A.B.R. in Nager Type Acrofacial Dysostosis Syndrome

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Abstract

The acrofacial dysostosis of nager is a very rare hereditary syndrome in which findings of mandibulofacial dysostosis are associated with defects of the limbs. The developmental defects of the mesoderm if accompany the neurectodermal malformations, result in mental retardation and sensorineural hearing impairment. The conductive type of hearing loss is mostly encountered in Nager's syndrome but here we present a case with sensorineural involvement, along with its analysis of auditory brainstem evoked response audiometry (ABR).

A 9 years old female presented with delayed speech and hearing at the ENT department K.G.'s Medical College, Lucknow. According to her parents there was a generalised delay of mile stones with speech and hearing in particular. The family history was insignificant as none of the maternal or paternal members in the past two generations had any such problem. We examined both the parents and one of the siblings but none revealed any developmental anomaly to account for any syndrome associated hearing loss. The child was mentally retarded with I.Q. Score of 40. The facial examination revealed absent eyelashes in the medial thirds of lower lids. The mandibular and malar hypoplasia was minimally present. The palpebral fissures were down slanting (anti-mongoloid slant) and the lower lid revealed coluboma on the left side only. The external ear was normal and so was the external auditory canal with the tympanic membrane. There were no palatal abnormalities. There was syndactyly of second and third toes on the left side and simian crease

was present bilaterally. The tuning fork tests revealed bilateral positive Rinne but absolute bone conduction test (ABC) test was unreliable.

The routine blood and urinalysis were within normal limits. The radiography showed hypolastic maxilla and mandible, hypoplasia of both radii, and vertebral anomaly in the form of short neck with fused upper three cervical vertebrae (Fig. 1 and 2). The chest radiography and bony contours of hands and feet (Fig. 3 and 4) were within normal limits. Pure tone audiometry was not possible in this uncooperative retarded child and hence she underwent ABR (by Cadwell 5200 A double channel electric response audiometer) under sedation. The tracings are depicted in the figure 5 and the hearing threshold was in the range of 70 to 80 dB in both the ears. The impedance studies did not reveal any abnormality. The cold caloric test was not possible. The other vestibular tests such as positional, head shake were not tried owing to the existing vertebral anomaly. The existing speech what so ever was limited to only mama and dada. The MRI (head) and fundoscopy were normal.

After assessment of hearing threshold this child was immediately taken up for speech therapy along with assisted hearing. In spite of mental retardation she performed reasonably well.

Discussion

The congenital conductive hearing impairment as encountered in this syndrome are due to various developmental abnormalities either involving the

Fig. 2. Lateral view of skull Maxillary and malar hypoplasia along with cervical vertebral anomaly (shot neck, fused upper 3 cervical vertebrae).

external or middle ear. These are mostly detected by either otoscopy (external auditory canal) or by impedance studies (middle ear). The congenital sensorineural hearing loss on the other hand may be due to the involvement of nervous system from cochlea up to the auditory cortex. Fortunately owing to the different origins of middle and inner ear, the malformations of neuroectoderm (inner ear) usually do not accompany the mesodermal involvement. The neuroectodermal malformations involving the auditory system may be detected either by brain imaging if gross anatomical defect is present or physiologically by ABR if no such defect is present to account for such pathology. The pure tone audiometry in this child was not reliable and hence ABR was selected as a tool

Fig. 1. Occipitontal view of skull showing Maxillary and malar hypoplasia.

Fig. 3. Radiography of hands showing normal bony contours

Fig. 4. Radiography of feet showing normal bony contours.

for assessment of hearing. As the impedance audiometry was normal, the likelihood of conductive element contributing to the hearing impairment would have been minimal. The psychiatric examination revealed severe mental retardation reflecting deranged physiology of brain probably due to developmental reasons. As the brain imaging did not reveal any gross pathology the hearing impairment was considered to be a part of mental retardation and therefore aberrant auditory conduction was suspected to be contributory. This aberrant auditory conduction was suspected to be contributory. This aberrant auditory conduction might have been due to malformed auditory pathways and this prolonged neuronal conduction may have been either due to lack of myelination or as a result of prolonged refractory period. As the ABR has been recorded even in a premature child by Weber (1982) the lack of maturation (myelination) of the nervous system as in this case was not considered to cause any hinderance in its recording. Because ABR testing with clicks result in only one point audiogram, it is not possible to distinguish among rising, flat and falling hearing tones (Eggermont 1982). Sensorineural hearing impairment are characteristically most severe in the high frequencies, so the click ABR threshold

may overestimate the mannitude of overall loss at speech frequencies. In contrast a significant low frequency loss may go undetected. Here the frequency of the click stimulus was selected at 3000 Hz, since at this frequency the accuracy of ABR is excellent for detecting average sensorineural hearing impairment of more than 30 dB. The preferred method of measuring hearing threshold as in this case was the measurement of that minimum threshold at which wave V was just recognisable. Alternatively the threshold calculation form the latency of wave V based on age matched standards would not have been suitable here as the myelination status was not predictable.

The ABR in this case revealed bilateral delayed wave V; their respective latencies being 6.42 msec. on right and 7.51 msec. on left. The latency of wave I on the left side was prolonged (2.11 msec), but the interwave latency (I-V) were 5.3 and 5.4 msec respectively on right and left sides. Prolonged latency of wave I denotes delayed conduction from cochlea to cochlear nucleus. This prolonged latency on the left side predicts either a delayed generation of impulses from cochlea or some delay in the conduction through cochlear nerve. The former may be due to some element of conductive loss and the latter may be the result of either a lack of proper myelination or prolonged refractory period. The interwave latencies of both the sides are comparable and hence the auditory pathways between these generator sites (of both the waves) viz cochlear nucleus and medial geniculate body are more or less equally effected. Hence the basic derangement of the auditory pathway on the left side (compared to right) lies somewhere between cochlea and cochlear nucleus. Moreover the wave form of left side is more discernable as compared to right. This denotes that the various generator sites on the left side are producing their characteristic wave pattern and hence depicting normal conduction between cochlear nucleus and medial geniculate body. On the contrary the wave pattern of the right side is not as clear as of the left. This may suggest that impulses are not being conducted normally between the true generators, but still the conduction is adequate enough to maintain the interwave latency I to V on the left side. This might be due to the redundancy or some alternative conduction in the auditory pathways. The figure 6 shows input neurons on the left and output neurons on the right. The input neurons

Fig. 5. Auditory brainstem evoked response audiometry of right side (upper tracing) and left side (lower tracing)

Latencies : $V=6.92$ msec (R+) 7.51 msec (L+)

Interwave latency 1 +) $V=5.3$ msec R+ 5.4 msec L+

A and B are supra-threshold to output neurons X and Z respectively since there are multiple synaptic connections releasing supra-threshold levels of neurotransmitter. Similarly both the input neurons individually are sub-threshold to it. Thus in case of damaged X and Z the impulse from input neurons would be conducted through Y. This alternative conduction path may bypass the actual generator site but still be able to conduct the impulses to their destination. Another hypothesis of alternative

conduction is by divergence in multiple tracts (Fig. 7). The multiple small peaks between waves I and V on the left side may represent various 'small generators' involved in the conduction of the electrical impulse through the alternative pathway.

Most of the reported cases of acrofacial dysostosis reveal only conductive component in hearing impairment (Chrzanowska et al 1993); Meyerson et al 1987, Lowry RB, Pavone et al 1986). The

Fig - 6

Fig. 7

conductive component is usually attributable to atretic ear canal (Meyerson et al 1987) or middle ear malformations. The incidence of dysplastic ears with external auditory canal defect is 85% and the conductive hearing impairment in only 60%. These are predominantly those with normal intelligence and without any neurological involvement. On the contrary Jackson et al (1989) have also reported Nager's syndrome with subnormal intelligence and Fryns et al (1996) with severe neurological deficit. The neurological defect consisted of spastic diplegia, hemiparesis of left arm and of agenesis corpus callosum (CT scan). This patient died at the age of 50 years due to complete AV block signifying associated nerve conduction abnormality. Thus the neuroectodermal involvement leading to sensorineural hearing impairment and mental retardation is rare in this extremely rare syndrome. There is a considerable variation and overlap between the various congenital abnormalities found in this syndrome but characteristic emphasis is made on specific association of the first arch syndrome with limb defects. The prognosis rests upon early rehabilitation, particularly of the speech and hearing. As far as the assisted hearing is

concerned, the approach adopted for hearing aid selection was that of Kilney (1982) and Mahoney (1985) which compares aided versus unaided ABR thresholds. In aided condition a specified input was delivered from an earphone suspended over the hearing aid microphone. Hearing aid gain was manipulated until a recognisable waveform was evident. However Beauchaine and Gorga (1988) have cautioned against the application of ABR to paediatric hearing aid selection. The other defects encountered may be developmental delay, feeding difficulties due to palatal abnormalities or evidences of upper airway obstruction.

The etiology is mostly sporadic as in this case but AR and AD inheritance (Lowry RB, 1977) have also been suggested. The prevention is not exactly known but genetic counselling is absolutely indicated. Hence a proper rehabilitation would include :-

1. Close surveillance at birth for prematurity, upper airway obstruction and feeding problems.
2. Hearing should be assessed as soon as possible and speech therapy offered when necessary.

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