CASE REPORT

The Gross, Fine, and Oral Motor Functions in a Patient with Megalencephalic Leukoencephalopathy with Subcortical Cyst A Case Report

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Abstract

Megalencephalic Leukoencephalopathy with Subcortical Cysts (MLC) is a rare autosomal recessive neurodegenerative disorder. As motor deficits are a core feature of MLC, the present study reported on an MLC1 patient's gross, fine, and oral motor functions. Our patient demonstrated macrocephaly, deterioration of motor functions with ataxia, spasticity, and intellectual disability. In addition to medical interventions, the patient received rehabilitation interventions of occupational therapy and speech therapy. Brain structures were analyzed with magnetic resonance imaging (MRI), and gross, fine, and oral motor functions were analyzed with Gross Motor Function Measurement (GMFM), Purdue Pegboard Test (PPT), and Oral Motor Assessment Scale (OMAS) at age two and after interventions at age five. The results showed that although the motor functions did improve due to the interventions, the patient still had weaknesses in gross, fine, and oral motor functions when compared to his peers. These findings emphasized the importance of early referral for rehabilitation of motor function in order to increase their independence, participation in daily tasks, and quality of life.

Keywords: Megalencephalic Leukoencephalopathy; Van Der Knaap syndrome; Motor disability

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Introduction

Megalencephalic Leukoencephalopathy with Subcortical Cysts (MLC), also known as Van Der Knaap's disease, is an infantile-onset autosomal recessive neurodegenerative disorder (1). It was described first in 1991 by Singhal et al. in the Agarwal community in India, but in 1995 Van Der Knaap published the first comprehensive description of MLC (2). Although the prevalence of MLC is reported to be highest in Turkey and the Indian Agrawal community, it is a rare disorder with no formal research on its incidence (3). In the Iranian population, Ashrafi et al. (2009) published the first case report of an MLC patient (4), which was followed by Kariminejad et al. (2015), who reported 18 patients from 16 families and claimed that MLC is common in the Iranian population (5). Consanguinity and inbreeding are probably involved in the increased incidence rate of this rare disorder (3).

Mutation in the *MLC1* gene, located on the long arm of chromosome number 22, band 13.33 (22q13.33), is the cause of type 1 MLC, which accounts for 75% of all cases (6). Brain magnetic resonance imaging (MRI) in these patients shows diffuse cerebral white matter signaling abnormalities and swelling of the abnormal white matter (3) with subcortical cysts, predominantly involving the anterior temporal lobe and frontoparietal lobe (2).

Studies have reported that the mean age of symptom onset is 16 months. However, the onset age ranges from birth to twenty-five years and is characterized by macrocephaly, occasional seizures, and motor disorders with ataxia and spasticity (2,5). Macrocephaly develops in the first six months in 24% of patients and the second six months in 70% of patients (4) and can be as large as 4 to 6 SD above the mean (7). Head growth usually returns to the normal rate after this period (2). Walking is often unstable and is followed by ataxia of the trunk and extremities, and minor signs of pyramidal dysfunction may emerge (7).

No treatment has been found to address the underlying defects, and interventions are mainly supportive in the form of drug therapy with acetazolamide and anticonvulsants in the presence of epileptic seizures and rehabilitation interventions such as occupational therapy and speech therapy to prevent side effects (1,7).

Despite the previous studies highlighting the progressive decline in motor functions and their adverse effects on daily activities (such as independence of movements, feeding skills, and speech) (2,5,7), none of them have specifically examined the impact of this disorder on the different kinds of motor functions.

The present study aims to report the gross, fine, and oral motor functions in an MLC1 patient.

Case presentation

The patient was a 2-year-old boy referred to the rehabilitation center in Mashhad, Iran. According to the case history, he was born of a consanguineous marriage at thirty-seven weeks of pregnancy. At birth, he was a mature infant, with weight, height, and head size of 2830g, 50cm, and 33cm, respectively. At five months, his head started to grow abnormally and revealed the occurrence of macrocephaly and hydrocephaly, but the accumulated fluids were absorbed spontaneously without the need for medical intervention. As illustrated in **Figure 1, head circumference at five years old (after the final intervention)** was 58 cm which is larger than the normal size for this age (51cm on average).

The genetic evaluation revealed a homozygous pathogenic variant in intron 5 of the MLC1 gene

(c.423+6T>C; IVS 5 ds T-G+6), which confirmed the diagnosis of MLC. None of the family members were affected by any major neurological disorders. Neurological evaluations around 12 months of age were conducted by a pediatric neurologist and demonstrated no sensory abnormalities; however, motor impairments, spasticity, and ataxia were evident in all four limbs of the child. Furthermore, brain MRI showed bilateral symmetrical white matter hyperintensity on T2/FLAIR, hypointensity on T1 with cystic changes, as well as CSF intensity in the subcortical region of the frontal and occipital lobes. The corpus callosum was also thinned **(Figure 2)**.

The patient's parents reported that the oral and pharyngeal reflexes, including sucking, biting, and gagging, were weak, while the rooting reflex looked normal. Moreover, the suck-swallow-breath cycles were not coordinated, and drooling was present, especially with liquids, due to the weakness of oral motor muscles. Parents also reported a delay in gross and fine motor movement development in limbs since seven months of age and a delay in starting vocalization and speech. Abnormalities in speech, including imprecise consonants, distorted vowels, consonant substitutions, slow speech rate (slow phoneme-to-phoneme transitions), inappropriate pauses between the words, strain, and struggle, from the beginning of speech production were also present. Furthermore, mild cognitive impairments and mental delay were documented on his health card records.

Therapeutic interventions were performed for three years to improve motor skills. The timeline of significant events after diagnosis is shown in **Table 1**.

3. Motor functions evaluation

3.1. The Gross Motor Functions

3.1.1. Clinical Observations

The child's parents transport him in a wheelchair.

3.1.2. Tool Assessment: Gross Motor Function Measure (GMFM) score sheet (GMFM-88 and GMFM-66 scoring) was used for gross motor evaluation. It is a useful tool for assessing motor functions to determine the effectiveness of intervention programs in children under 17 years old with cerebral palsy (CP) and other neurological disorders (8). It was translated into Persian by Dehghan et al. in 2011 (9). Items are grouped into five categories: A. lying and rolling (17 items), B. sitting (20 items), C. crawling and kneeling (14 items), D. standing (13 items), and E. walking, running, and jumping (24 items) and scored on a four-point ordinal scale in the form of 0 = cannot initiate, 1 = initiates, 2 = partially completes item, 3 = completes item independently (10). Any item which is omitted, the child is unable to do, or they are unwilling to attempt to do is scored as 0. A maximum of three trials are carried out for each item. The final score is from 0 to 100, calculated from the sum of the percentages of the five tests divided by five. In GMFM, depending on the age, patients are classified at five levels: under two years, 2-4 years, 4-6 years, 6-12 years, and 12-18 years of age (**Table 2**) (11). Higher scores indicate better gross motor functions (12).

3.2. The Fine Motor Functions

3.2.1 Clinical Observations

Hand dexterity is one of the fine motor skills consisting of speed, accuracy, and coordination of hands, arms, and fingers. The patient was functionally limited in daily activities due to inadequate hand dexterity.

3.2.2 Tool Assessment: The Purdue Pegboard Test

(PPT) is a tool developed by Joseph Tiffin in 1948 and is the most widely used fine motor assessment tool due to its high validity and reliability, clear and well-defined variables, and the use of cognitive skills, including processing speed and attention control (13). The obtained validity coefficients ranged from 0.07 to 0.76 among studies (14), and reported three-trial administration increases the reliability of the results (13).

PPT consists of five subtests: right hand, left hand, both hands, right + left + both hands, and assembly. According to the guidelines, the subject can conduct three practice trials before starting each part of the test (15). The testing board consists of a board with two cups, one on the right and one on the left containing twenty-five pins and two central holes, one on the left with forty washers, and a second hole on the right with twenty collars. In the one-handed subtests, first, the dominant hand and then the non-dominant hand were tested, and the maximum number of nails placed inside the holes on the board in 30 seconds was counted. In the two-handed subtest, both hands were used simultaneously to put the nails in both columns of holes in 30 seconds. The fourth subtest included the sum of the scores of the dominant, non-dominant, and both hands. The assembly subtest consisted of placing nails, washers, and collars with both hands for 60 seconds. The scores for each test were calculated as the number of nails for the one-handed subtest, the pair of nails for the two-handed subtest, and the number of assembly components (nails, washers, and collars) for the assembly subtest (14).

The patient had low scores in all five stages of PPT, indicating weak hand dexterity, which can lead to daily life limitations (**Table 5**).

3.3 The Oral Motor Functions

3.3.1 Clinical Observation

An informal assessment of the oral-facial structures and functions was conducted by an experienced speech therapist (16). The results are presented in **Table 3.**

3.3.2 Tool Assessment: Oral Motor Assessment Scale (OMAS) was used to evaluate oral motor skills during feeding. Kaviani et al. (17) estimated this tool's reliability to be about 95%. OMAS assesses mouth closure, lip closure onto utensils, lip closure during deglutition, swallowing (solid, semisolid), mastication, straw suction, and control of liquids during deglutition (18). 0 to 3 scores are allocated for each skill; the final score is the sum of the scores obtained during three evaluations (18) (**Table 6**).

Oral motor skills are scored as follows: passive with a score of 0, demonstrating severely compromised skills, sub-functional with a score of 1, demonstrating moderately compromised skills, semi-functional with a score of 2, demonstrating slightly compromised skills, and functional with a score of 3 demonstrating very slightly compromised (19).

The patient's score was 1 (from a total of 21), representing a passive score (**Table 6**).

Therapeutic interventions

In addition to medical interventions from seven months of age (Levocarnitine), the patient received rehabilitation interventions, including occupational therapy and speech therapy, from two years old until age five (three years in total). The occupational therapy sessions were held daily for 45 minutes to improve gross and fine motor functions. The speech therapy session was performed triweekly for 45 minutes to address the oral motor and feeding deficits.

4.1. Follow-up

MRI was performed at age five to investigate the brain structure, showing diffuse swelling of the cerebral hemispheric white matter and multiple subcortical cysts in both hemispheres located in the anterior temporal, frontal, and parietooccipital lobes **(Figure 3)**.

The patient's post-intervention gross motor score in GMFM was 34.30, a level four in the performance classification system, which illustrated one level improvement **(Table 2, 4).**

Furthermore, PPT scores revealed improvement in fine motor skills following the intervention **(Table 5)**. Finally, the patient scored 15 (from a total of 21) in OMAS in the follow-up assessment, showing a final predominance of semi-functional skills and an improvement in oral motor skills (**Table 6**).

Discussion

the present study aimed to evaluate the gross, fine, and oral motor functions in a patient with MLC1. To our knowledge, this study is the first case report specifically focused on these functions in a case with MLC1 and investigated the efficacy of medical and behavioral treatments.

The obtained results indicate that the patient had significant weaknesses in all motor functions, although gross, fine, and oral motor skills improved in response to the interventions.

The patient demonstrated weaknesses in gross motor functions, including lying, rolling, sitting, crawling, kneeling, standing, walking, running, and jumping. These limitations may lead to dependence on mobility and self-care and adversely affect daily activities. Golubović et al. (2020) suggested that in patients with neurological disorders, the levels of motor impairment, the ability to move around, and passivity and dependency are directly related to their participation levels and may lead to significantly reduced involvement in everyday activities (20).

The patient's fine motor functions were significantly weak, consequently limiting the hand skills such as speed, accuracy, grasping, and coordination between hands, arms, and fingers in daily activities. These findings seem to be consistent with Park et al. (21), who highlighted that hand dexterity can be used as an index to assess the speed and accuracy of hand functions and hypothesized that the fine motor disabilities of the hands might lead to disturbance in hand coordination and upper limb functions during daily activities.

This study's patient also demonstrated weak oral motor functions, leading to feeding problems such as weakness in closing lips, controlling liquid and solid foods during deglutition, sucking from a straw, and mastication. These findings account for a feeding disorder due to oral motor disability, as proposed by Lacerda (2017), who suggested that oral motor deficits in children with motor deficits lead to feeding problems such as drooling, recurrent coughing, and a lack of coordination in sucking, swallowing and chewing muscles, and can be considered the leading cause of death in these children (22). Furthermore, Hillary (2004) reported that in children with motor deficits, weakness of tongue movement, partial lip obstruction, abnormal oral reflexes, and inappropriate sitting posture might cause feeding problems (23).

In line with previous studies (7,5), our patient's head started to grow at five months, as well as his genetic findings showed a mutation in the MLC1 gene (2-4,6). MRI report was also in line with previous studies of MLC1 and, despite receiving interventions, showed no significant differences

at ages two and five, which could be due to the degenerative nature of this disorder (2,5,7). In contrast with Kariminejad (5), who reported that most individuals with MLC have occasional epileptic seizures, our patient did not have a history of seizures.

As the clinical manifestations of MLC patients can be seen in patients with other neurologic conditions such as Alexander's disease, Canavan disease, and Glutaric aciduria, it is necessary to consider these as differential diagnoses of MLC1 (2-4,7).

In conclusion, although the patient's gross, fine, and oral motor skills improved after medical and rehabilitative interventions, he had significant weaknesses in feeding, speech, and daily activities compared to his peers. Therefore, referring MLC1 patients with motor disorders for early rehabilitation interventions seems vital in enhancing their independence, communication opportunities, and quality of life.

Disclosure of potential conflicts of interest

The authors declare that they have no competing interests.

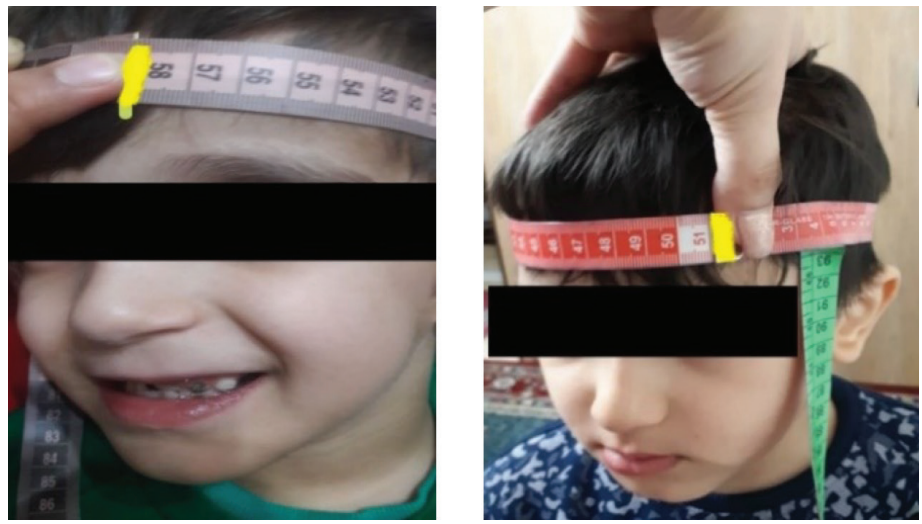

Figure 1*: A) The macrocephalic head of the patient (58 cm), B) The head size of normal boy (average 51 cm)*

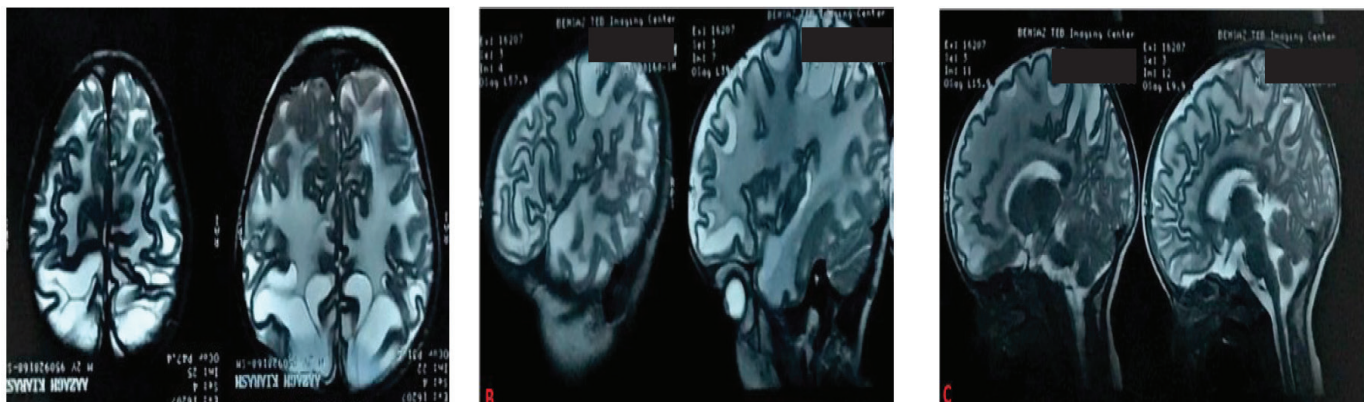

Figure 2*: MRI of Megalencephalic Leukoencephalopathy with subcortical Cysts (MLC1) patient at the age of two.*

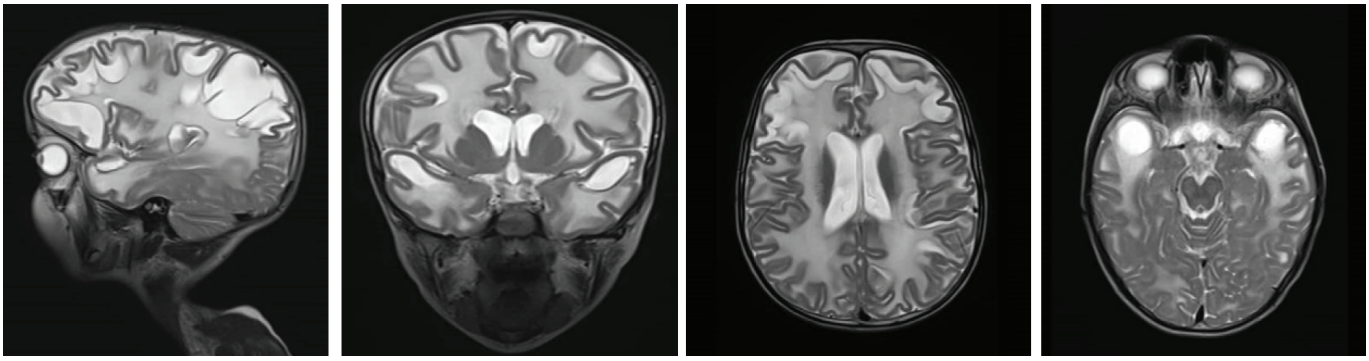

***Figure 3**: MRI of Megalencephalic Leukoencephalopathy with subcortical Cysts (MLC1) patient at the age of 5.*

Table 1. Timeline of significant events after diagnosed

Medical intervention	Prior 2016 (7 months of age)
Started motor deficits	Prior 2016 (7 months of age)
Significant motor impairment with spasticity and ataxia	~ 2016 (~1 year old)
Brain MRI	2017 (2 years old)
Motor functions evaluation	2017 (2 years old)
Therapeutic interventions (medical, speech therapy and occupational therapy)	2017- 2020
Brain MRI	2020 (5 years old)
Motor functions evaluation	2020 (5 years old)
MRI: Magnitude Resonance Image	

Table 2. Gross motor function classification system levels

Level 1	Walks without restrictions; limitation in more advanced gross motor skills
Level 2	Walks without assistive devices; limitation in walking outdoors and in the community
Level 3	Walks with assistive mobility devices; limitation in walking outdoors and in the community
Level 4	Self-mobility with limitation; children are transported or use power mobility outdoors and, in the community.
Level 5	Self-mobility is severely limited even with the use of assistive technology

Table 3: Informal assessment of oral-facial structures and functions

Task	Assessment Items	Observations
Evaluation of Face	Symmetry: normal/ droops on right/ droops on left	Droops on right & left
	Abnormal movements: none/ grimaces/ spasm	Grimaces
	Mouth breathing: yes/ no	Yes
	Checking the jaw function during the function of opening and closing the mouth	
	Range of motion: normal/ reduced	Reduced
	Symmetry: normal/ deviates to right/ deviates to left	Normal
	Movement: normal/ jerky/ groping/ slow/ asymmetrical	Jerky, Slow
	Temporomandibular joint noises: absent/ grinding/ popping	Absent
	Dentition observation	
	Molar occlusion: normal /class /class II/ class III	Normal, Class I
	Incisor occlusion: normal/ overbite/ under bite/ cross bite	Normal
	Teeth: all present/ dentures/ teeth missing	Teeth missing
	Arrangement of teeth: normal/ jumbled/ spaces/ misaligned	Misaligned
	Hygiene	Normal
	The client was asked to *pucker* up his lips	
	Range of motion: normal/ reduced	Reduced
	Symmetry: normal/droops bilaterally/ droops right/ droops left	Droops bilaterally
	Strength (press tongue blade against lips): normal/ weak	weak
	The client was asked to puff cheeks and hold air	
	Lip strength: normal/reduced	Reduced
	Nasal emission: absent/ present	Present

Task	Assessment Items	Observations
Evaluation of Tongue	Surface color: normal/ abnormal	Normal
	Movement: normal/ absent/ jerky/ spasms/ writhing/fasciculation	Jerky
	Size: normal/ small/ large	Normal
	Frenulum: normal/ short	Normal
	The client was asked to protrude the tongue	
	Excursion: normal/ deviates to right/ deviates to left	Not able to excursion
	Range of motion: normal/ reduced	Reduced
	Speed of motion: normal/ reduced	Reduced
	Strength (apply opposing pressure with tongue blade): normal/ reduced	Reduced
	The client was asked to retract tongue	
	Excursion: normal/ deviates to right/ deviates to left	Not able to excursion
	Range of motion: normal/ reduced	Reduced
	Speed of motion: normal/ reduced	Reduced
	Client was asked to move tongue tip to the right	
	Excursion: normal/ incomplete/ groping	Incomplete
	Range of motion: normal/ reduced	Reduced
	Strength (apply opposing pressure with tongue blade): normal/ reduced	Reduced
	Client was asked to move the tongue tip to the left	
	Excursion: normal/ incomplete/ groping	Incomplete
	Range of motion: normal/ reduced	Reduced
	Strength (apply opposing pressure with tongue blade): normal/ reduced	Reduced
	Client was asked to move the tongue tip up	
	Movement: normal/incomplete/groping	Incomplete
	Range of motion: normal/reduced	reduced
	Client was asked to move the tongue tip down	
	Movement: normal/ incomplete/ groping	Incomplete
	Range of motion: normal/reduced	Reduced
	Observation of rapid side-to-side movements	
	Rate: normal/ reduced/ slows down progressively	Slows down progressively
	Range of motion: normal/reduced on left/reduced on right	Reduced bilateral

Task	Assessment Items	Observations
Evaluation of Pharynx	Color: normal/ abnormal	Normal
	Tonsils: absent/ normal/ enlarged	Normal
Evaluation of Hard and Soft Palates	Color: normal/ abnormal	Normal
	Rugae: normal/ very prominent	Normal
	Arch height: normal/ high/ low	Normal
	Arch width: normal/ narrow/ wide	Normal
	Growths: absent/ present	Absent
	Fistula: absent/ present	Absent
	Cleftting: absent/ present	Absent
	Symmetry at rest: normal/ lower on right/ lower on left	Normal
	Gag reflex: normal/ absent/ hyperactive/ hypoactive	Normal
	Client was asked to phonate using /ɑ/	
	Symmetry of movement: normal/ deviates right/ deviates left	Normal
	Posterior movement: present/ absent/ reduced	Reduced
	Lateral movement: present/ absent/ reduced	Reduced
	Uvula: normal/ bifid/ deviates right/ deviates left	Normal
	Nasality: absent/ hyper nasal	Hyper nasal

Table 4: Gross Motor Function Measurement-88 Score

Dimensions	Prescores (%)	Post scores (%)
A. Lying & Rolling	0.86	1.00
B. Sitting	20.66	58.33
C. Crawling & Kneeling	25	69.19
D. Standing	2.56	17.89
E. Walking Running & Jumping	2.77	25.11

Table 5: Purdue Pegboard Test score

Test	Prescores (n)	Postscores (n)
Right Hand	2	10
Left Hand	1	8
Both Hands	0	5
Right plus Left Plus Both Hands	3	23
Assembly	0	5

Table 6: Oral Motor Assessment Scale and the patient's scores

Predominance of type	Passive 0	Sub-functional 1	Semi-functional 2	Functional 3	Pre-Score and classification	Post-Score and classification
Mouth closure	No reaction	Locks and holds the utensil tightly	Holds and releases the utensil quickly	Capable of opening and closing the mouth softly onto the utensil	1 Sub-functional	3 Functional
Lip closure on utensil	Does not close	Does not close but holds with teeth	Closes but in an unsatisfactory manner with partial loss of the food	Closes satisfactorily with total removal of the food	0 Passive	2 Semi-functional
Lip closure during deglutition	Does not close	Does not close and tongue interposes	Does not close properly but tongue does not interpose	Closes satisfactorily	0 Passive	2 Semi-functional
Control of food during deglutition (solid/soft)	Always loses all food	Always loses most of the food	Loses some of the food	Does not lose	0 Passive	2 Semi-functional
Mastication	Without movement	Exclusively munches	Performs movement without tongue control	Chews functionally	0 Passive	2 Semi-functional
Sucking straw	Without active movement	Tries but does not manage	Sucks and manages in an intermittent fashion	Sucks continuously	0 Passive	2 Semi-functional
Control of liquid during deglutition	Always loses everything	Loses most of it	Loses little	Does not lose	0 Passive	2 Semi-functional

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Author's Contribution

Reihaneh Saber-Moghadam: conceptualization, methodology, investigation, writing– original draft, writing– review and editing, visualization, analysis. Toktam Maleki Shahmahmood: methodology, writing– review and editing, investigation, analysis, visualization. Pooria Sarvghadi: methodology, analysis, investigation, visualization. Mehran Beiraghi Toosi: project administration, supervision.

Conflict of Interest

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials

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