IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 11 Ver. VII (November. 2016), PP 62-65
www.iosrjournals.org

Deafness Dystonia Optic Neuronopathy Syndrome – A Case Report

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Abstract: *Deafness dystonia optic neuronopathy (DDON) syndrome is an extremely rare X linked single gene disorder characterized by prelingual or post lingual sensorinural hearing loss since childhood (SNHL),optic neuropathy, progressive dystonia, and behavioral problems. Herein we report a case of 20 year old Indian male who presented with complaints of increased hearing since he was 9 years old and visual difficulty which had started recently approximately at 19 years of age with associated behavioral problems. Investigations revealed bilateral profound hearing loss with optic atrophy. The case showed the typical features of DDON syndrome. Symptomatic management was planned. The case was further referred for genetic testing and was counseled regarding possible prognosis and management. The patient is kept on follow up for assessment. This rare case indicate the need to keep DDON Syndrome in mind while investigating ever simple case of SNHL at early childhood associated with any kind of visual problems.*

Key words*: Deafness, optic neuropathy, syndrome, genetic.*

I. Introduction

Deafness Dystonia Optic Neuronopathy (DDON) syndrome is a X-linked recessive syndrome also known as Mohr-Tranebjærg syndrome. It is a single-gene disorder occurring primarily in males. It is known to result from mutation in TIMM8A or a contiguous gene deletion syndrome at Xq22, which also includes X-linked agammaglobulinemia caused by disruption of BTK, located telomeric to TIMM8A[1,2].

The clinical features of DDON syndrome include sensorineural hearing loss (SNHL), dystonia, optic neuropathy and behavioral problems. This is a very rare genetic disorder. A recent comprehensive review identified 91 affected individuals from 37 families [3]. Here we describe a case of 20 year old Indian male with clinical findings and investigations suggestive of DDON Syndrome. To best of our knowledge this is the first reported case in India.

II. Case

A 20 year old male born to non consanguineous parents reported in the ENT Deptt. at M.M Medical College and Hospital, Solan . He was the first child, with FTNVD, cried immediately after birth. No family history of any congenital disorder. His scholastic performance was below average and he had left school since ten years of age. His developmental milestones except speech were normal. Speech milestones were delayed with first meaningful word at 2 years of age. Hearing loss (progressive in nature) was noticed by the parents when the patient was 9 years of age. They also reported history of frequent attacks of upper respiratory tract infection. There was no significant prenatal or postnatal history related to hearing loss. As reported the patient started having diminution of vision for past 2-3years.

They also reported behavioral changes for past few years like increased aggressiveness, compromised ability to concentrate and increased time to understand simple tasks indicating mild intellectual disability. Patient was examined and various audiological tests were performed and he was also referred for ophthalmological and psychological evaluation. Examination and Investigations: Clinical assessment revealed no ear, nose and throat abnormality. Audiological tests were done. Pure tone audiometry showed profound SNHL with pure tone average of 98 db in right ear and 95 dB in left ear, postlingual in nature (Fig 1). Tympanometric findings showed bilateral A type tympanogram. Ipsilateral and contralateral stapedial reflexes were absent in both ears. Abnormal findings were observed on auditory brain stem response testing where peak V could not be obtained even at 100 dB nHL in both ears for click stimuli which confirmed loss of profound degree esp. at 2-4 KHz (Fig 2). Speech and language skills were developed to acceptable levels. Patient could comprehend simple and complex sentences when spoken at ear level with speech reading to certain extent. Expressive vocabulary was restricted but he could form simple sentences with mean length of utterance (MLU) of 3-4 words.

During the assessment patient was not very active and gave delayed clumsy responses. Axial Computed topographic scan Head and temporal bone showed no abnormality (Fig 3).Ophthalmological examination showed visual acuity of 6/36 in both eyes by Snellen's chart with no further improvement. On Slit lamp examination anterior segments (both eyes) were normal. Stereoscopic fundus examination both eyes revealed disc pallor suggestive of optic atrophy (Fig 4). Foveal reflexes and blood vessels were normal. On Ishihara's charting there was partial red-green color deficiencies. Based on the presence of hearing loss, optic atrophy and mild behavioral changes DDON was suspected as all these clinical features and investigations are suggestive of DDON syndrome. Symptomatic management was planned. Patient was counseled regarding the prognosis. The benefits of use of hearing aid/Cochlear Implantation (CI) & Low Vision Aids were discussed. Patient was counseled regarding use of total communication, educational and developmental programs and was referred for genetic testing at higher institute.

III. Discussion

Mohr and Mageroy described an X-linked recessive disorder in 1960 with childhood onset of sensorineural hearing impairment, which was believed to be non-syndromic and was designated DFN-1, indicating that it was the first described X-linked non-syndromic form of hearing loss[1]. Tranebjaerg et. al. reinvestigated it and identified associated neurologic, visual, and behavioral findings [4]. Thus the syndrome was renamed Mohr-Tranebjaerg syndrome and later deafness-dystonia-optic neuronopathy (DDON) syndrome [5]. DDON occurs in inherited X-linked recessive pattern. In males, one altered copy of the gene in each cell is sufficient to cause the condition that is why this condition is more common in males. The diagnosis of DDON syndrome is established with the following clinical findings a) Progressive SNHL with prelingual or postlingual onset. b) Absent stapedial reflex. c) Abnormal ABR findings. c) Normal evoked otoacoustic emissions, indicating normal outer hair cells [6] d) Normal-appearing optic nerves in children; in adults, the optic nerves become pale. Normal appearance of the retina [7]. e) dystonia/ataxia. f) Gradual slow onset of personality changes, paranoia, dementia. g) Gradual decrease in visual acuity associated with optic atrophy h) Normal findings on Neuroimaging (CT and MRI) of the inner ear [1, 4]. In the majority of males from age 40 years or more CT showed general brain atrophy [8]. j) Agammaglobulinemia occurs when DDON syndrome is caused by a contiguous gene deletion syndrome. Serum immunoglobulins concentration is typically less than 200 mg/dL; although decreased serum IgG and IgA concentrations can be seen in children with a constitutional delay in immunoglobulin production, low serum IgM concentration is almost always associated with immunodeficiency. Patients show slowly progressive decrease in visual acuity beginning approximately at the age of 20 and dementia beginning approximately at age 40.

Psychiatric symptoms as paranoia may appear in childhood and progress. The HL appears to be consistent in age of onset and progression, whereas the neurologic, visual, and neuropsychiatric signs vary in degree and rate of severity [5]. As seen in the reported case there was post lingual hearing impairment in early childhood with the beginning of diminution of visual acuity noticed at approximately 18 years of age. Few psychiatric features had begun to appear but there were no indications of dystonia, dementia as yet. Some of the patients are known to have certain additional features. Spinal cord dysfunction was present in an individual of DDON syndrome with prolonged somatosensory evoked potentials (SEPs) and disturbed central motor conduction to lower extremities in motor evoked potentials (MEPs) [9]. The lifespan of individuals with DDON syndrome show extreme variation and depends on the severity of the disorder. Patients with severe cases have known to survive into their teenage years, while those with milder cases have lived into their sixties [4]. Treatment of this rare genetic disorder is symptomatic. For hearing loss hearing aids and Cochlear Implantation have only variable success because auditory neuropathy is known to be the cause of the hearing loss. James T Brookes reported marginal improvement with continued low scores in standardized speech, language audiometric tests in a four year old child with CI [10]. Thus patients are provided with educational and developmental programs for sensory deficits and training in tactile sign language. Dystonia and associated symptoms are known to improve with GABA β-agonists. Regular neurologic evaluation and assessment for dementia and/or psychiatric manifestations and annual developmental and speech/language assessments in childhood are the line of intervention. Genetic counseling is given to the related families. Prenatal testing for pregnancies at increased risk is possible for families in which the disease-causing mutation has been identified. The diagnosed case should be followed up regularly.

IV. CONCLUSION

The clinicians should keep the possibility of DDON Syndrome in mind while evaluating patients with hearing loss and visual deficits especially at early age who might develop the same clinical features and these cases should be kept on regular follow-up.

Figures And Images

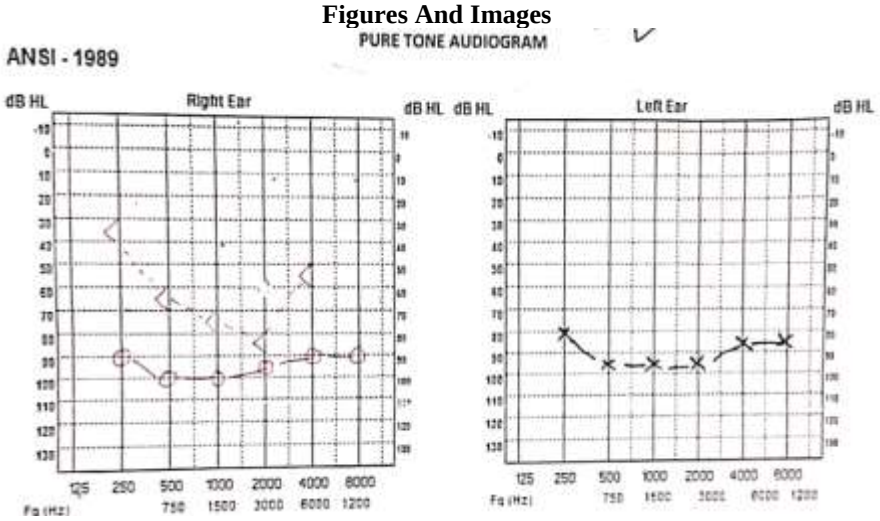

Figure 1:Pure tone audiometry (PTA) of the patient indicating bilateral profound hearing loss with Pure Tone Average of 98dB in Right ear and 95dB in Left ear .

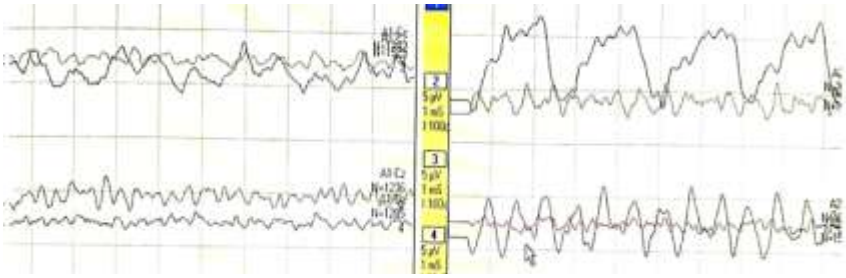

Figure 2 : Brain stem evoked audiometry showing abnormal results .The traces of waveform at 100 and 90dbnHL show absence of peak V in both ears .

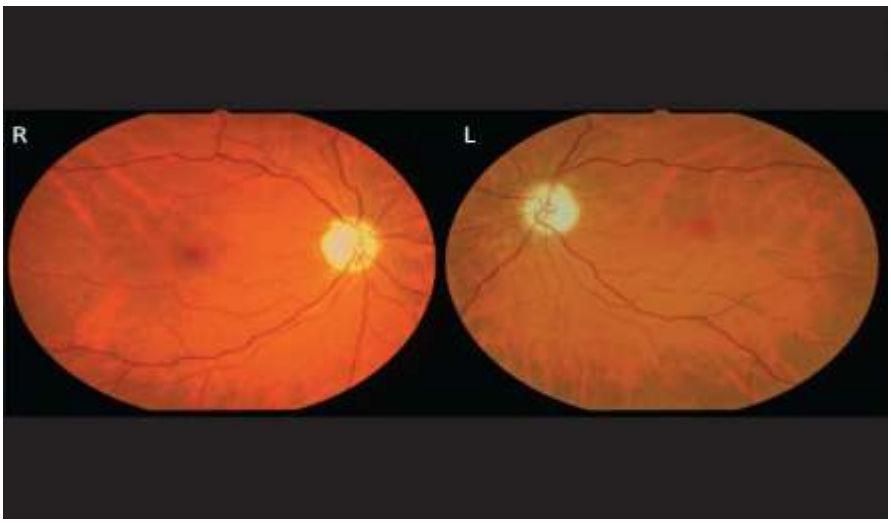

Figure 3: Bilateral Optic Discs show gross pallor.

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