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Case Report

Deciphering Special Abilities in Apert Syndrome Using Neuropsychological Psychodiagnostics

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Abstract

Apert syndrome (AS), an autosomal dominant malformation syndrome, is a rare congenital anomaly with peculiar skeletal presentations. It is caused by mutations in genes encoding fibroblast growth factor receptor 2 (FGFR2). Relevant literature exists in studying comorbidities like dental abnormalities, hearing impairment, hyperhidrosis, cardiac, gastrointestinal malformations, and anomalies of the genitourinary tract. However, there is a lack of consensus on the impact of AS on the neuropsychological functioning of patients. The aim of the current case report was to present a novel case of a high functioning male with Apert Syndrome, and analyse the impact of 'Nurture' on Intelligence, perceptual and fluid reasoning, spatial processing and visual motor integration, set shifting, reaction time and executive functioning among other cognitive functions.

Keywords: *Apert Syndrome (AS); Fibroblast Growth Factor Receptor 2 (FGFR2); Neuropsychological Psychodiagnostics*

Background

Apert syndrome (AS) is an autosomal dominant malformation syndrome, characterized by multisuture craniosynostosis [1] (premature fusion of coronal sutures) [2], midfacial hypoplasia, abnormal skull base development and syndactyly of hands and feet [3]. It is a rare congenital anomaly with peculiar skeletal presentations [4]. The condition is caused by mutations in genes encoding fibroblast growth factor receptor 2 (FGFR2) [5]. Although primordial symptoms make it evident, a formal diagnosis is made with a genetic analysis, wherein mutations of Ser252Trp or Pro253Arg in FGFR2, confirm the diagnosis [6]. These mutations may be inherited or newly caused. Older paternal age may influence new mutations [7].

Comorbidities such as dental abnormalities, hearing impairment, hyperhidrosis (excessive sweating) [8] are common in persons with AS. Narrowing of the nasal passages and tracheal anomalies may lead to airway obstruction. Structural cardiac abnormalities, gastrointestinal malformations, and anomalies of the genitourinary tract may be present. Speech and language disturbance may also persist [9].

Existing literature lacks a consensus on the intellectual and cognitive functioning of persons with Apert syndrome, some studies suggest these patients have a normal range intelligence or mild intellectual disability (ID) with cognition at par with peers; and report

of moderate-to-severe ID is rare [10], while others claim high prevalence of Mental Retardation (MR) and low performance on cognitive tasks, such as that of attention [11-13]. This gap exhibits a need to further study the neuropsychological functioning of patients with AS.

In the given study, a case of Apert Syndrome in a male of early 20s from a South-East Asian country has been reported. The authors have assessed the global neuropsychological functioning of the patient with an attempt to understand the contributing factors to the same as an outpatient service.

Case Presentation

X, a male in his early 20s was referred from the Outpatient Medical/Clinical services of Paediatric Surgery to Medical/Clinical service of Neurology and further to Para-Clinical service of Clinical Neuropsychology at a Tertiary Care hospital for neuropsychological evaluation. As a part of psychodiagnostics, clinical history was taken, including birth, developmental, familial and genetic history. The psychodiagnostic assessment followed three steps- (i) Clinical history taking and interview, (ii) Psychometric testing, and (iii) Clinical Observation. The reason for referral by the clinicians/medical doctors was Assessment of possible Learning Disability. Additionally, a list of patient and informant concerns were noted down. These primarily revolved around his performance at Academic Institute, for which they wanted accommodations and requested for a change in the evaluation pattern as guidelines for his age group were not present.

The mother underwent full-term, normal pregnancy at age 32. During the 4th month of pregnancy, doctors speculated the presence of excess body fluid. X was born by caesarean delivery. Birth cry was present and birth weight was normal. The patient's first degree relatives are architects and engineers. He was diagnosed with Apert Syndrome at birth. The informant reported most developmental milestones were delayed due to surgeries and weakness during recovery. He had his first surgery at the age of 2 months, uncommon for this condition. At age 2.5 years, X was taken to a speech therapist. His understanding of number skills was delayed. Seizures were reported since early teenage years. Epileptic medication was prescribed. After 3 years of epileptic onset, the frequency of seizures declined, post which medication was tapered. He was also diagnosed with hearing impairment around the same time. Last seizure reported was a year before this case presentation, and medication was re-started. He was unaware of seizures during sleep. No frothing was reported. He mentioned a constant fear of getting seizures during sleep.

X studied in the regular Board pattern until middle school. He had been provided a scribe by the school. He had a major surgery in IXth standard, post which, the patient shifted to National Institute of Open Schooling (NIOS), Ministry of Education, with English, fine arts, home science, Hindi, painting, and data entry as core subjects. With immense support and training and exceptional awareness by his parents, X is presently enrolled in a high ranking law university. His current academic concerns were difficulty articulating and writing long answers.

The informants report the patient to be a friendly person who takes initiatives and wants to do tasks independently. He is highly familiar with technology, and can make airline bookings, uses a calculator for payments. He is reported to have strong observational skills, reads newspaper daily well and is well aware of world affairs. When focusing on one thing, gets fully absorbed in the visual details, and finds it difficult to come out of it. He often makes socially age inappropriate statements or out of context statements, like a younger child, and has difficulty falling asleep. His parents take turn to stay with him to ensure his sound sleep. Sense of touch and smell are strong. Informant reports patient is very particular about spellings. He strives for perfection on routine things, such as being very particular about on creases on the bedsheet. The parents feel this attention to detailing and perfectionism must be used towards a professional advantage. There is a difficulty in abstract thinking and assignment of multiple variables. Difficulty was observed in conceptualizing concepts not visible to the eye. The informant reported the patient to lack slightly in understanding of social protocol and hierarchical positions. He faced difficulty understanding humor, abstract thinking, and assignment of multiple variables and conceptualizing concepts not visible to the eye. These difficulties factor in to negatively impact his academic performance. Despite all difficulties, he has taken admission into a professional course. He is reported to have balance problems and often bumps into things. He has difficulty conforming to time limits.

X's first degree relatives were exceptionally well-informed about the condition, and eager to help him in all ways possible.

At the time of assessment, the patient was accompanied by his mother on three different dates of evaluation. He was dressed appropriately, hygiene was well kept, and walked with a minor irregularity in gait. He was oriented to time, person and place. Insight was partially present. The patient was cooperative and communicative throughout the assessment and rapport could be easily established. His attention could be aroused and sustained. He was right handed. Speech was not very clear, but understandable. Eye contact was occasional. Patient had recently started using a hearing aid. The patient presented with structural abnormalities in hands, feet and head that are visible to the clinician's eye. Gripping problem was observed due to physical deformity. He was distracted by noise during the assessment. Patient's hand-eye coordination was slow.

Spatial orientation was intact and the patient could follow instructions. The patient was detail focused. While evaluating the patient, it was observed that the patient had fluctuating motivation, which was later confirmed by objective testing. Hence, a special effort was made to keep his motivation in check. Behavioral and psychiatric screening was conducted and the patient was found to have borderline problems in domains of anxiety and somatic domains. Clinical disturbances were observed in academic and social domains.

Investigations

On psychometric evaluation using standardized, culture-fair tests (Table 1), the patient was found to have Intelligence Quotient (IQ) in average range (IQ = 110) on a performance test, whereas a score of 66 was obtained on a Full IQ assessment that included arithmetic, reasoning and verbal performance. The Full Scale IQ (FSIQ) is the most representative of general intellectual functioning. The patient scored a raw score of 54, with a corresponding composite score of 56 and a percentile rank of 1, indicating that the patient performed better than 1% of the population. On the verbal comprehension scale, which is a measure of verbal concept formation, verbal reasoning and knowledge acquired from one's environment, the patient obtained a percentile rank of 13. On perceptual reasoning, which measures perceptual and fluid reasoning, spatial processing and visual motor integration, the patient obtained a percentile rank 0.2. On the verbal memory scale, the patient obtained a percentile rank of 58. On processing speed, the percentile rank was 0.1. Set shifting, reaction time and executive functioning were found to be impaired. Immediate recall was found to be intact. Delayed recall was impaired. Problem areas in Learning disability assessment were expressive language and arithmetic, whereas the patient had intact performance on hand-eye coordination, figure-ground perception, figure constancy, position-in space, spatial relations, auditory perceptions, cognitive abilities, memory and receptive language. Spellings and reading fluency were intact but below grade level, and written expression is impaired.

S. No.	Assessment Protocol
1.	Standard Progressive Matrices (SPM)
2.	Colour Trails Test (CTT)
3.	Rey-Osterrieth Complex Figure test (CFT)
4.	Auditory Verbal Learning test (AVLT)
5.	Diagnostic test of Learning disability
6.	Dyslexia Pupil Portfolio
7.	Achievement Motivation Scale (n-ach) (AMSn-DM)
8.	Wechsler Adult Intelligence Scale (WAIS)
9.	Hamilton Depression Rating Scale (HDRS)
10.	Hamilton Anxiety Rating Scale (HAM-A)
11.	Behavioral Checklist screening
12.	Personality Trait Inventory (PTI)
13.	Mini-International Neuropsychiatric Interview (M.I.N.I.)

Table 1: *Assessment protocol.*

Discussion

The aim of the current case report was to present and analyse a novel case of a high functioning male with Apert Syndrome. The authors felt the need to report this due to the lack of consensus in the present literature regarding the neuropsychological functioning in persons with Apert syndrome. The patient came for a neuropsychological psychodiagonistics with the objective of compensatory guidelines to be submitted to the University Committee to ensure the evaluation pattern changed to a more inclusive one. A comprehensive multi-disciplinary clinical assessment was conducted (Table 2). The high performing case presented shows the social and economic aspects are relevant in the mental prognosis of these patients. It was exceptional to see the patient reach this level of academic achievement despite facing numerous difficulties through life. It is noteworthy, that the parents of the patient were informed, dedicated and updated regarding the rules and provisions available. This demonstrates the effect of parental education and importance of environment and nurture in the performance of patients. Literature suggests cognitive function development is directly related to the quality of family environment provided to patients with Apert syndrome, more than physical malformations [14]. When the patients live in institutions, they present lower IQ scores, as compared to stimulating home environments [15-17]. The existing literature shows a diversity of neuropsychological outcomes in individuals with AS. While some studies show children who have syndromic craniosynostosis have FSIQs similar to the normative population. They are, however, at increased risk for developing learning difficulties, by internalizing, social, and attention problems. Higher levels of behavioral and emotional problems have been shown to be related to lower levels of intellectual functioning [18].

Test	Score	Interpretation Status
SPM	48; PR=75	Intact
CTT1	PR = 5-8	Impaired
CTT2	PR<5	Impaired
CFT1	32; PR<5	Impaired
CFT2	25; PR=25-40	Intact
CFT3	16; PR<5	Impaired
AVLT1	45; PR<5	Impaired
AVLT2	9; PR=5-10	Impaired
AVLT3	7; PR<5	Impaired
AVLT4	12; PR<5	Impaired
VCI	PR=13	Low Average
PRI	PR=0.2	Low average
FSIQ	66; PR=1	Sub-Average
AMSn-DM	103; Z= -1.39	Low
D-ld	94	Intact

Table 2: *Result on neuropsychological assessment.*

X obtained a score of 110 on the performance IQ scale despite having deficits in other cognitive domains (an average range of 90-110). The fact that X was able to enter a premier law institute can be understood to be due to special abilities that he has. Moreover, the level of education and awareness showed by the parents was commendable and would have contributed to X's achievements.

Neuropsychological aspects are important to take into account while understanding the overall functioning of Apert syndrome patients, but many studies lack this aspect of testing [19-21]. Independence is not the only aspect important for healthy neuropsychological

functioning. Social, personal, cognitive, family and vocational aspects are also important. Psychometric assessment, clinical interview and history taking highlight probable non-cognitive factors confounding the results. These range from recent medical problem, life events, motivation, and distractibility to previous night's sleep. It is essential that patients with disability are not seen as a burden. When the focus is shifted to their strengths and ability to do well in the society, the performance and quality of life exponentially improves. Lest they feel a double burden of the stigma associated and performance in life. The quality of family environment and parental education is seen to be the most significant factor directly involved in mental development of patients with Apert syndrome [22]. The relevance of assessing diverse neuropsychological functions must be noted here. A single assessment for global functioning may not be an adequate measure to gauge the strengths and weaknesses of the patient for a better quality of life management. The authors recommend multidisciplinary assessment of children with Apert syndrome across a broad range of dimensions [23] to obtain a profile of each child's strengths and weaknesses to ensure that appropriate educational placements and early interventions are implemented. Considering patterns of development over time at key ages is also argued to be of central importance [24]. Multi-disciplinary management integrating various aspects of anatomic, physiological, surgical and neuropsychological needs to be undertaken as a part of the continuum of care model [25].

While inclusive education has already been implemented, there lacks a tendency of authorities, policy makers as well as the general public to focus on the strengths and abilities of such individuals. There exists a need for a quantum shift of focus from 'disability' to the 'special ability' of the same person.

Conclusion

This case report provides valuable insights into the neuropsychological functioning of a high-functioning individual with Apert Syndrome, emphasizing the influence of a nurturing environment and informed caregiving on cognitive and social outcomes. Despite significant challenges, the individual demonstrated remarkable academic and adaptive achievements, highlighting the role of personalized support and early interventions. The findings underscore the relevance of a strengths-focused approach, advocating for inclusive practices and multidisciplinary assessments to unlock the potential of individuals with Apert Syndrome. This case reinforces the notion that fostering abilities over emphasizing disabilities can transform lives, shifting the narrative towards empowerment and societal contribution.

Key Points

- Apert syndrome, a rare congenital anomaly, comes under multiple disabilities, and requires a multi-disciplinary care as per the continuum of care model.
- This case report addresses the age old debate of influence of 'Nature Vs Nurture' and highlights the impact of a nurturing environment, experiences and social factors on the global neuropsychological functioning of a patient with Apert Syndrome.
- There exists a need for a quantum shift of focus from 'disability' to the 'special ability' of patients.

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