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Pontine Tegmental Cap Dysplasia: A Case Report from the Audiology Clinic

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Abstract: ***Background and Objective: Pontine tegmental cap dysplasia(PTCD) is a newly identified congenital condition ensuing a wide spectrum of clinical manifestations, marked by unique and specific anatomical malformations of the hindbrain. Symptomatology includes sensory, motor, cognitive and behavioral deficits. The severe end of the spectrum constitutes fatal outcomes as well, as evidenced by the literature. One such case, who visited the department of audiology, is the object of the present study. This study aims at describing the clinical presentations of this patient in relation to the previously reported diagnostic features of PTCD providing justification to the diagnosis. Method: Single case study methodology was adapted and comprehensive audiological investigations were performed using physiological and electrophysiological assessment procedures. Results and Conclusion: The child was found to have profound hearing loss bilaterally in conjunction with almost all the features pertinent to PTCD.***

Keywords: Pontine tegmental cap dysplasia, hindbrain, axon, guidance

1. Introduction

Malformations of the brainstem and cerebellum are very rare and are often poorly reported due to technical constraints. They usually result in severe clinical manifestations due to the involvement of cranial nerves, pyramidal tracts[2]and other cerebro-cerebellar circuits[5].Extensive works on the classification of the recognized midbrain-hindbrain disorders have been executed. Featuring and distinguishing one out of the several reported conditions demands advanced imaging techniques and upgraded knowledge in the realms of embryology and molecular genetics. With the state of the art advances in neuroimaging methods, this has been proved possible. Pontine tegmental cap dysplasia (PTCD) was successfully separated from other overlapping malformations, and the clinical and radiological phenotypes described.

PTCD is a rare hindbrain disorder alleged to have stemmed from defective axonal guidance mechanisms[4] of the embryonic development process. Neuronal cells generated in the ventricular zone [3] migrate to reach and position themselves in different cortical locations thus establishing functional connections during the inside-out formation of the brain[10]. In this work up, neurons project long axons that navigate by interacting with multiple signaling molecules, which produce chemical guidance cues to decide the fate of axons. The process is called axon guidance.

PTCD is a recently reported congenital brain malformation preponderantly involving the rhombencephalon identified by a cluster of peculiar clinicoradiological features.PTCD is a disorder marked chiefly by hindbrain malformations, the main neuroimaging features being, hypoplastic or dysplastic vermis, commonly noted as 'shrunken cerebellum', absent or malformed inferior olives (evident by the absence of lateral bulging of medulla), absent or malformed inferior, middle cerebellar peduncles, lateralized superior peduncles, resembling the 'molar tooth sign', ventralhypoplasia of pons, and typical focal vaulting of the pontinetegmentum(the so called 'cap') projecting into the fourth ventricle, which is the diagnostic signature of the malformation[9]. Also, additional findings like ectopic transversely oriented commissural fibres and cranial nerve involvement were also reported. According to Barkovich et al., PTCD can be put under group III of his classification called 'localized brain malformations that significantly affect the brainstem and cerebellum'

History and Course

Very firstly described by Barth et al in 2007, PTCD is yet an understudied condition in medical literature today. The condition initially was covered under the non-specific umbrella term, pontocerebellarhypoplasias (PCH) [6], since both the latter and the former involve the same anatomical structures, brainstem and cerebellum, and share similar features like reduction in pontine prominence and cerebellovermal dysplasia. Several studies on PTCD are being continuously published over the years, confirming, convincing and refining the earlier made assumptions of pathogenesis and symptomatology. Till date, nearly 30 cases have been identified with PTCD [11]. Researchers are currently reviewing all the previously reported cases of midbrain-hindbrain malformation anticipating that PTCD may have been misdiagnosed as PCH or Möbius syndrome[6] and that the prevalence of PTCD might actually be greater than estimated.

Pathognomonic Mechanisms

The possible pathogenesis of this rare condition can be explained by abnormal axonal migration as evidenced by absence of transverse pontinefibres, absent superior cerebellar peduncles decussation and ectopic pontinefibres. Several molecular mechanisms, genes and genomes were studied anticipating attributions to this disorder. Genes like ROBO3, NPHP1, NTN1, HGPPS and DCC were eliminated from the candidate list earlier thought of causing the disorder. Presently, group of genes called Hoxgenes [6] are studied expecting that these genes could be another mechanism by which these malformations develop [7]. Several molecular mechanisms are also under study possibly

involving in axonal migration defects such as netrin-1/DCC operating sign molecules and mutations in genes encoding ciliary proteins may also pose candidacy for impaired axonal migration[1].It is doubted that point mutations in a single gene or micro-rearrangrments may be the cause of PTCD [8].

Clinical Manifestations

PTCD is characterized by a wide range of clinical features resulting in varying degrees of disability. The degree of brainstem dysplasia correlates well with the developmental disability [5]. Patients typically present with neonatal hypotonia, pyramidal and cerebellar signs, cranial nerve deficits and extracranial malformations involving cardiac, gastrointestinal, genitourinary systems and costovertebral anomalies [9]. The cranial neuropathies result in the variable association of sensory-neural deafness, vision impairment, facial paralysis and difficulties in chewing and swallowing. Severe developmental delay has been reported in most cases with bilateral deafness resulting in language impairments. Cognitive deficits are reported in almost all cases with varying severity ranging from near normal intelligence to moderate-severe mental retardation. Almost all cases had dysarthria and phono-articulatory deficits. Adaptive and behavior problems were also observed.

2. Case Report

This male child, a case of global developmental delay, 1 year old, born second to a non-consanguinous parentage was referred to the Institute of Speech and Hearing. Parents brought the child with complaint of not responding to soft and loud sounds since birth. Birth history was collected which was uneventful with a full term normal vaginal delivery. Birth weight was 3.5kgs as reported. Birth color was normal and birth cry was immediate and parents could not comment further on child's perinatal events. Postnatally, child had difficulties in taking feeds which led him to Neonatal Intensive Care Unit admission for about a week. The child presented with generalized hypotonia which was central in nature. Child could not suck at breast and is fed milk with spoon until now. Histories of breath-holding spells followed by seizures were also reported. Involuntary movement of lips and upper limbs, reduced tonicity of all four limbs with hyperactive deep tendon reflexes were observed on motor examination. A convergent squint on left eye was also noticed. There was no facial asymmetry and no pooling of secretions. Developmentally, the child showed delayed acquisition of motor milestones with head control achieved at 10 months of age. No other motor skill was reported to be achieved. Speech and language milestones were also delayed. The child did not coo and did not exhibit adequate social smile for age. Child did not respond to loud sounds and could not recognize familiar voices, which provoked suspicion for possible hearing loss.

MRI was done; the impression was *pontine tegmental cap dysplasia.* The findings were,

- Abnormal brainstem with hypoplastic pons and flattened ventral surface. Shrunken cerebellum and focal bulging of the pontinetegmentum projecting into the fourth ventricle - pontine tegmental cap dysplasia.
- Vertical orientation and medial positioning of head and body of left hippocampus with round hippocampal head - Hippocampal malrotation, above features show associations with malformations of cortical development and temporal lobe epilepsy.

The child was examined at upgraded institute of otorhinolaryngology. No ear, nose and throat abnormalities were detected. Tympanic membranes were intact bilaterally as revealed by otoscopy. No significant otologicalhistory was reported. The child had not undergone any sort of audiologicalmanagement thus far. Detailedaudiological investigations were performed at Institute of Speech and Hearing, the results of which are as follows: Both external ears were free from structural anomalies and cerumen impaction. Immittance audiometry was done to assess middle ear function, which showed'B'type tympanogram on right ear and 'C' type tympanogram on left ear. The findings were suggestive of middle ear effusion on right ear and Eustachian tube dysfunction on left ear. Acoustic middle ear muscle reflexes were absent bilaterally for both ipsilateral and contralateral stimulations. Distortion Product Otoacoustic emissions(DPOAE) were obtained from both ears. The results showed absent OAEs at all frequencies, which were suggestive of outer hair cells dysfunction in both ears. Auditory brainstem responses were acquired under sedation from both ears. No replicable peaks could be traced even at an intensity of 100dBnHL for click stimuli at the repetition rate of 11.1 clicks/second from both ears. Suggestive of bilateral profound hearing loss.

3. Discussion

The results of all the behavioral, objective and subjective assessmentswere consistent with the impressionofpontine tegmental cap dysplasia. The child demonstrated central hypotonia which was attributable to pontine/hindbrain circuit malformations. Involuntary movements of the limbs and lips observed could be due to defects in the control circuits which involve cerebellum and other hindbrain structures. Vacant stare and breath holding spells could explain the hippocampal abnormalities. Only one case of all of the previously reported cases had hippocampal abnormalities. This child, the object of the present study also presented with hippocampal malrotation and orientation abnormalities, thus making a total of two cases with hippocampal involvement. Irrespective of the intact auditory canals and contents, hearing loss of profound degree was observed in this child. All the cases reported till date presented with hearing loss of profound degree, not less, irrespective of the involvement of auditory canals and other auditory structures, suggesting possibilities of genetic origin involving genes coding for auditory functions. Other structural anomalies of the brain were also consistent with the condition in question. No vertebral and other visceral abnormalities were noticed in this patient and no peripheral nerve involvement was observed. Reported in literature were three patients whohad been implanted with cochlear implants and were provided with listening training to overcome hearing disability. The procedure was beneficial and improved the patients' communicative functions and quality of life. Further research is indicated in the realms of

genetics and molecular biology, to arrive at capable diagnostic methods and prognostic indicators.

References

[1] A. JamesBarkovich, et al (2009). A developmental and genetic classification for midbrain- hindbrain malformations. Brain.132;3199-3230.
[2] BhayanaA,et al (2018).Clinicoradiological aspects of pontine tegmental cap dysplasia: Case report of a rare hindbrain malformation. Indian J of Radiol Imaging,28;18-21.
[3] Celine Plachez, Linda J R. (2005).Mechanisms of Axon Guidance in the Developing Nervous System. Current Topics in Developmental Biology,69, 267-346.
[4] Engle EC. (2010).Human Genetic Disorders of Axon Guidance.Cold Spring Harbor Perspectives in Biology;2:a00174,doi:10.1101
[5] Jessica L. Klein, et al. (2016).Clinical and neuroimaging features as diagnostic guides in neonatal neurology diseases with cerebellar involvement. Cerebellum & Ataxias,3:1
[6] P.Jissendi-Tchofo, et al (2009).Pontine Tegmental Cap Dysplasia: MR Imaging and Diffusion Tensor Imaging Features of Impaired Axonal Navigation. American Journal of Neuroradiology.30:113-19.
[7] Peter G. Barth, et al (2007).Pontine tegmental cap dysplasia: a novel brain malformation with a defect in axonal guidance. Brain,130,2258-2266.
[8] Pin Fee Chong, et al (2015).A case of pontine tegmental cap dysplasia with comorbidity of oculoauriculovertebral spectrum. Brain & development,37,171-174.
[9] Rodolfo M Queiroz,et al (2017).Pontine tegmental cap dysplasia accompanied by a duplicated internal auditory canal. RadiologiaBrasileira.doi/10.1590/0100-3984.2016.0015
[10] Stephen C. Noctor, et al (2002).Dividing Precursor Cells of the Embryonic Cortical Ventricular Zone Have Morphological and Molecular Characteristics of Radial Glia. The Journal of Neuroscience, 22(8),3016-3173.
[11] Sylvie Picker-Minh, et al. (2016).Pontine Tegmental Cap Dysplasia in an Extremely Preterm Infant and Review of the Literature. Journal of Child Neurology.20, 334-340.