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Attention deficit hyperactivity disorder and specific learning disability co-occurring in a case with Silver-Russell syndrome

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ABSTRACT

This case presentation discusses the management of comorbid attention deficit hyperactivity disorder (ADHD) and specific learning disability (SLD) in a female adolescent diagnosed with Silver-Russell syndrome (SRS).

A 13-year-old female patient presented to the child psychiatry outpatient clinic eight months ago with complaints of reading and writing difficulties and forgetfulness. When she was four years old, she was diagnosed with SRS. Somatotropin therapy was initiated for the patient. Based on psychiatric examination, family interviews, psychometric assessments, and information obtained from school, the patient was diagnosed with ADHD and SLD. The patient was started on methylphenidate treatment, gradually titrated to a dose of 27 mg/day. She was also referred for special education for the SLD diagnosis. In the literature, it has been reported that in most children with SRS, intelligence is within the normal range, and they often receive diagnoses of ADHD and/or SLD. Studies have shown that although, executive function disorders are not significantly associated with SRS in comparison to control groups, there is an increased risk. Children and adolescents with this rare congenital disorder are at risk for psychiatric disorders, and periodic evaluation by a child psychiatrist is recommended.

Keywords: Silver-Russell syndrome, Attention deficit hyperactivity disability, Specific learning disorder, Child, Neurodevelopmental disorders

1. INTRODUCTION

Silver-Russell syndrome (SRS) is a heterogeneous congenital disorder characterized by growth retardation, low birth weight, short stature, and dysmorphic facial features. Approximately 60% of patients diagnosed clinically with SRS can have an underlying molecular cause identified. The most common underlying mechanisms include loss of methylation at chromosome 11p15 and maternal uniparental disomy for chromosome 7 [1]. The prevalence of the condition is estimated to be 1 in 30,000 to 1 in 100,000 live births [2]. Studies have shown that individuals with SRS are at significant risk for both motor and cognitive developmental delay, as well as learning difficulties [3]. Due to these risks, individuals with SRS need developmental assessments from infancy onward. Moreover, research has shown that negative body image concerns in children and adolescents with SRS can lead to psychosocial problems, anxiety disorders, social anxiety, and depression [4].

Attention deficit hyperactivity disorder (ADHD) is a mental disorder characterized by age-inappropriate attention problems, excessive motor activity, and/or impulsivity (such as inability to delay gratification, acting without thinking, and impulsivity) that become evident in preschool and school-aged children and persist throughout life. It is classified under the title "Attention-Deficit/Hyperactivity Disorder" in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). It has three subtypes: "Predominantly Inattentive Presentation," "Predominantly Hyperactive/Impulsive Presentation," and "Combined Presentation," which includes symptoms from both groups. According to DSM-5 criteria, for the predominantly inattentive presentation, at least six out of nine symptoms should be present; for the predominantly hyperactive/impulsive presentation, at least six out of nine symptoms should be present; and for the combined presentation, both sets of criteria should be met. Symptoms should be present in two or more settings before

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the age of 12 for at least six months and should impair social, academic, or occupational functioning. ADHD, one of the most common mental disorders in childhood, is associated with impairments in behavior, emotions, academic performance, and social functioning. When left untreated, it can lead to ongoing difficulties in adulthood as well [5, 6].

Specific learning disability (SLD) is a neurodevelopmental disorder that arises from the interaction of genetic, epigenetic, and environmental factors. In the DSM-5, learning disability is addressed in various subcategories, including difficulties in reading, reading comprehension, writing, written expression, understanding numbers and calculations, learning numerical reasoning, and academic skills. It involves challenges not only in academic areas but also in motor, sensory, and perceptual domains. Reading difficulty (dyslexia) is the most common among these disorders [5, 7].

Specific learning disability can be defined as specific deficiencies in perceiving and processing information. Additionally, individuals with SLD experience problems in auditory and visual perception, memory, fine and gross motor skills, attention, language and communication, abstraction, and social skills. Delay in language development, difficulty in word finding and naming, mixing up basic words, word-syllable conversion (e.g., saying "vami" instead of "mavi", saying "fison" instead of "sifon") difficulty in learning letter-sound relationships; difficulty in motor skills, inability to use scissors, inability to use fork and spoon, coordination difficulties, difficulties in understanding similarities and differences, and confusion in directions can be given as examples [8].

Due to its neurodevelopmental nature, SLD can exhibit different characteristics throughout life, starting from early stages of life. Studies in the literature have found that children with SRS have a higher frequency of SLD and ADHD disorder compared to the general population [9].

In this case presentation, the management of a female adolescent followed up with SRS diagnosis along with coexisting ADHD and SLD was discussed in light of the literature.

2. CASE REPORT

A thirteen-year-old girl was brought to the child psychiatry outpatient clinic eight months ago with complaints of difficulty in reading and writing and forgetfulness. It was learned from her medical history that she was born via cesarean section due to prematurity at 36 weeks of gestation following an uncomplicated and planned pregnancy. She was born weighing 2160 grams (-1.9 SDS) and measuring 43 cm (-2.3 SDS), and did not experience any perinatal or postnatal medical issues. It was learned that the patient, who was breastfed for about four months, started walking at fifteen months of age, began speaking meaningful single words at sixteen months of age, and received toilet training at the age of three. At the age of six, due to insufficient growth in height and weight, she was referred to pediatric endocrinology. During the physical examination, her weight was measured as 12.5 kg (-3.7 SDS) and her height as 96 cm (-4.1 SDS). Broad forehead, relative macrocephaly, and triangular facial appearance were observed, and the patient was diagnosed with Silver-Russell syndrome using the Netchine-Harbison clinical scoring system [1].

Recombinant growth hormone therapy (somatropin) for short stature, which she had been using for seven years, was stopped five months ago. In the family history, it was found that the mother, aged 31, is physically and mentally healthy, has a primary school education, and is a housewife; the father, aged 36, is physically and mentally healthy, has a high school education, and working in the auto electrical business to support the family. It was also noted that the patient's two brothers are healthy. No specific features are identified in the family history.

In the educational history, it was noted that the patient attended kindergarten for two years, had difficulty learning colors, numbers, and shapes, had good relationships with peers, did not have any separation anxiety from parents, learned to read and write in the second term of the first grade, but lagged behind peers in school subjects and literacy, is currently in the sixth grade with low academic performance, struggles to focus on lessons in class, easily gets distracted while studying, has difficulty sustaining attention on tasks, exhibits forgetfulness in completing household chores, and has trouble following teachers' instructions or completing school assignments properly.

In the psychiatric examination, it was observed that the patient's overall appearance appeared younger than her age, her self-care was appropriate for her age and sociocultural background, she was cooperative, her speech was coherent and goal-directed, her mood was euthymic and congruent with affect, her consciousness was clear, her orientation to person, place, and time was intact, her associations were organized, there were no perceptual disturbances, and, her intelligence level was clinically normal.

Upon examination of the Sentence Completion Test administered to the patient, it was observed that there were letter reversals, capitalization errors, and failure to leave spaces between words. According to information obtained from the school, it was revealed that the patient's academic performance was well below the class average, and she experienced difficulties in listening to, understanding, and interpreting information. The teacher-completed Turgay's DSM-IV ADHD and Disruptive Behavior Disorders Screening Scale (T-DSM-IV-S) [10] revealed a score of 21 out of 27 points on the attention deficit subscale, 4 out of 27 points on the hyperactivity and impulsivity subscale, 6 out of 24 points on the oppositional defiant disorder subscale, and 4 out of 45 points on the conduct disorder subscale.

T-DSM-IV-S completed by the patient's mother revealed a score of 18 out of 27 points on the attention deficit subscale, 2 out of 27 points on the hyperactivity and impulsivity subscale, 4 out of 24 points on the oppositional defiant disorder subscale, and 4 out of 45 points on the conduct disorder subscale. Higher scores are associated with greater symptom severity. According to the Wechsler Intelligence Scale for Children (WISC-R) [11] administered to the patient, the verbal IQ was 85, performance IQ was 85, and the total IQ was 85. In the clinical assessment of the patient's SLD, the Specific Learning Difficulties Clinical Observation Battery (SLD-COB) was administered [12].

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During the mathematics test, the patient made errors while doing addition using pen and paper, and also made errors in multiplication, whether mentally or using pen and paper. She read 72 words per minute, but comprehension was below average. According to the norm value for 5th grade Turkish children, 104.35±25.46 words per minute is considered normal [12]. In the writing test, she exhibited difficulties such as letter reversals, mixing upper and lower case letters, omitting punctuation marks, and not leaving spaces between words. Her clock drawing was inaccurate. She correctly distinguished between left and right, but showed differences in lateralization (preferring the right hand, left eye, and right foot). She made errors in prioritization and sequencing. According to the clinical assessment of the patient, difficulties were observed in the areas of reading, writing, and mathematics.

Based on the psychiatric examination, family interviews, psychometric assessments, and information obtained from the school, the patient was diagnosed with ADHD, predominantly inattentive presentation, and SLD with impairments in reading, mathematics, and written expression. The patient was referred to special education for a diagnosis of specific learning disorder. Furthermore, psychostimulant medication (methylphenidate HCL) therapy for ADHD was initiated, and the medication dose was gradually titrated up to 27 mg/day. At the patient's follow-up visit two months later, according to the information obtained from the school, the T-DSM-IV-S rating scale subtest scores showed improvement, with the inattention subscale score decreasing to 4, the hyperactivity-impulsivity subscale score decreasing to 0, the oppositional defiant disorder subscale score decreasing to 2, and the conduct disorder subscale score decreasing to 1. According to the T-DSM-IV-S rating scale-parent form, the inattention subscale score decreased to 3, the hyperactivity-impulsivity subscale score remained at 0, the oppositional defiant disorder subscale score decreased to 1, and the conduct disorder subscale score decreased to 1. On the other hand, although, the patient had been referred to special education due to SLD, it was learned that the family did not send the patient to special education because they thought there was no problem with her education. The family stopped the child psychiatry follow-ups at their own request.

Informed consent was obtained from the patient and parents for the case presentation.

3. DISCUSSION

Silver-Russell syndrome is a congenital condition characterized by significant growth retardation that persists both intrauterinely and postnatally, along with distinct physical features such as prominent forehead, micrognathia, ear anomalies, and a characteristic triangular face [13]. Growth hormone (GH) deficiency may be present in individuals with SRS who exhibit intrauterine growth retardation [14]. Although, GH deficiency was not detected in our case, she used somatropin for seven years due to short stature. Research indicates that individuals with GH deficiency may experience cognitive impairments, and GH therapy has been shown to partially improve these functions to some extent [15].

Reviewing the literature, it has been reported that in many children with SRS, intelligence is normal, and they often have diagnoses of ADHD and/or SLD [9]. However, additional studies are needed to elucidate the relationship between comorbid psychopathologies in this field. Treatment guidelines for ADHD in children and adolescents recommend psychosocial interventions initially for young children and older children with mild to moderate symptoms; for more severe ADHD symptoms, psychostimulants alone or in combination with psychosocial interventions may be necessary. Methylphenidate and dexamphetamine (or dextroamphetamine) are considered first-line treatments for children with ADHD [16].

The adverse effects of psychostimulant medications are generally dose-dependent and may include decreased appetite, abdominal pain, headache, irritability, anxiety, and sleep problems. Concerns may arise regarding the potential impact of methylphenidate treatment on growth and development in our case; however, a meta-analysis has shown that methylphenidate treatment does not affect growth or alter weight-for-age percentiles [17]. In our case, no changes in height or weight were observed during follow-up measurements.

In a study conducted by Bogdanov et al., which investigated 16 children with SRS referred due to attention problems and learning difficulties, 50% of the cases were diagnosed with both ADHD and learning difficulties, 37.5% had only language-based learning difficulties, and 12.5% were diagnosed solely with learning difficulties [9]. The disorder most commonly associated with SLD is ADHD [18]. The co-occurrence of these two disorders has been found to range from 7% to 92% in research studies. DuPaul et al., in their study, reported the frequency of co-occurring ADHD with SLD as 18-60% and found the prevalence of SLD in individuals with ADHD to be seven times higher than that of the general population [19]. In recent studies conducted in Türkiye, the frequency of ADHD co-occurring with SLD ranges from 42.4% to 84.6%, while the frequency of SLD co-occurring with ADHD is reported to be 23.6% [20]. Similarly, in our case, there is a co-occurrence of ADHD and SLD.

Individuals with ADHD experience difficulties in executive functions such as problem-solving, planning, organizing, maintaining flexibility, sustaining attention, and working memory [21]. Studies have shown that although there may not be significant executive function impairments in children and adolescents with SRS compared to control groups, there is an increased risk of such impairments [22]. Additionally, studies have shown that adolescents and adults with SRS may develop low self-esteem, anxiety disorders, and major depressive disorder due to their dysmorphic appearance [23, 24].

When reviewing the literature, it is observed that there has been a primary focus on medical symptoms and interventions related to SRS, with limited attention given to cognitive abilities, academic and social developmental needs. In future research involving individuals with SRS, systematic neuropsychological

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assessment should be considered to evaluate sensory and motor skills, cognitive level, and psychosocial adjustment. A better understanding of SRS, which affects individuals throughout their lives, is necessary, particularly in terms of the specific interventions needed in school settings, such as special education, speech therapy, vocational and physical therapy, social skills training, and/or counseling [25].

Given the high likelihood of psychiatric comorbidities in children and adolescents with the rare congenital disorder SRS, we believe that referring them to a child and adolescent psychiatrist for psychiatric evaluation and implementing early treatment interventions are crucial for the benefit of the cases.

Compliance with Ethical Standards

This research was conducted ethically in accordance with the principles of Helsinki World Medical Association Declaration.

Patient Consent: The patient and her guardian gave their written consent for clinical information related to this patient to be reported in a medical publication.

Conflict of interest statement: The authors have no conflict of interest to declare.

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Authors contributions: BGO: Conception and design, NDV and AA: Data collection, BGO and HA: Analysis and interpretation of results, NDV, BGO, AA and HA: Draft manuscript preparation. All authors reviewed and approved the final version of the manuscript.

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