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CASE REPORT

Early Intervention in a Child With Aymé-Gripp Syndrome: A Case Report

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Abstract

Aymé-Gripp syndrome is an autosomal dominant inherited disease. The *de novo* pathogenic variant of the MAF gene, located at 16q23.2, is considered the primary common cause of this disease. The pathogenic variant causes interference with lens and eye development and embryonic development. Patients with Aymé-Gripp syndrome typically present with bilateral cataracts, bilateral congenital sensorineural hearing loss, and Down syndrome-like facial features. Dual sensory impairment is observed in these patients. Delayed developmental milestones in the aspect of gross motor, fine motor, speech, and language, cognitive function, and social interaction can be detected early in life. Here we presented a 4-year-old male diagnosed with Aymé-Gripp syndrome. This case report provides an important vivid image of children with rare inherited diseases, multiple comorbidities, sensory impairment, and developmental disabilities. Furthermore, the physiatrist could collaborate with the therapists, special education teachers, and other specialists, providing a comprehensive intervention and individualized rehabilitation program to prevent the patients from deterioration or enhance their function and quality of life.

Keywords: Aymé-Gripp syndrome, Developmental disability, Early intervention, Dual sensory impairment

1. Introduction

Aymé-Gripp syndrome is an autosomal dominant hereditary disease characterized by congenital bilateral cataracts, bilateral sensorineural hearing loss, Down syndrome-like facial appearance, as well as neurodevelopmental abnormalities.[1–3] Defect in different organ systems is a common manifestation. The impairment of the central nervous, cardiopulmonary, musculoskeletal, and genitourinary systems often occurs, causing intellectual impairment and developmental delay.[1,4]

Since the incidence of Aymé-Gripp syndrome is extremely low, there are limited investigations into this disease, and the research related to the prognosis and the principle for early intervention and rehabilitation of this disease is lacking.[4] We hereby reviewed the clinical course and the rehabilitation progress of a case diagnosed with Aymé-Gripp syndrome to provide a

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clear representation of this rare genetic disease.

2. Case report

A male patient had pericardial effusion and tachycardia at a gestational age of 34 weeks and 1 day while his mother received a pregnancy checkup. He was born via cesarean section at the gestational age of 35 weeks and 4 days, presenting with respiratory distress upon birth. His Apgar score was five at one minute after birth and eight at five minutes after birth. He was admitted into an intensive care unit, receiving intubation for desaturation, subxiphoid draining for pericardial effusion, and anti-epileptics for an episode of neonatal seizure. Broad-spectrum antibiotic treatment was also given for several episodes of severe infection, including ventilator-associated pneumonia, urinary tract infection, and bacteremia. Pericardiectomy was arranged at the age of 4 months for refractory pericardial effusion. Upper airway obstruction was found during the weaning process; hence, a tracheostomy was performed at five months. During admission, a brain MRI revealed a small posterior fossa and cerebellum with hypoplasia of the inferior cerebellar vermis. Epileptiform discharge was documented on the electroencephalography.

The patient had the facial appearance of a cleft palate, hypognathia, low-set ears, kinky hair, and anonychia. A bilateral congenital cataract was found while he was hospitalized in the intensive care unit, and surgical repair was performed at two years and two months. His cleft palate was surgically repaired at 10 months. Bilateral sensorineural hearing loss was diagnosed through distortion-product otoacoustic emissions at one year and one month.

After discharge from the intensive care unit, the patient received multidisciplinary outpatient treatment and follow-up. Aymé-Gripp syndrome was diagnosed by next-generation sequencing at another hospital at one year and seven months.

The patient was brought to our outpatient department of pediatric rehabilitation at six months with the presentation of generalized hypotonia, congenital facial anomaly, delay in motor development, and dysphagia with an indwelling nasogastric tube. A comprehensive developmental-behavioral evaluation was conducted at eight months, revealing global developmental delay. Visual and auditory impairments were noted. He had poor sensory and perceptual integrity. The patient had no vision-vision fixation, visual following, or auditory localization. The patient had a poor ability of swallowing and sound production.

The patient received multidisciplinary rehabilitation programs initially in another local clinic, including physiotherapy, occupational therapy, and speech and language therapy. At the age of three years old, the patient changed to the branch of our hospital to continue rehabilitation. The gross motor score of the comprehensive developmental inventory for infants and toddlers (CDIIT) test was 13, 1 percentile, indicating a significant delay in development.[5,6] After one year of rehabilitation, the patient had another comprehensive developmental-behavioral evaluation at four years and one month old, which revealed global developmental delay. The gross motor score of CDIIT was 22, first percentile, indicating mild improvement in gross motor development.[5,6] The delay in fine motor, speech, language, cognitive, and psychosocial function remained without further decline.

At four years and three months, due to severe delay in development, the patient started special education. The special education teacher conducted an individualized education program (IEP) to further enhance the patient's development. The therapists and the special education teachers made clear observation of this patient. They found that despite the patient had severely impaired visual and auditory function, the patient could respond to moving objects and red light, and could respond to the sound produced at his right side ear. The patient's tactile system was better compared with visual and auditory system. The auditory function was also better than the visual function. He could perform rolling and crawling in prone and supine positions, and could transfer himself from supine to sit. But assistance was needed while the patient changed his position from sit to stand. Under the use of ankle-foot orthosis, the patient was able to walk for 1 to 2 strides. Patient had tracheostomy and no verbal expression. Simple physiological needs,

such as food, drink, sleep, rest, could be expressed by body language, touching his parents or teachers, and hand movements The body language include facial expressions and gestures to convey information. Some emotions, such as happiness, sadness and anger could be observed by subtle facial expression. Therapists, teachers and parents could observe eyebrows raising, mouth angle twitching, pursed lips as the access code of signal transduction.

Rehabilitation programs were arranged, including physiotherapy, occupational therapy, and speech and language therapy. Physiotherapy focused on trunk balance and ambulation training. Swiss ball was used to facilitate patient's balance. Partial body weight supported treadmill training was provided for ambulation training. Occupational therapy focused on posture training, transfer, movement facilitation and multisensory stimulation. Speech and language training focused on auditory stimulation to preserve the remanent auditory function. The speech and language pathologist used the adaptive single switch device for auditory stimulation training and augmentative communication training. For communication, the patient mainly communicates with other people by body language. For feeding training, the patient was taught to recognize the foods by touching and smelling under supervision, then consume it with the assistance of the caregiver.

Because of the severe visual and hearing loss, the early intervention program was mainly performed through tactile, vestibular, and proprioceptive system-based training. Snoezelen multisensory intervention was delivered to the patient through a specially designed room with high-tech instruments. We selected toys that generate vibration and sound to produce tactile and auditory input. For visual training, the patient was educated to play a special-designed computer game in a dark room. The strong-light figures on the screen changed with a cueing tone after clicking the mouse. The multisensory environment and the video game helped the patient establish casualty and increase sensory input. Patient had superior tactile sensory system and liked to touch things with different texture. He used bilateral hands and the head to touch things in the outside environment. Patient used his head to rub things very often, like some self-stimulating behavior. The occupational therapist designed different texture setting to promote patient's motivation to move. Playing swing was also provided for vestibular stimulation. For discrimination of people, wristband with different texture were wore in different individuals, helping the patient distinguish among parents and special education teachers.

Currently the patient had got a new pair of eyeglasses. His visual and auditory systems had mild improvement after early intervention program. The patient could gaze his eyes on moving objects with more concentration, and could respond to specific words and vocabularies while listening to them. His rehabilitation training and special education classes, under the goal of improving the independence in daily living, still based priorly on tactile, proprioceptive, and vestibular interventions. Visual and auditory stimulation were also used for improving his social communication abilities.

3. Discussion

Aymé-Gripp syndrome is a rare autosomal dominant inherited disease with the presentation of visual and hearing impairment and complex clinical features, including skeletal defects, joint deformities, short stature, seizure disorder, and brain anomalies.[1,3,7,8] Patients with Aymé-Gripp syndrome may present a facial feature of Down-syndrome like face, including flat facial appearance, short nose, long philtrum, narrow mouth, and low-set and posterior rotated ears.[1] Cataracts, sensorineural hearing loss, pericardial effusion, seizures, and dental abnormalities were also reported.[1,9] The actual prevalence is unknown due to the scarce number of patients.[3] Cognitive impairment and developmental delay are common in patients with Aymé-Gripp syndrome because of multiple system dysfunction, neurological impairment, poor intellectual development, and sensory impairment.[1,7]

The developmental process of children was divided into several domains, including gross motor, fine motor, speech and language, and social interaction.[10] Visual and auditory systems are vital for sensory input,

playing a crucial role in child development, especially in the early months of life.[11] Sensory integration and multisensory processing are also important for incorporating different types of sensory input in order to facilitate the process of development.[12] The maturation of multisensory processes starts early in life and develops through puberty.[13] Disruption of sensory inputs leads to impaired multisensory perception and processing development, hindering individuals from reaching developmental milestones while maturing.[14] Patients with congenital diseases such as Aymé-Gripp syndrome often suffer from impairment in visual input, auditory input, or both, making them to have severe delay from development compared to normal children.[1,15]

The combination of visual and auditory impairment is called dual sensory loss or dual sensory impairment (DSI).[16] Patients with deaf-blind condition could not be educated appropriately in traditional special education programs.[16] The children with DSI mainly communicate through touching; therefore, tactile communication technique as well as the application of proprioceptive and smell stimulation play an important role in the rehabilitation of these children.[16,17] The goal of rehabilitation is to develop compensatory strategies to help the children navigate their environment through enhancing their overall sensory experience.[18] Auditory and visual cues could be used in patients with severe visual and auditory impairment but not total deaf-blind status.[19,20] Assistive devices and technology such as glasses and cochlear implant, as well as augmentative and alternative communication devices, could be considered in the assistance of rehabilitating processes.[20]

This patient had severe impairment of body structure, including cerebellum, eyes, hearing structures, facial appearance, heart, and respiratory system. Visual and hearing impairment, as well as global developmental delay, result in severe limitations in capacity for receiving preschool education and carrying out daily life activities. There is no current literature describing the functional outcome of patients with Aymé-Gripp syndrome because of the small number of patients. Nevertheless, early intervention especially multisensory-based rehabilitation are still necessary since adequate rehabilitation strategies offer an opportunity for a delayed child to promote sensory processing, motor, speech, and communication development, and to prevent the children with multiple system dysfunction from further decline.[21] Our patient had scanty reserve of visual and auditory sensations, and developed a special communication strategy through touching, specific gesture, and body language after years of rehabilitation and special education. The rehabilitation and education were delivered mainly through tactile communication and facilitation of vestibular system and proprioception. Although the patient still need assistance in most of the activities in daily living, the patient's family reported that the patient had better response to the environment after rehabilitation.

There are only a few reports on Aymé-Gripp syndrome because of the low incidence of the disease. Research on the prognosis and the principle for early intervention of this disease are lacking. For such children with inherited rare diseases, which cause multisensory impairment, early intervention with an interdisciplinary approach, as well as the engagement of family members and special education, is necessary for slowing down the natural course of functional deterioration, and even amelioration of academic performance, development, and social interaction.

4. Conclusions

For children diagnosed with Aymé-Gripp syndrome or other hereditary syndromes manifesting as dual sensory impairment, developmental delay is expected, and is commonly observed. Early intervention with an interdisciplinary approach helps maintaining these children's function and may even improves these children's developmental outcomes.

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Conflict of interest

There is no conflict of interest concerning this study.

References

1. Amudhavalli SM, Gadea R, Gripp K. Aymé-Gripp syndrome. In: Adam MP, et al., eds. *GeneReviews(®)*. University of Washington, Seattle. Copyright © 1993-2022.
2. Gripp KW, Nicholson L, Scott CI. Apparently new syndrome of congenital cataracts, sensorineural deafness, Down syndrome-like facial appearance, short stature, and mental retardation. *Am J Med Genet* 1996;61(4):382−6.
3. Chaudhry C, Kaur P, Srivastava P, Kaur A. Ayme gripp syndrome in an Indian patient. *Am J Med Genet* 2021;185(4):1312−6.
4. Niceta M, Stellacci E, Gripp KW, Zampino G, Kousi M, Anselmi M, et al. Mutations impairing GSK3-mediated MAF phosphorylation cause cataract, deafness, intellectual disability, seizures, and a down syndrome-like facies. *Am J Hum Genet* 2015;96(5):816−25.
5. 王天苗, 廖華芳. 嬰幼兒綜合發展測驗之判定準確度及切截點分析. 特殊教育研究學刊 2007;32(2):1−15.
6. 王天苗. 嬰幼兒綜合發展測驗之預測效度研究. 特殊教育研究學刊 2005;29:1−24.
7. Amudhavalli SM, Hanson R, Angle B, Bontempo K, Gripp KW. Further delineation of Ayme-Gripp syndrome and use of automated facial analysis tool. *Am J Med Genet* 2018;176(7):1648−56.
8. Niceta M, Barbuti D, Gupta N, Ruggiero C, Tizzano EF, Graul-Neumann L, et al. Skeletal abnormalities are common features in Ayme-Gripp syndrome. *Clin Genet* 2020;97(2):362−9.
9. Wang Q, Qin T, Tan H, Ding X, Lin X, Li J, et al. Broadening the genotypic and phenotypic spectrum of MAF in three Chinese Han congenital cataracts families. *Am J Med Genet* 2022;188(10):2888−98.
10. Scharf RJ, Scharf GJ, Stroustrup A, Milestones Developmental. *Pediatr Rev* 2016;1:25−37.
11. Lewkowicz DJ. Perception of dynamic and static audiovisual sequences in 3- and 4-month-old infants. *Child Dev* 2008;79(5):1538−54.
12. Jorquera-Cabrera S, Romero-Ayuso D, Rodriguez-Gil G, Triviño-Juárez J. Assessment of sensory processing characteristics in children between 3 and 11 Years old: a systematic review. *Front Pediatr* 2017;5:57.
13. Nardini M, Bales J, Mareschal D. Integration of audio-visual information for spatial decisions in children and adults. *Dev Sci* 2016;19(5):803−16.
14. du Feu M, Fergusson K, Sensory impairment and mental health. *Adv Psychiatr Treat* 2018;9(2):95−103.
15. Konig AL, Sabir H, Strizek B, Gembruch U, Herberg U, Bertrand M, et al. Isolated cytokine-enriched pericardial effusion: a likely key feature for Ayme-Gripp syndrome. *Am J Med Genet* 2022;188(2):624−7.
16. Brabyn JA, Schneck ME, Haegerstrom-Portnoy G, Lott LA. Dual sensory loss: overview of problems, visual assessment, and rehabilitation. *Trends Amplif* 2007;11(4):219−26.
17. Watkins S, Clark TC. A coactive sign system for children who are dual-sensory impaired. *Am Ann Deaf* 1991;136(4):321−4.
18. Omar R, Peng WE, Ishak WS, Saat N. Profile and quality of life of children with dual sensory impairment or deafblindness in visually impaired special centres. *J Sains Kesihatan Malaysia* 2019;17(2):157−63.
19. MPJ Vervloed, Janssen N, Knoors H. Visual rehabilitation of children with visual impairment. *J Dev Behav Pediatr* 2006;27(6):493−506.
20. Lieu JEC, Kenna M, Anne S, Davidson L. Hearing loss in children: a review. *JAMA* 2020;324(21):2195−205.
21. Dionne-Dostie E, Paquette N, Lassonde M, Gallagher A. Multisensory integration and child neurodevelopment. *Brain Sci* 2015;5(1):32−57.