International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 12-12-2020; Accepted: 25-12-2020; Published: 18-01-2021
www.medicalsciencejournal.com
Volume 7; Issue 1; 2021; Page No. 30-32

Manifestation of hearing loss in Joubert syndrome: Case report

Priyanka Jaisinghani[1], Jithin Raj Balan[2]

[1] Dst Inspire Fellow, All India Institute of Speech and Hearing, Manasagangothri, Mysuru, Karnataka, India

[2] Audiologist, All India Institute of Speech and Hearing, Manasagangothri, Mysuru, Karnataka, India

Abstract

Joubert Syndrome (JS) is a rare autosomal recessive condition presenting features of ataxia, mental-motor retardation, hypotonia, opthalmological issues and respiratory problems. The hallmark of this syndrome is 'molar tooth sign' in MRI due to malformations of cerebellar vermis. It is caused by mutations in genes primarily responsible for ciliary function. Therefore, multi-organ issues such as retinal, renal, oral, hepatic, digital and cerebral organs can also coexist. We present a case report of a child diagnosed with Joubert Syndrome, having symptoms of hypotonia, truncal ataxia, poor mental abilities, poor motor abilities and delayed speech and language with hearing loss. The results of audiological evaluation revealed bilateral severe to profound hearing loss. JS being one of the ciliopathy there are chances of having associated damage in sensory hair cells of cochlea resulting in significant hearing loss. Moreover, consanguinity in this case is expected to have increased the expression of autosomal recessive disorder such as JS. Since, there is dearth of literature regarding occurrence of congenital hearing loss in JS, the present case report throws light on this association. It becomes difficult to identify hearing loss when multiple disabilities coexist such as in Jouberts syndrome. Therefore, we suggest pediatricians and other health practitioners to recommend these cases for audiological screening to rule out any hearing loss at the earliest. Whereas, for JS with hearing loss an Audiologist to initiate the intervention by fitting of amplification device followed by intensive listening training and speech and language therapy to ensure a better quality of life.

Keywords: joubert syndrome, molar tooth sign, ciliopathy, hearing loss

Introduction

Joubert Syndrome (JS) is a rare autosomal recessive neuro-developmental disorder aftermath to malformations of cerebellar and brainstem structures [1]. The presence of molar-tooth sign in Magnetic Resonance Imaging (MRI) study is considered as pathognomonic sign for this condition. This classical feature is explained by cleft appearance in between the cerebellar hemispheres due to the absence of the vermis. Additionally, vermian hypoplasia and enlarged 4th ventricle also appears as 'bat wing' in CT and MRI [2]. The agenesis of cerebellar vermis either complete or partial acts as a prognostic indicator in individuals having JS [3].

Joubert Syndrome manifests itself with primary symptoms of ataxia, mental-motor retardation, hypotonia, opthalmological issues and respiratory problems [1]. It has been also reported that postpartum apnoea signifies the prognosis of individuals with JS. Mechanical ventilation is essential for recurring and long lasting apnoea which is associated with JS. Apart from the classical symptoms, certain conditions exist in a few cases of JS, such as anomalies in central nervous system (corpus callosum agenesis, occipital encephalosis), occular coloboma, retinal dystrophy, renal disease, polydactyly, hepatic fibrosis and tumours in tongue [4, 5]. Facial dysmorphism is also reported in several cases with JS [2, 6]. It is recommended that detail evaluation should be carried out for pediatric cases to rule out multi-organ involvement and other brain anomalies using Brain MRI. Eye examination, ultrasonography of abdomen and ECHO examination are also recommended [7].

JS has prevalence of about 1 in 100,000 live births and its chance of recurrence in a family is 25% [5]. Till date approximately 200 cases with JS have been reported across the globe but this might be an underrated estimation [8]. Currently 13 genes have been attributed to Joubert Syndrome and all are associated with ciliary function in some or the other way. They are AHI1, ARL13B, CC2D2A, CEP290, INPP5E, KIF7, NPHP1, OFD1, RPGRIP1L, TCTN1, TCTN2, TMEM67 (MKS3), and TMEM216 [9]. Therefore JS is part of the ciliopathies; set of diseases which are caused due to damage of the motile and immotile (sensory/primary) cilia.

Case Report

We present a case study of a male child of age 1 year 8 months who was brought to our setup with complaints of delayed speech and language, poor motor abilities and hearing loss in both ears. He also had poor socialization skills. At the time of visit it was observed that child expressed needs through vocalization and crying. The child belongs to an Indian family of southern state Karnataka and parents are first degree consanguineously married. The child is a full term baby delivered through caesarean section with normal birth weight and birth cry. His speech milestones were delayed with babbling achieved correctly by the age of 6 months but first word was not yet achieved. Similarly, motor development was also delayed with neck control only partially achieved at the time of visit and sitting with support was achieved by 10 months of age. Following case history the child was sent for detailed evaluations.

Speech and language skills were examined and it was observed that child could recognize family members, could identify few common objects and also, he could understand emotions. Expression was only through vocalizations and he

said 'amma' non-meaningfully. Receptive and Expressive Emergent Language Scales (REELS) test was administered. The child had comprehension of 6 months and expression of 3 to 4 months. Under psychological evaluation, Developmental Screening Test (DST) was administered and child had developmental age (DA) of 3 months with developmental quotient (DQ) of 25. His Intelligence quotient (IQ) was 30 and mental age (MA) was 6 months. Physiotherapist reported that child was completely dependent for mode of locomotion with poor holding and gripping abilities. Pediatrician confirmed the presence of hypotonia and truncal ataxia. Neurologist recommended for Magnetic Resonance Imaging (MRI) brain in T1W Axial plane and T2W Axials, Coronals and Saggitals. MRI findings showed evidence of vermian hypoplasia-dysplasia with hypoplasia of the cerebellum. The superior cerebellar peduncles were elongated and thickened with a parallel orientation and deep interpeduncular fossa. The fourth ventricle was also enlarged. Further, the mesencephalon was elongated with narrow postmesencephalic isthmus. Also, the posterior fossa and retrocerebellar spaces were seen enlarged. Altogether the findings were found to be consistent with JOUBERTS SYNDROME. Due to poor socioeconomic status gene analysis was not carried out hence the causative mutated gene remains unknown in this case.

We present here the audiological profile of this child diagnosed with Jouberts Syndrome. Audiological assessment was carried out using the following test battery:

1. Otoscopic Examination
2. Tympanometry and Acoustic Reflex Testing using GSI-Tympstar version 2.0
3. Transient and Distortion Product Oto-Acoustic Emissions using ILO-292 diagnostic OAE
4. Click and 500Hz tone burst ABR using Biologic Navigator Pro AEP 7.2 system
5. Behavioral Observation Audiometry using GSI-Audiostar Pro via free field speakers.

Under otoscopic examination normal tympanic membrane with cone of light was seen in both ears. Immittance evaluation results were 'A' type normal typanograms in both ears with ear canal volume of 0.8ml in right and 0.9ml in left. Both the ipsilateral and contralateral reflexes could not be elicited in both ears. These findings were suggestive of normal middle ear function. Transient and Distortion product otoacoustic emissions were measured and they were absent in both ears. This indicated outer hair cells dysfunction in both the ears. Behavioral observation audiometry (BOA) was carried out in sound field as the child was not co-operative for the conditioned audiometry. The results of sound field behavioral observation audiometry are mentioned below.

Table 1: BOA responses elicited using different stimulus

Stimulus	Intensity	Response Observed
500 Hz	80-85	Eye movements, Searching sound source
1000 Hz	95-100	
2000 Hz	110	
4000 Hz	120	
Live Speech	85-90	

Further, auditory brainstem response could not be elicited using click stimulus as well as 500 Hz tone burst stimulus even at maximum stimulation level of 90dBnHL for clicks and 80dBnHL for the tone burst. Accordingly, based on these findings the provisional diagnosis was bilateral severe to profound hearing loss. Following the diagnosis, the child was fitted with high gain digital behind the ear (BTE) hearing aid and is presently under intensive listening training and speech language therapy.

Discussion

As mentioned prior, JS is one of the ciliopathies resulting in damage to motile or immotile sensory cilias. The motile cilias are present over the epithelium of various kinds of cells and help in mucal transport. The damage to these motile cilias result in complications such as retinal disease, cystic kidney disease, respiratory tract disease, cerebellar malformations, neural tube defects, polydactyly and cerebellar malformations [10]. Similarly, sensory cilias also play a critical role as hair cells in cochlea [11]. Cochlear stereocilia are microvilli containing actin filaments and not the true primary cilia which are derived from tubulin. However, kinocilium is derived from the true primary cilia and organize or orient the stereocilia over the surface of the hair cells. The kinocilium localizes to more acentric position from its original central position over the apical cell surface. This further leads to assymetrical patterning of the stereocilia. Once the stereocilia morphogenesis is completed the kinocilium degenerates but its basal body remains intact. It is reported that in mice this basal body for damaged hair cells is capable to regenerate the kinocilium and hence has role in repair function [12]. Henceforth, damage to these sensory cilia might terminate this repair process and also formation and patterning of stereocilia thereby leading to permanent hearing loss.

Several ciliopathies like, Usher syndrome, Alstrom syndrome and Bardet–Biedl syndrome henceforth have sensorineural hearing loss as an additional feature. Therefore, JS being a ciliopathy there are chances of having associated hearing loss. At present, very few studies in literature have reported the presence of sensorineural hearing loss (SNHL) in individuals having Joubert Syndrome. A retrospective study across 22 cases was carried out to assess the presence of hearing loss feature in individuals having JS which could be present in cliopathies [13]. 14 cases underwent audiological evaluation out of which 3 adolescents had very mild SNHL, 6 younger children had conductive hearing loss due to middle ear infections whereas, 3 cases were hypersensitive to sound. Overall, the presence of hearing loss in patients with JS was not noteworthy. But, at younger age due to middle ear pathology conductive loss should be prevented keeping in mind the speech and language development and those who had normal hearing at younger age are suggested for continuous follow up at later stage. A 6 year old Indian child who is one of the two siblings diagnosed with Joubert syndrome of consanguineous parents is reported as having congenital sensorineural hearing loss [14]. However, authors suggest that SNHL in this case could be due to separate entity of parental consanguinity and its co-occurrence with JBS could be just coincidence. They came to this conclusion by knowing that even few follow up cases with JS did not report hearing loss. In the present study also, though there was positive consanguinity but this is presumed to have increased the expression of autosomal recessive disorder Jouberts Syndrome.

In Indian context until now 14 cases with Joubert syndrome have been reported in lietrature, four cases at Srinagar [8], three siblings at Mangalore, Karnataka [3], two at Tamil Nadu [15], two siblings at Mumbai [14], one at Hyderabad [16], one at Rajasthan [17] and one at Punjab [18]. Amongst all these cases only one is reported to have congenital sensorineural hearing loss but the degree of hearing loss is not mentioned [14].

At times it becomes difficult to identify hearing loss due to the presence of multiple disabilities such as in case of JS wherein, mental retardation, truncal ataxia, hypotonia and delayed speech and language coexist. There are chances of missing the hearing impairment at early ages of life when maximum speech and language development occurs. The present study highlights the existence of congenital hearing loss in cases with JS and thereby there is a need to modify the recommendations made by pediatricians and other medical professionals to include hearing assessment also in the further investigations. Until now there is only single study which has reported congenital hearing loss in JS [14]. The present study adds on to this and suggests hearing screening for all the cases with JS at the earliest so that management can also commence early.

With the advent of electrophysiology hearing thresholds can be attained even for new born or infants using Auditory Brainstem Response. Further, Oto-acoustic emission is a test to assess functioning of cochlear hair cells in the absence of middle ear pathology. JS being a ciliopathy as already mentioned might have associated hearing loss due to damage of sensory hair cells in cochlea. Therefore, along with other assessments hearing assessment is mandatory to ensure normal functioning of cochlear hair cells. It is necessary to identify the hearing loss at an early stage so that appropriate intervention can be initiated and maximum utilization of the critical period is made. Management by fitting of amplification device followed by listening and speech language therapy will improve their quality of life by reducing the communication breakdown.

Acknowledgements

Our sincere acknowledge to the participant and his parents to be part of the study. We also acknowledge All India Institute of Speech and Hearing, Mysore (affiliated to University of Mysore) for the infrastructure required to carry out the study.

References

1. Joubert M, Eisenring JJ, Robb JP, Andermann F. Familial agenesis of the cerebellar vermis: a syndrome of episodic hyperpnea, abnormal eye movements, ataxia, and retardation. Neurology. 1969; 19:813-25.
2. Maria BL, Quisling RG, Rosainz LC *et al*. Molar tooth sign in Joubert syndrome: clinical, radiologic, and pathologic significance, J. Child Neurol. 1999; 14(6):368-376.
3. Ganesan SL, Narayan A, Tedla JS, Sharada N. Joubert syndrome: A case report. Indian Journal of Physiotherapy and Occupational Therapy-An International Journal. 2010; 4(4)150-151.
4. Parisi MA. Clinical and Molecular Features of Joubert syndrome and Related Disorders. Am J Med Genet C Semin Med Genet. 2009; 15:326-40.
5. Brancati F, Dallapiccola B, Valente EM. Joubert Syndrome and related disorders. Orphanet J Rare Dis. 2010; 5:20.
6. Saraiva JM, Baraitser M. Joubert syndrome: a review, Am J Med Genet, 1992, 43(4).
7. Cullu N, Calik M, Akal A. Joubert syndrome: the clinical and radiological findings.
8. Choh SA, Choh NA, Bhat SA, Jehangir M. MRI Findings in Joubert Syndrome. Indian Journal of Pediatrics. 2009; 76:231-5.
9. Sang L, Miller JJ, Corbit KC *et al*. Mapping the NPHP-JBTS-MKS protein network reveals ciliopathy disease genes and pathways. Cell. 2011; 145:513-528.
10. Tobin JL, Beales PL. The nonmotile ciliopathies. Genetics in Medicine. 2009; 11(6):386-402.
11. Flock Å, Duvall AJ. The ultrastructure of the kinocilium of the sensory cells in the inner ear and lateral line organs. The Journal of cell biology. 1965; 25(1):1-8.
12. Sobkowicz HM, Slapnick SM, August BK. The kinocilium of auditory hair cells and evidence for its morphogenetic role during the regeneration of stereocilia and cuticular plates. Journal of neurocytology. 1995; 24(9):633-653.
13. Kroes HY, Van Zanten BG, De Ru SA, Boon M, Mancini GM, Van der Knaap MS *et al*. Is hearing loss a feature of Joubert syndrome, a ciliopathy?. International journal of pediatric otorhinolaryngology. 2010; 74(9):1034-1038.
14. Kher AS, Chattopadhyay A, Divekar A, Khambekar K, Bharucha BA. Joubert syndrome with polydactyly and optic coloboma in two sibs, Indian J Pediatr. 1994; 61(6):729-732.
15. Raghavan DV, Doshi VV, Nambi S. Joubert syndrome with autism in two siblings: A rare presentation. Indian Journal of Psychiatry. 2016; 58(1):90.
16. Arora R. Joubert Syndrome: Imaging Features and Illustration of a Case. Polish Journal of Radiology, 2014, 79, 381.
17. Sharma NC. Joubert's Syndrome- A Case Presentation. Ind J Radiol Imag. 2006; 16:243-244.
18. Singh P, Goraya JS, Saggar K, Ahluwalia A. A report of Joubert syndrome in an infant, with literature review. Journal of pediatric neurosciences. 2011; 6(1):44.