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Analysis of Functioning in a 12-year-old Boy with Coffin-Siris Syndrome

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Abstract

A case of a 12-year-old, Caucasian, male diagnosed with Coffin-Siris Syndrome (CSS) is described from a neuropsychological perspective. Results yielded additional DSM-5 diagnoses of Autism Spectrum Disorder (ASD), Attention-Deficit Hyperactivity Disorder (ADHD), Developmental Coordination Disorder, Language Disorder, and Specific Learning Disorders with an impairment in reading, written expression, and math. Notable prenatal, developmental, and medical history also contribute to the case presentation and offer a unique perspective to the etiology of CSS and accompanying diagnoses.

Keywords: Coffin-siris syndrome; Genetic disorders; Autism spectrum disorder

Introduction

Coffin-Siris Syndrome (CSS) is a rare genetic disorder typically characterized by hypoplastic or absent 5th digit nails or phalanges, moderate to severe developmental, intellectual, and/or speech delay, hypertrichosis, and coarse facial features, yet there is a large degree of clinical variability [1-4]. The establishment of clinical criteria for diagnosing CSS has evolved in recent literature but has been inconclusive [5].

Recent studies have deciphered several gene variants and phenotypes related to the etiology of CSS development. Specifically, CSS has been traced to the BRG1/BRM associated factor (BAF), which regulates gene expression by controlling chromatin dynamics [6]. Mutated BAF complexes begin to occur during neurodevelopment and have been linked to various neurodevelopmental disorders, including CSS [3,4]. CSS possesses several genes within the BAF complex including, *ARID1A*, *ARID1B*, *SMARCA4*, *SMARCB1*, and *SMARCE1* [1,4,5].

Some discussion has emerged regarding two types of phenotypical development. Classical CSS or Type A has been differentiated from Variant CSS (Type B) due to the coarseness of facial features. Specifically, individuals in Type B tend to possess a thin brow and thin vermilion of the upper lip [3,5]. Gene variant *ARID1B* has been related in intellectual disability and symptoms of Autism Spectrum Disorder in a case example of a 16-year-old female who meets diagnostic criteria for CSS [54]. Further, out of seven case examples 100% had developmental delay, speech delay, and/or intellectual disability ranging from mild to severe, while 71% having features of Autism Spectrum Disorder [4].

Developmental deficits among case reports have also been variable, ranging from moderate to severe in the areas of speech and cognitive abilities [3,5]. Some case reports noted co-occurring symptoms of Autism Spectrum Disorder (ASD); however, no case reports have attempted to differentiate CSS and ASD or established that they co-occur [4]. Given the sparsity of research and lack of consistency in diagnostic criteria, Vergano & Deardorff, 2014 [5] stated,

“Ongoing efforts will need to be aimed at improving understanding of the natural history and organizing international collaborations. This will enable early establishment of the diagnoses, careful characterization of these patients and enable a global approach to improving the care and therapies for these individuals to optimize their health and intellectual potentials (p. 255).”

Thus, there is importance in utilizing neuropsychological assessment to establish a comprehensive understanding of an individual's functioning [3,5]. With less than 100 cases being reported in literature, it is crucial that the functioning of an individual with CSS be reviewed. Here, an overview of a clinical case of CSS with comorbid neurodevelopmental diagnoses will be reviewed.

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Table 1: List of Neuropsychological Assessments.

Wechsler Intelligence Scale for Children -5 th Edition (WISC-V) [9]	Receptive One-Word Picture Vocabulary Test (ROWPVT) [14]
Kaufman Test of Educational Achievement – 3 rd Edition (KTEA-3) [10]	Expressive One-Word Picture Vocabulary Test (EOWPVT) [15]
Wide Range Assessment of Memory and Learning - Second Edition (WRAML 2) [11]	Brief Rating Inventory of Executive Functions – 2 nd Edition (BRIEF-2) [16]
Gray Silent Reading Test (GSRT)	Conner's CBRS [17]
Symbol Imagery	Social Responsiveness Scale (SRS-2) [18]
NEPSY-2 [12]	Autism Spectrum Rating Scale (ASRS) [19]
Delis-Kaplan Executive Functioning Systems Subtests (D-KEFS) [13]	Short Sensory Profile [20]
Autism Diagnostic and Observation Schedule- 2 nd Edition (ADOS-2)	

Case Introduction

The patient was a 12-year-old, Caucasian, male, who resided with his biological father, step-mother, and three younger biological siblings. None of his siblings had a diagnosis of any genetic conditions, nor neurodevelopmental delays. His biological mother was incarcerated at the time of the evaluation. Social history was remarkable for unspecified abuse; therefore, the patient did not have any contact with his biological mother.

Prenatal history was remarkable for drug and alcohol use. In addition, the patient's biological mother attempted to terminate the pregnancy at the end of her first trimester with an abortion drug. She began engaging in prenatal care when she was 4-5 months pregnant. The patient was born full-term weighing 8.4 pounds. He was placed in the NICU for breathing problems. The patient was born with right-sided weakness, which may have been attributable to having a stroke in utero. Upon being released from the hospital, he was said to have difficulty regulating his temperature and required heat blankets. The patient was described as a limp baby, who had low muscle tone and poor muscle control in his neck, trunk, legs, chest, arms, and fingers. Subsequently, he experienced difficulty with sucking, chewing, and continued to drool after 2½ months. However, he grew normally and did not have difficulty gaining weight. Language, toileting, and motor milestones occurred late. The patient did not speak his first words until he was 5 years old. He did not begin crawling until he was 17 months old and was unable to run until age 5. The patient also has a history of enuresis and soiling accidents.

The patient was diagnosed with CSS as an infant. He has accompanying ataxia and speech issues. Medical history is remarkable for high and prolonged fevers, visual deficits, respiratory issues, seizures, apraxia, and frequent ear infections. At the time of the evaluation, he continued to experience rapid onset fevers with a temperature as high as 103°. Additionally, he has been hospitalized for MRSA and pneumonia. Absence seizures occurred from age 2 to 4. No head injuries were reported. Current medical complaints included headaches, dizziness, weakness, nausea, stomachaches, chronic diarrhea, sleep difficulties, and vision issues. The patient was on a modified ketogenic diet to help with symptoms. Subsequently, he took 20mg of Norditopin for hypopituitarism. Family history was unremarkable for genetic disorders, autism spectrum disorder, learning problems, and attention problems.

Behaviorally, the patient is said to have difficulty regulating his emotions and displays behavioral rigidity. He was described as organized and has difficulty adapting to changes in routine. In addition, various restricted interests were reported as well. Self-help skills are said to be poor, as he has difficulty grooming. Several sensory sensitivities were also noted and include; food textures, loud

singing, certain lighting, and fabric texture.

Methods

A full neuropsychological evaluation, including an Autism Diagnostic and Observation Schedule – 2nd Edition was administered. Review Table 1 for the full list of tests.

Case Results

The patient was referred for an independent neuropsychological evaluation to obtain a third-party assessment of his cognitive, academic, social-emotional functioning, and attention/executive functioning skills. Results from the assessment yielded a complex neuropsychological profile that could not be easily delineated by a single psychological diagnosis consistent with DSM-5 criteria [7]. General findings from the evaluation are described below.

Unlike similar cases of CSS, the patient displayed intact cognitive abilities; however, he displayed difficulties with speech articulation and social abilities. All difficulties have been observed in multiple settings. Similar to other reported cases, the patient appeared to have difficulties with expressive speech and speech impairment [3]. Despite his difficulty with speech, his verbal abilities were a relative strength in his cognitive profile.

Objective social-perceptual tasks were completed to obtain a deeper understanding of the patient's interpersonal and social functioning. He displayed difficulty recognizing faces and identifying and understanding other's emotions via facial expressions and perspective taking. Raters on additional questionnaires also endorsed symptoms related to ASD including social problems, sensory sensitivities, restricted interests, stereotypical behaviors, and reduced interest in social interaction, which was further supported through the Autism Diagnostic Observation Schedule Second Edition (ADOS-2) administration [8]. Specifically, on the ADOS-2, the patient displayed diverted eye contact, restricted interests and stereotypical behaviors, inappropriate social gestures, idiosyncratic and pedantic speech, and restricted affect, which was consistent with parent and teacher reports. Overall, results support a diagnosis of Autism Spectrum Disorder (Severity 2) with accompanying language impairment and without intellectual impairment.

The patient was also given a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), combined type, with associated executive functioning deficits. Working memory, which refers to one's ability to maintain and manipulate information in mind for the purpose of completing a task, encoding information, or generating sequential steps to achieving a goal was impaired. On objective measures of attention and executive functioning, the patient displayed impairment in selective and sustained attention, and planning and organization. Some tasks in executive functioning domains were not

administered due to articulation difficulties and fine-motor deficits. However, parent and teacher ratings also suggested that the patient exhibits executive functioning challenges in shifting, initiation, self-monitoring, emotional control and regulation, and organization of materials, further providing evidence to the diagnosis of ADHD.

The patient also performed significantly below expectation based on his cognitive abilities, on tasks of math, reading, and writing, which is consistent with a diagnosis of Specific Learning Disorder in these areas. Finally, per developmental history, his clinical profile represented symptoms related to a developmental coordination disorder and a language disorder.

Discussion

The exemplified patient displays a complex profile that provides additional information about cognitive, executive, behavioral, social, emotional, and academic functioning in individuals diagnosed with CSS. Comparatively, the patient displayed characteristics similar to those reported in literature but aligned primarily with Type B CSS phenotypes. Neuropsychological evaluations are essential for individuals with CSS to not only determine an individual's ability to function in daily conditions, but to provide recommendations that can aid the individual in success interpersonally, academically, and functionally. Additional research is necessary to determine further comorbidities and to rule-out other potential factors (e.g., prenatal care, comorbid medical conditions).

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