seen in both genders but is twice as much in males (M/F:2) [3]

It is known that cerebellum plays an important role in coordination and motor functions. It has also been reported that recent studies have also been involved in modulation of mood,cognition and psychiatric disorders. It appears that the cerebellum has a regulatory role,either directly or indirectly, by increasing or supplementing the functions of the other brain regions. The disorder in the cerebellum may cause many psychiatric disorders including schizophrenia,bipolar disorder, depression, anxiety and attention deficit hyperactivity disorder [4].

Many studies have shown that there are changes in the cerebellum in ADHD. Even some

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studies report that the severity of ADHD is related to the volume of the cerebellum and posterior fossa [5]. The fact that cerebellar volumes of patients receiving psychostimulants are higher than those who do not, suggests that cerebellar functions are important in the etiology of ADHD. A longitudinal study which ADHD and healthy controls were compared during 2-14 years by Mackie and colleagues found that ADHD group had smaller vermises than controls in every visit and this finding remained unchanged during the developmental period. In addition, patients with small vermis lobules due to stroke or other developmental anomalies are reported to have decreased attention directing ability [6].

Neurobehavioral development of children with Joubert syndrome is not fully defined. Children with Joubert syndrome have been shown to have intelligence ranging from IQ <30 to 85 and have been identified as one of the original findings of mental retardation disease. There are three possible consequences of Joubert syndrome; 1- Patients die at a young age, 2- they have to live serious developmental strains with vision and motor problems 3- Patients show mild developmental delay. Their parents report hyperactivity, aggression, and addiction in these children. Neurocognitive problems such as fluent speech problems, verbal memory, picture-word matching problems are also seen [3,7].

In this case report, it is aimed to discuss the emergence mechanisms and treatment of mental retardation, attention deficit hyperactivity disorder and conduct disorder seen in patients with Joubert syndrome. The permission of the parents is taken for this case report.

Case

O.S. 6-year-old boy was evaluated at the child psychiatry clinic with complaints of extreme mobility, irritability, rapid cramping, unwillingness to school, escape from school, and harm to peers and animals. It has been learned that a patient with no family history has a late of speech skills and social, academic, and daily adjustment function Is back from peer groups and also due to central minimal mitral insufficiency. The patient's mother reported that he has been hyperactive, impulsive since the age of 3, and that his attention was back from her peers and that these situation has destroyed participation in the school and peer communication. Physical examination included hypertelorism, blue sclera, nasal pustule, low ear and clinodactyly. Considering the evaluation of intelligence (2013 St. Binet: 63) and DSM-IV-based Screening and Assessment Scale for Behavioral Disorders in Children and Adolescents filled by parents and teachers, ADHD conduct disorder and Mild Mental Retardation were diagnosed. Treatment with long-acting (OROS) methylphenidate 18 mg/day + risperidone 1 mg / day was planned. After 3 months, conduct disorder and ADHD symptoms and scale scores decreased. In magnetic resonance imaging (MR), molar tooth appearance is seen in the cross sections of sagittal and axial T1A, T2A and Flair axial sections at midbrain level. Cerebellar vermis is hypoplastic and displaced. The fourth ventricle was seen as dilated and extended posteriorly. In addition, the fourth ventricle is continuous with cisterna magna (Figure 1 and 2). The findings described in the cross sections of the middle brain are thought to be compatible with Joubert syndrome.

Discussion

Although mental retardation or developmental delay is accepted as a component of Joubert syndrome, there is insufficient study of psychiatric problems in children with Joubert syndrome. In this case, radiological findings support JS. In this patient, ADHD, MR and conduct disorder are seen together. In the event, ADHD and Behavioral disorder were either incidental to JB, or the presence of cerebellar dysfunction in JB caused or contributed to the manifestation of ADHD and impaired behavior. The most prominent brain anomalies in Joubert syndrome are pontomesencephalic connections originating from primitive isthmus and superior cerebellar peduncles and cerebellar vermis. The molar tooth image is caused by deep cleft, thickened and reoriented superior cerebellar peduncles and vermian hypoplasia of the Brainstem isthmus [8]. In addition to radiological findings, there may be hypotonia, ataxia, abnormal breathing, visual problems. The most dominant feature is the developmental delay [2].

Studies on the role of cerebellum in attention and motor response are increasing. Neocerebellar fields in healthy volunteers are active during information coding and recall [9]. A global decline in brain volume has been

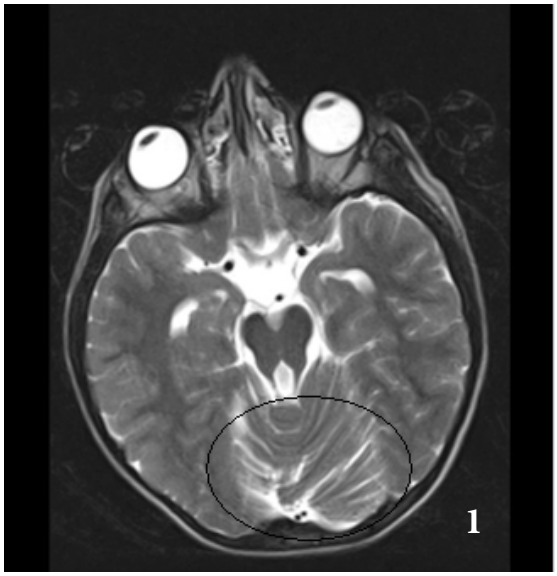

Figure 1. Cerebellar peduncles and vermis hypoplasia in Joubert's syndrome

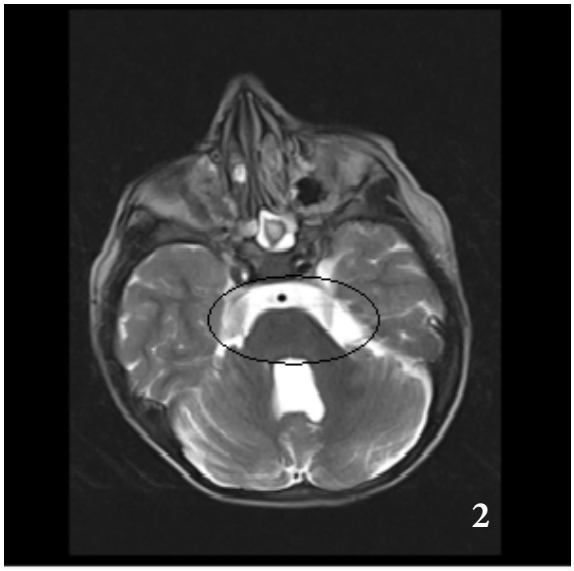

Figure 2. Midbrain changes in Joubert's syndrome

demonstrated in ADHD. Areas of decline are especially prefrontal cortex, basal ganglia, cerebellum and temporapariatel areas. In addition, problems in completing a timing task in ADHD were associated with the cerebellum [10]. In neuroimaging studies performed on schizophrenia, it has been shown that there are pathologies in the cerebellum vermis, particularly in relation to the dysfunctions associated with certain tasks. Cerebellar dysfunction also causes various developmental problems such as ADHD, autism, and dyslexia. Studies have shown that inferior-posterior vermis of cerebellum in children with ADHD is smaller when compared to the control group [11]. In patients with ADHD, structural delayed fronto-striatal, fronto-temporo-parietal, and fronto-cerebellar nerves were shown in the structural MR studies compared to control groups. It is known that the above-mentioned networks are mediated by cognitive functions. In ADHD, decreased volume and increased cortical density are observed in the frontal brain regions, parieto-temporol area, basal ganglia, posterior cingulate, cerebellum, and splenium of the corpus callosum [12].

In ADHD treatment, there are two options, stimulated and non-stimulated. They do not only improve attention, but also improve executive functions. The use of methylphenidate has also been reported in neuro-behavioral problems associated with various neurological problems (traumatic brain injury and stroke) [13]. Long-term methylphenidate treatment causes an improvement in the structural abnormality of the gray matter in the anterior cingulate cortex, thalamus and cerebellum [14]. It is also reported that risperidone has moderate efficacy in behavioral disorders accompanying mental retardation with ADHD comorbidity or not [15].

This article mentions a case of Joubert syndrome with many psychiatric problems treated with methylphenidate and risperidone. Psychopharmacotherapy has been shown to be useful in psychiatric problems in the Joubert syndrome.

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