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Case Report

Neuropsychological Profile in Hutchinson-Gilford Syndrome: Analysis of a Rare Case

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Abstract: Hutchinson-Gilford Syndrome, also known as Progeria Syndrome, is a rare genetic disorder that leads to premature aging and accelerates the cellular aging process, affecting the cognitive, motor, and social functions of affected children. This study presents the neuropsychological assessment of two 3-year-old patients diagnosed with the syndrome, aiming to map their cognitive, emotional, and behavioral profiles. The evaluation included interviews with family members, clinical observation, and the application of tests such as the Bayley-III Scale and the Son-R Test. The results indicated significant delays in cognitive, motor, and communicative abilities in both patients, with developmental ages below their respective chronological ages. Based on these findings, a multidisciplinary approach involving speech therapy, occupational therapy, and physical therapy is recommended to stimulate the affected areas and develop family support strategies to promote better social and functional adaptation.

Keywords: Hutchinson-Gilford Syndrome; Progeria; Neuropsychological Assessment; Therapeutic Interventions; Cognitive Development.

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1. Introduction

Hutchinson-Gilford Syndrome, also known as Progeria Syndrome, is a rare and fatal genetic disorder characterized by accelerated and premature aging, which manifests in children during the early years of life. According to the latest data from the Progeria Research Foundation [1], approximately 149 children and young adults have been identified with the syndrome worldwide [1]. The condition is caused by a mutation in the LMNA gene, leading to the production of an abnormal protein called progerin. This protein affects the nuclear structure of cells, resulting in structural fragility that accelerates cellular aging [2]. The estimated prevalence is 1 in 4 to 8 million births, and affected individuals typically have a limited life expectancy, generally reaching only adolescence or early adulthood due to severe cardiovascular complications [3].

The clinical signs of the syndrome are unmistakable and include alopecia, thin and wrinkled skin, joint stiffness, early-onset osteoporosis, and cardiovascular disorders such as atherosclerosis, which resemble the aging process seen in elderly adults [4]. In addition to physical characteristics, Progeria Syndrome can significantly impact the neuropsychological development of patients. Studies indicate that while intellectual functioning is often preserved, there is a prevalence of deficits in motor skills, socio-emotional abilities, and behavioral regulation, which influence social adaptation and quality of life [5].

The rarity and complexity of Hutchinson-Gilford Syndrome pose significant challenges for clinical practice and neuropsychological research, as each case may reveal particularities in behavioral manifestations and adaptive difficulties [6]. The literature on this condition remains limited, especially regarding neuropsychological implications, reinforcing the importance of case studies that can document in detail the cognitive, emotional, and adaptive profiles of patients with this syndrome. Such reports contribute to a broader understanding of the condition, helping to guide appropriate therapeutic and psychoeducational interventions [5, 6].

This case study seeks to fill this gap by conducting a detailed neuropsychological assessment of a child with HGPS, exploring cognitive, motor, communicative, and socio-emotional skills. The assessment was conducted through family interviews, clinical observation, and the administration of standardized tests, including the Bayley-III Scale and the Son-R Test. The investigation aimed to understand how the syndrome affects neuropsychological development and what strategies can be adopted to improve the quality of life and adaptation of these children to social and educational environments. The primary objective of this study is to identify preserved and impaired developmental areas in the child, contributing to the planning of interventions that promote well-being and adaptive development.

2. Case Report

2.1 Clinical Context

The cases presented involve the neuropsychological evaluation of two 3-year-old female children diagnosed with Hutchinson-Gilford Syndrome, a rare genetic disorder also known as Progeria Syndrome. Both patients underwent neuropsychological assessments to outline their cognitive, emotional, and behavioral profiles. The family history of both does not reveal any incidence of psychiatric conditions or neurodevelopmental disorders, and they are the only individuals in their families diagnosed with this syndrome. The disease, characterized by premature and accelerated aging due to a genetic mutation, directly impacts physical health and overall development. The patients are monitored by a multidisciplinary team, including a pediatrician, cardiologist, physiotherapist, occupational therapist, and speech therapist.

The physical conditions of the patients present clinical particularities such as visual hypersensitivity, joint stiffness, and early-onset osteoporosis, which affect both mobility and participation in daily activities. Within the family context, both children live with close relatives who provide continuous support in their routines. Due to their clinical conditions, they require constant monitoring to meet the specific needs imposed by the syndrome. It is crucial to assess their adaptive and socio-emotional abilities to develop individualized and continuous support plans. Additionally, both children displayed affectionate and socially responsive behavior, despite difficulties with emotional self-regulation and communication.

The neuropsychological assessments aimed to map each patient's cognitive, behavioral, and motor abilities to identify preserved and impaired developmental areas. This mapping allows for a better understanding of the syndrome's impact on neuropsychological development and the establishment of interventions that help improve the quality of life and social adaptation of the patients. The instruments selected for these assessments, such as the Bayley-III Scale and the Son-R Test, were applied to determine the extent of delays in communication, cognition, motor skills, and socio-emotional development, providing a comprehensive overview of their developmental profiles.

2.2 Assessment Instruments

For the neuropsychological evaluation of the patients, various procedures were conducted, including anamnesis interviews, clinical observation, and the application of specific tests. Initially, detailed interviews were conducted with close family members to

gather information about the children's developmental history, family contexts, and observed behavioral characteristics in daily life. Subsequently, the children were observed in both structured and free activities, focusing on social interactions, emotional reactions, and behaviors during tasks. The test sessions were adapted to respect each patient's individual conditions and were conducted in an environment that promoted comfort and familiarity, aiming to minimize the potential impact of anxiety on performance.

The main instruments used were the Bayley-III Scale and the Son-R Test, both chosen for their ability to assess fundamental developmental areas in children of this age group. The Bayley-III Scale is a widely used battery for measuring cognitive, motor, and socio-emotional development in children up to 42 months old. It was applied to examine potential developmental delays compared to the expected typical development for the patients' ages. This instrument allowed for a detailed analysis of cognitive abilities such as memory and attention, as well as motor skills and socio-emotional aspects. The Son-R Test, a non-verbal intelligence test, was administered to estimate the children's intelligence quotient (IQ) and assess non-verbal reasoning, providing a broad understanding of their cognitive potential.

During observation sessions, data were recorded on the patients' interactions, including their social behaviors, responses to commands, and levels of initiative in activities. Emotional reactions, such as frustration tolerance and responses to challenging situations, were carefully monitored and documented, offering insights into their emotional self-regulation capacities and adaptive abilities. Verbal and non-verbal communication was also observed, highlighting the presence of echolalia and a preference for repetitive verbal expressions in both children. These observations complemented the test data, providing an integrated view of each child's strengths and challenges, with essential information for guiding future interventions.

3. Discussion

The neuropsychological assessment of the patients revealed profound impairments in various areas of development. The condition, characterized by premature cellular aging, directly influences cognitive (Table 1), motor, communicative, and adaptive development, leading to neuropsychological profiles marked by significant delays and functional difficulties that require multidisciplinary support.

Figure 1. Cognitive Performance – Developmental Age vs. Chronological Age.

Assessed Skill	Developmental Age (months)	Chronological Age (months)
General Cognitive	23	48
Receptive Communication	19	48
Expressive Communication	19	48

Legend: Cognitive and communicative performance of the patient, highlighting the difference in relation to chronological age.

The data obtained through the Bayley-III Scale demonstrated developmental delays in the patient's cognitive abilities. The observed developmental ages were significantly below the chronological age of 48 months. The assessments of general cognitive skills suggested consistent difficulties in basic executive functions, such as working memory, focus, and processing new information. Difficulties in executive functions, including working memory and processing new information, may be associated with premature aging and cellular damage that adversely impact the developing brain. Progeria is also known to affect multiple body systems, which may further amplify cognitive challenges by interfering with the child's physical and emotional well-being [7].

The patient exhibited slower response times and difficulties maintaining attention on tasks requiring immediate responses, limiting problem-solving abilities and adaptability to environmental changes. These deficits indicate limitations in organization skills and

mental flexibility, which are frequently associated with the syndrome's impact on neural development. A study by Ullrich et al. (2013) evaluated neurological characteristics of HGPS patients, revealing that neurological alterations can occur subclinically, possibly contributing to the observed cognitive deficits, such as response slowing and attention difficulties [8].

The cognitive and communication skills of the patient are delayed by approximately 29 months. Receptive and expressive communication, which involves understanding instructions and responding verbally, is impaired. The patient exhibits echolalia and repeats words as a compensatory strategy, making linguistic processing difficult and impacting social interaction. This affects both comprehension and the formulation of appropriate responses in social interactions. Communication in children with progeria presents complex challenges, influencing both social interactions and language skills. It was observed, for instance, that the patient tends to demonstrate greater receptivity in familiar settings but hesitates in interactions with unfamiliar individuals, which may hinder integration into broader and more diverse environments [9, 10]. These deficits manifest in both expressive and receptive communication, as evidenced by echolalia and difficulty interacting effectively with strangers. Such limitations are a direct consequence of the syndrome's impact on linguistic and social abilities, constituting one of the most significant challenges for emotional development and social integration in these children [4].

Case studies further illustrate this scenario. Wang et al. [11] reported the case of a 4-year-old child with HGPS who suffered a cerebral infarction, leading to blurred vision and communication disorders. MRI scans revealed multiple abnormalities in the bilateral frontoparietal cortex, semioval center, lateral ventricles, and deep frontal and parietal lobes, suggesting that cerebrovascular events can exacerbate communication deficits in HGPS patients [11]. Furthermore, research on the otologic and audiological manifestations of HGPS identified low-frequency conductive hearing loss in almost all evaluated patients, which may impair speech perception and, consequently, hinder the development of communication skills [12].

Despite the evident cognitive delay, some aspects of non-verbal processing demonstrate relatively better potential than expected. The evaluation using the Son-R test indicated that although children with progeria present cognitive impairments, certain executive functions related to non-verbal tasks—such as logical reasoning and problem-solving—may be less affected [5]. This preservation, albeit modest, creates opportunities for intervention strategies aimed at strengthening these abilities. In this context, speech therapy plays a crucial role. By promoting the development of language skills and improving social interaction, it facilitates emotional expression and engagement, which is essential for expanding social integration opportunities and enhancing emotional development in these children [13].

The patient's motor development also exhibited significant limitations (Table 2). Fine and gross motor skills were evaluated and found to be delayed compared to typical age-related development. In the fine motor test, the patient's skills corresponded to a developmental age of 23 months, falling short of what is necessary for tasks requiring precision and manual coordination, such as holding and manipulating small objects. In contrast, gross motor skills, assessed as equivalent to 16 months, showed an even more significant delay (Table 2).

Table 2. Motor Skills – Fine and Gross Motor Development.

Assessed Skill	Developmental Age (months)	Chronological Age (months)
Fine Motor Skills	23	48
Gross Motor Skills	16	48

Legend: Motor development delay in the patient's fine and gross motor skills.

This impairment directly affects mobility and the ability to perform broad and coordinated movements, limiting participation in play and educational activities, which are essential for social integration and physical development. Supporting this, a study published in the American Journal of Medical Genetics by Malloy et al. (2023) observed that young individuals with HGPS exhibited limitations in range of motion, decreased grip and pinch strength, reduced walking endurance, and impaired gross motor skills compared to their age-matched peers [14]. These limitations directly impact mobility and participation in recreational and educational activities, which are crucial for social integration and physical growth. Therefore, therapeutic interventions should focus on improving motor skills to enhance the quality of life for HGPS patients [14].

Research by Kreienkamp and Gonzalo [15] highlights that while HGPS does not fully replicate normal aging, it shares several similarities, including bone and joint alterations. These complications may indirectly influence cognitive functioning [15]. The fragility of gross motor skills is concerning, as it restricts environmental exploration and engagement in activities requiring body coordination. This motor profile reinforces the need for interventions focusing on physiotherapy and occupational therapy to improve muscle strength, postural stability, and motor control [15]. Occupational therapy aims to enhance motor coordination and independence in daily tasks, using activities that promote muscle strength, mobility, and motor control. It plays a crucial role in increasing autonomy and improving the quality of life for children with progeria, who often face motor challenges and difficulties adapting to physical environments [4].

The patient's adaptive life skills were also assessed, with a focus on essential areas for autonomy. Table 3 summarizes the adaptive skills of the patients, highlighting a considerable discrepancy between their developmental and chronological ages. Limitations were observed in self-care skills and participation in community activities, requiring constant support. In daily routines, difficulties were evident in following instructions and completing more complex tasks without supervision. The self-care domain, where developmental ages were estimated at 28 months, showed limitations that compromise independence in personal hygiene and feeding activities, necessitating caregiver assistance for basic tasks.

Table 3. Adaptive Behavior – Daily Living Skills.

Skill Area	Developmental Age (months)	Chronological Age (months)
Self-Care	28	48
Community Life	22	48
Daily Routine	24	48
Social Interaction	25	48

Legenda: Developmental age in daily adaptive skills versus chronological age.

Community life skills correspond to a developmental age of 22 months, showing a 26-month delay compared to chronological age. Daily routine skills correspond to a developmental age of 24 months, with a 24-month delay compared to chronological age. Social interaction skills correspond to a developmental age of 25 months, presenting a 23-month delay in relation to chronological age. Thus, it is evident that Hutchinson-Gilford Syndrome significantly impacts neuropsychological development, resulting in marked delays in critical areas for adaptive and social functioning [9]. Despite the identified limitations, it is important to highlight that the patient demonstrated strong emotional bonds with her family members and a preserved ability to express empathy, characteristics that can be leveraged to promote advances in social interaction and communication.

The exploration of preserved abilities is crucial for an intervention plan aimed at enhancing the patient's quality of life and fostering functional adaptation [9]. According to the Progeria Research Foundation [13], children with Progeria face challenges in self-care, education, work, recreation, leisure, and social participation due to physical limitations. Occupational therapy plays an important role in thoroughly assessing the child's abilities and, when necessary, adapting tasks or developing specific equipment to facilitate participation in daily activities [13]. There are no studies proving the effectiveness of occupational therapy interventions in children with Progeria. Despite their interest in participating in various activities, these children face specific difficulties due to physical limitations, as evidenced in occupational, physical, and medical assessments. Thus, it is essential for an experienced occupational therapist to thoroughly evaluate each child's abilities in order to propose adaptations or develop new equipment that facilitates participation in daily activities [13].

The results of the neuropsychological assessments of the patient with Hutchinson-Gilford Syndrome (Progeria Syndrome) align with many findings in the literature on this rare condition, which is characterized by premature cellular aging, resulting in severe impairments in cognitive, motor, and adaptive areas [4].

4. Final Considerations

The results of neuropsychological assessments indicate that patients with Hutchinson-Gilford Syndrome exhibit substantial delays in cognitive, motor, and communication areas, with a significant discrepancy between their chronological ages and developmental levels based on the conducted assessments. In cognitive terms, patients showed difficulties in basic executive functions, such as working memory and attention, while fine and gross motor skills were below the expected level for their age, compromising their ability to perform daily activities independently.

Expressive and receptive communication was also impaired, with echolalia and difficulty understanding and formulating clear responses, affecting social interactions and the ability to adapt to the environment. These findings are consistent with the literature on the syndrome, which describes significant developmental delays in key areas, requiring specialized and continuous monitoring to maximize the patients' adaptation and functionality.

For future follow-up, it is essential to implement a multidisciplinary intervention plan, with a focus on speech therapy, occupational therapy, and physiotherapy. Speech therapy should be prioritized, aiming to improve receptive and expressive communication skills, using therapeutic approaches that enhance language comprehension, verbal production, and social interaction. Occupational therapy and physiotherapy should be integrated, focusing on motor development, especially fine and gross motor skills. Stimulation of motor coordination and strength should be included through adapted activities that promote muscle strengthening, mobility, and autonomy in daily activities, such as feeding and hygiene. These interventions should be continuously adjusted according to the progress of the patients and their motor and cognitive development.

Beyond therapeutic interventions, family support must be considered a central element in the developmental process of these children. Parents and caregivers should receive guidance on how to provide a constantly stimulating environment, with daily practices that integrate functional communication and motor development. It is suggested that structured and play-based activities be introduced to stimulate both social interaction and motor exploration, adapted to the patients' developmental levels.

Family training should include guidance on how to use augmentative and alternative communication, when necessary, to facilitate children’s interactions, as well as early stimulation techniques to promote motor and communication skill development. The active engagement of the family in the therapeutic process can significantly contribute to the patients' progress, helping them achieve greater autonomy and quality of life. Due to its rarity, research on this condition faces several limitations. One of the main constraints is

the small sample size, which makes it difficult to obtain statistically significant results and generalize findings. Clinical variability among patients may influence data interpretation, making it challenging to establish uniform disease progression patterns and treatment responses.

Another significant limitation is the lack of comprehensive longitudinal studies tracking patients over time. This knowledge gap prevents a deeper understanding of the disease's natural history and the long-term effects of therapeutic interventions. Additionally, many existing studies are observational or based on case reports, limiting the ability to infer causal relationships and assess the effectiveness of possible treatments. To overcome these limitations, future research must focus on increasing sample sizes through international multicenter collaborations, allowing for the collection of more robust and representative data. Investments in longitudinal studies are crucial to monitor disease progression and evaluate the long-term effects of new therapies.

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