Case Report

Speech-Language Profile of A Child With Coffin-Siris Syndrome

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Abstract:
The purpose of this paper is to review medical, audiological and speech-language records of a 25 month old boy (AR) with Coffin-Siris syndrome and to report the significant progress he made in the development of receptive and pragmatic language. A genetic evaluation showed de novo nonsense mutation of ARID1B. Auditory brain stem response recording suggested bilaterally normal hearing. AR showed significant improvement in speech-language with speech-language therapy. Improvement in receptive and pragmatic language was disproportionately more than expressive language. This report highlights the importance of early identification and intervention for children with Coffin-Siris syndrome.

Abbreviations:
CT: Computerized Tomography; ELA: Expressive Language Age; HIS: Intelligent Hearing systems; Hz: Hertz; KHz: Kilo Hertz; MRI: Magnetic Resonance Imaging; nHL: normal Hearing Level; NIMAHNS: National Institute of Mental Health and Neuro Sciences; REEL: Receptive-Expressive Emergent Language; RLA: Receptive Language Age

Introduction: Grange Coffin and Evelyn Siris were the first to describe the Coffin-Siris syndrome which is a rare genetic disorder that results in developmental delay and hypoplasia or absence of the fifth fingernails and fifth distal phalanges [1]. Characteristic features of this variable condition include developmental disability, and abnormalities of the fifth fingers or toes, and characteristic facial features. Some of the other symptoms frequently seen in this condition include mild to severe mental retardation, hirsutism but with sparse scalp hair, hypotonia and coarse facial features including broad nasal bridge, microcephaly, antverted and broadnasal tip, a wide or large mouth with thick/prominent lips, and thick and laterally placed eyebrows. According to [2], two subtypes of CSS may be seen, one characterized by “classic” coarse facial features, and a second which displays "variant" facial features. Coffin-Siris syndrome is a condition that affects several body systems (ophthalmological, neurological, cardiac, renal, auditory and pulmonary). Most patients are females (female - male ratio: 4:1; [3]), but the severity is similar in both sexes [4, 5]. Just about 140 cases have been reported so far [6].

Though Coffin-Siris syndrome appears to be characterized by an autosomal dominant pattern of inheritance [7], autosomal recessive inheritance cannot be discounted. It is said that the condition is not usually inherited from an affected parent, but occurs from de novo mutations in the gene during early embryonic development [6]. Mutations in the ARID1A, ARID1B, SMARCA4, SMARCB1, or SMARCE1 gene lead to Coffin-Siris syndrome. Each of these genes indirectly regulates gene expression. It is suggested that mutations of these genes results in abnormal chromatin remodeling which in turn alters the activity of several genes and cellular processes. This may explain the variability manifested by children with Coffin-Siris syndrome.

Past case studies have made a general statement that children with Coffin-Siris syndrome are delayed in their speech development (as is the case with gross and fine motor skills, social adaptation), but this observation has not been substantiated. Fleck et al. [8] reported significant delay in expressive language in relation to receptive language in these children.
Six of the 16 children aged more >2 years in the Fleck et al. study were unable to speak while in the remaining, first spoken word appeared between 15 and 60 months. Swillen et al. [9] reported the psychological and behavioral characteristics of 12 children and adolescents with Coffin-Siris syndrome, aged between 2.7 and 19.4 years. Three of these children were mildly mentally retarded and the others moderately retarded. Swillen et al obtained data on the language skills of these children on the sub-scale 2 of the questionnaire “Sociale Redzaamheidsschaal” [10] (an adaptation of the Cain-Levine Social Competence scale, [11]). Children aged between 2.5 and 6 years in this study showed severe delay in speech onset, used less than six words, babbled, but showed only slight interest in language. On the Bayley Developmental Scales, 5 children under 6 years of age preferred visuo-spatial tasks than language items. However, children aged between 7 and 19 years in their study spoke in short sentences. Vocabulary and language comprehension of these children appeared to be appropriate to their mental level though language expression was reduced. Based on these observations, Swillen et al concluded that the degree of developmental delay is variable and not always severe in children with CSS syndrome.

We report here a child with Coffin-Siris syndrome in whom we could document not only the status of speech-language development, but also the change in the status of speech-language as a result of speech-language therapy. This report also brings out the importance of genetic analysis in the diagnosis of the condition particularly because the clinical features were not conclusive of Coffin-Siris syndrome.

**Case Report:**

**Medical History:** AR, aged 2.1 years was brought to the Department of Speech Pathology and Audiology at the National Institute of Mental Health and Neurosciences (NIMHANS) with a complaint of delayed speech and language development. Before AR came to NIMHANS, he had been thoroughly examined at three other hospitals, and a diagnosis of Coffin-Siris syndrome had already been made. AR presented with perinatal history of breech delivery (full term gestation), neonatal seizure, and hypocalcaemia at the time of birth (Hospital 1), difficulties with feeding and muscular hypotonia. He was kept in neonatal intensive care unit for investigations relating to seizures. A CT scan of the head did not show any abnormality of the brain structures. AR was discharged from the hospital after the parents were counseled. AR developed pulmonary complications when he was 7 months old and investigations showed a moderate pulmonary artery hypertension along with some minor cardiac complications. Parents continued to be concerned about the motor development of the child and therefore, sought physiotherapy consultation (Hospital 2). Physiotherapy continued till AR was 10 months old. Then the parents noticed that AR was holding his neck in a particular position and so consulted a neurologist who advised an MRI. An MRI scan carried out at the age of 10 months showed a normal study of brain parenchyma. The parents were advised to continue physiotherapy for the child.

A follow-up clinical evaluation after one year (at the age of 1 year 10 months - Hospital 3) showed that the boy had a coarse facial appearance, broad nose, depressed nasal bridge, thick lips, wide mouth, per orbital puffiness, micrognathia, long eyelashes, puffy eyelids, abnormal ear positions, reduced muscle tone (mild degree), short and stubby fingers, short stature, gastrointestinal abnormalities, ophthalmic anomalies (myopia), inappropriate dentition, abnormal facial hair growth, large head circumference (clinically- Figure 1), and hypoplasia of 5th finger (Figure 2). The child was delayed in his motor as well as speech development. The child was noted to have mild to moderate intelligence. A neurologist (Hospital 3) diagnosed the child with Coffin-Siris syndrome based on the typical clinical picture that the child presented. However, as the child did not manifest some of the symptoms characteristic of Coffin-Siris syndrome like microcephaly, sparse scalp hair, hypoplasia of the fifth finger nail, among others, the diagnosis of Coffin-Siris syndrome in this child needed further tests and examination. A genetic evaluation showed de novo nonsense mutation in the gene ARID1B [NM_017519:c.6151C>T(p.Q2051X)] and the diagnosis of Coffin-Siris syndrome was confirmed.

![Profile of the Head: Full Cheeks, Low Set Ear, Up-Turned Nose, Depressed Nasal Bridge. The Head Circumference Appears to be Large, but it is Within Normal Limits (+1 SD) as Per WHO Growth Charts.](image-url)
Figure 2: Right Hand: Hypoplasia of the 5th Finger, Stubby and Short Fingers, Hypoplastic Nail in Fifth Digit (not Very Pronounced).

Clinical evaluation at NIMHANS was unremarkable and did not add to what has already been known about AR’s condition. No test could be administered for assessing IQ as AR was not cooperative. The child was advised continued physiotherapy and psychomotor education. However, as the parents were concerned about the status of speech-language development in their child, a thorough evaluation of speech-language and hearing functions was made at the Department of Speech Pathology and Audiology.

Auditory evaluation: The child was inconsistent in his responses to auditory stimuli. Behavioral pure tone testing was not a feasible idea with the child. Therefore, auditory brainstem responses (IHS, Mundelein, IL) was carried out to rule out any auditory neuropathy component as well as to track hearing thresholds. A standard protocol (active electrode between forehead and ipsilateral mastoid, ground electrode on opposite mastoid, band pass filter between 100 Hz and 3 kHz; both condensation and rarefaction click stimuli at a rate of 11.1 clicks per second through ER3A insert earphones; electrode impedance < 5kOhms) was employed to track thresholds. Clear and replicable 5th peak could be traced up to 30dB nHL which suggested bilaterally normal hearing.

Speech-language evaluation: AR showed inadequate pre-linguistic skills of eye contact, attention span, sitting behavior, name call response etc. Clinical evaluation of speech-language showed that the child was non-verbal in his communication (using gestures and pulling mother’s hand to draw her attention). The child identified some objects (pointed to ball, phone, brush etc. on request), and demonstrated that he understands the function of some objects (the child pointed to the ‘pen’ when we asked him to show the object with which we write). Expression was limited to production of vowels /a/ and /u/ during self-play. The child had a receptive language age (RLA) of 5-6 months and expressive language age (ELA) of 4-5 months on Receptive Expressive Emergent Language test [12]. The Receptive-Expressive Emergent Language Test (REEL-3) is designed to help identify infants and toddlers who may have language impairments. It has a subtest each on receptive language and expressive language as well as a subtest on inventory of vocabulary. REEL checklist is available in many Indian languages with their own norms.

Speech-language therapy: AR was admitted for speech and language therapy program. Initially, the child did not cooperate in therapy and resisted sitting in a closed room. Therefore, speech-language stimulation was carried out in open and day-to-day routine contexts. Speech-language therapy focused on improvement of receptive-expressive as well as pragmatic aspects of language (attention span, eye contact). Receptive language skills of ‘following commands’, ‘understanding simple questions’, ‘recognition of people and objects in the child’s vicinity’, and ‘categorization’ were worked upon. Similarly, expressive language skills of ‘vocalization in conjunction with pointing and gesturing’, ‘imitation of environmental sounds (vehicle sounds, animal sounds)’, ‘usage of mono- and bisyllabic words’, and ‘usage of pronouns’ were worked upon. Techniques employed in speech-language therapy included parallel talk (talking with the child on whatever he is doing), demonstration (perform the act and show), prompting (giving verbal or non-verbal cues), imitation, modeling, labeling and shaping of responses.

After 30 sessions of therapy (each of 45 minutes), AR did show improvement in all these aspects, but showed disproportionately greater improvement in receptive language compared to expressive language. He was able to identify parents and family members [both by face and voice: pointing to father or mother on request, or showing his chin (where the beard grows) on hearing his father’s voice], recognized many animals, vehicles, common objects in the house, and birds (pointed to the picture of the animal or other objects on verbal instruction), followed simple one step command (Eg., close the door), understood functions of many objects (example, pen for writing), simple questions (where is the ball?) and understood some prepositions in the context (in, on, under - Eg., ‘keep the pen under the book). Improvement in expressive language was evident as in nonverbal imitations, pointing towards known objects when asked to, and in vocalization although inconsistently.
Communicative intent was emerging. Pragmatic language also improved as evident in the recognition of some emotions [as evident in the child stopping whatever work he was doing when his father or mother raised their voice (anger), laughing or jumping when patted on the back, wiping the eyes of the mother when she pretended to cry etc.] as expressed in voice, social smile, and interaction with his peers. The child had a RLA of 8-9 months and an ELA of 6-7 months (just some vocalization) on REEL test after 30 sessions of therapy. Speech-language therapy continued. At the end of 60 sessions of therapy, the child obtained a RLA of 14-16 months and an ELA of 9-10 months (scattered from 10-11 months – scattered means that AR did some activities of 10 months level and some activities of 11 months level) on REEL test.

**Discussion:** Clinical observation was suggestive of macrocephaly and evaluation showed a head circumference of 49 cm at 29 months. According to Guszkiewicz et al. [13], the head circumference was normal or suggested microcephaly in all the individuals with Coffin-Siris syndrome reported till 2004. Guszkiewicz et al were the first ones to report a child of Coffin-Siris syndrome with macrocephaly. They opined that macrocephaly (with no family history) and an additional symptom of rectal dislocation in their subject suggested a new variant of Coffin-Siris syndrome. Though the head to body size ratio of AR gives a clinical impression of macrocephaly, he had normal head circumference of 50 cms at 30 months (within +1 SD according to Who Growth chart [14]).

Though a diagnosis of Coffin-Siris syndrome was made based on the typical dysmorphic features of the face and fingers of both hands, it may be noted that AR did not present some characteristic features associated with Coffin-Siris syndrome like microcephaly, sparse scalp hair etc. This may also indicate a variant form of Coffin-Siris syndrome in this instance.

This report also documents that intervention for speech-language can benefit children with Coffin-Siris syndrome if the diagnosis and intervention is carried at the earliest. The remarkable improvement that the child has shown in the comprehension of language in contrast to the changes in the expressive aspects of language is noteworthy. The child also showed very significant improvement in the pragmatic aspects of language as well as pre-linguistic skills for language which however could not be objectively quantified. At present, the child continues to be on speech-language therapy.

It is recognized that there could be several intervening factors which might have influenced change in speech-language of AR along with speech-language therapy. There are no studies in the past which have investigated changes in speech-language profile with or without speech-language therapy over a period of time. Therefore, there are no standards with which the results of the present study can be compared making it difficult to state that the improvement seen in AR was a result of speech-language therapy. Parental stimulation could be a contributing factor. But speech-language stimulation revolved around concepts dealt as a part of speech-language therapy. The child was under medication for control of hyperactivity for some time, but there are no studies which have documented the effects of such medication on speech-language. Spontaneous recovery of intellectual or cognitive abilities is not known in children with intellectual delay / disability and therefore, it can be assumed that AR did not show any spontaneous recovery. Furthermore, changes in the speech-language profile of AR have been documented at two points of time in the present study - once after 30 sessions and a second time after 60 sessions of speech-language therapy. There is quantifiable change in speech-language at these two points of time. Therefore, it is reasonable to assume that the change in the speech-language status of AR is a result of speech-language therapy.

**References:**


