Variation of hearing function in children with Apert Syndrome: A case report of three patients

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SUMMARY

Introduction: Apert syndrome is a rare disorder characterised by craniosynostosis, midfacial hypoplasia and symmetrical syndactyly of both hands and feet. Hearing loss is also a common symptom in patients with Apert syndrome. This case series aims to describe the clinical characteristics of hearing loss in patients with Apert syndrome. Case report: We present three children with Apert syndrome: (1) a 3-year-old boy with bilateral profound sensory neural hearing loss (SNHL), (2) a 2-year-old girl with otitis media effusion (OME) and mild conductive hearing loss (CHL) and (3) a 4-month-old boy with prolonged interpeak wave latency of wave I-III in the right ear based on brainstem evoked response audiometry (BERA) examination. Conclusion: As hearing loss is a common complication in patients with Apert syndrome, early and periodic screening of hearing function and speech and language development are imperative in these patients.

INTRODUCTION

Type 1 acrocephalosyndactyly, commonly known as Apert syndrome, is a rare craniosynostosis affecting about 9.9 to 15.5 infants per 1,000,000 live births. This syndrome, caused by the mutation of fibroblast growth factor receptor 2 (FGFR2) and inherited in an autosomal dominant manner, is classically characterised by craniosynostosis (fusion of premature cranial sutures), midfacial malformation and syndactyly of the hands and feet.[1–3]

Patients with Apert syndrome usually presents with acrocephaly, frontal bossing, midfacial retrusion, shallow orbits, proptosis, hypertelorism, down-slanting palpebral fissure, strabismus, flat nasal bridge, septal deviation and low-set ears. In addition, oropharyngeal examination may reveal bifid uvula, dental crowding, and orofacial clefts – including submucous cleft palate, cleft palate and pseudo cleft. These patients may be distinguished from other craniosynostosis syndromes by their unique hand deformities comprising of three syndactyly types: spade (type I), mitten (type II), and rosebud (type III).[4,5]

Otologic and audiologic symptoms are common in Apert syndrome. These include malformations of the outer, middle and the inner ear resulting in hearing loss. This warrants the need to perform prompt comprehensive audiologic investigation in children with Apert syndrome. These examinations may include impedance audiometry, pure tone audiometry, otoacoustic emission (OAE), brainstem evoked response audiometry (BERA) and auditory steady state response (ASSR) tests. Computed tomography (CT) scan of the temporal bone may also help visualise the middle and the inner ear and exclude other potential causes of hearing loss.[2,3]

Although there were several studies that reported the variation of hearing impairment in patient with Apert syndrome, our case report aims to add more information regarding anatomical finding, variation, and degree of hearing impairment in Apert syndrome. We reported three Apert syndrome patients with variation and clinical findings in hearing assessment.

CASE PRESENTATION

First Case

A 3-year-old boy diagnosed with Apert syndrome presented to the ear, nose and throat (ENT) clinic for audiologic investigation. The patient had delayed speech and was only able to say a few simple words with poor articulation. He was only able to respond when called with loud voice but was able to understand commands through sign language. The child was delivered vaginally at term with a birth weight of 3000 grams. There was no history of icterus, neonatal intensive care unit stay or ototoxic drug use. At birth, the patient had flat head syndrome and syndactyly of both hands and feet. The child had a history of front orbital advancement (FOA) surgery at the age of 24 months and syndactyly repair at the age of 35 months. He also had motor developmental delay in which the patient could walk only at the age of three years.

Physical examination revealed craniosynostosis, midfacial retrusion, hypertelorism, downslanting palpebral fissures, flattened nasal bridge and low-set ears (Figure 1). Patient also present with syndactyly of the hands and feet. The nasal cavities were narrow with inferior turbinate oedema, without secretions or septal deviation. Oropharyngeal examination revealed bifid uvula and pseudo cleft with adenotonsillar hypertrophy. Patient had normal ear canal with intact

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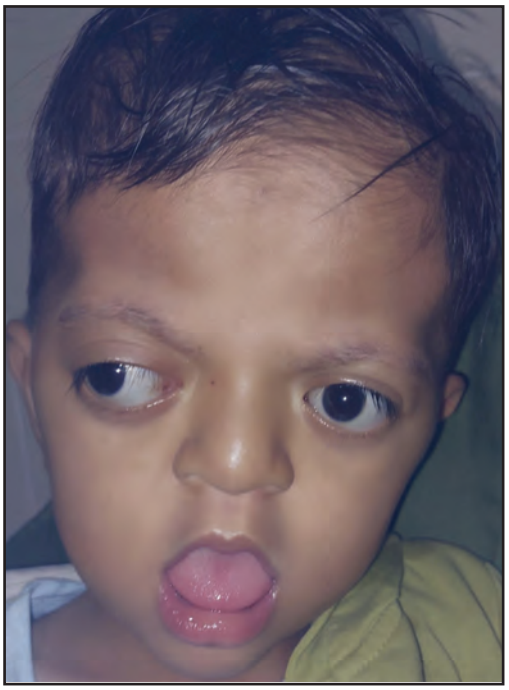

Fig. 1: Clinical findings of the first case showing craniosynostosis, midfacial retrusion, hypertelorism, and downslanting palpebral fissures, flattened nasal bridge, and low-set ears.

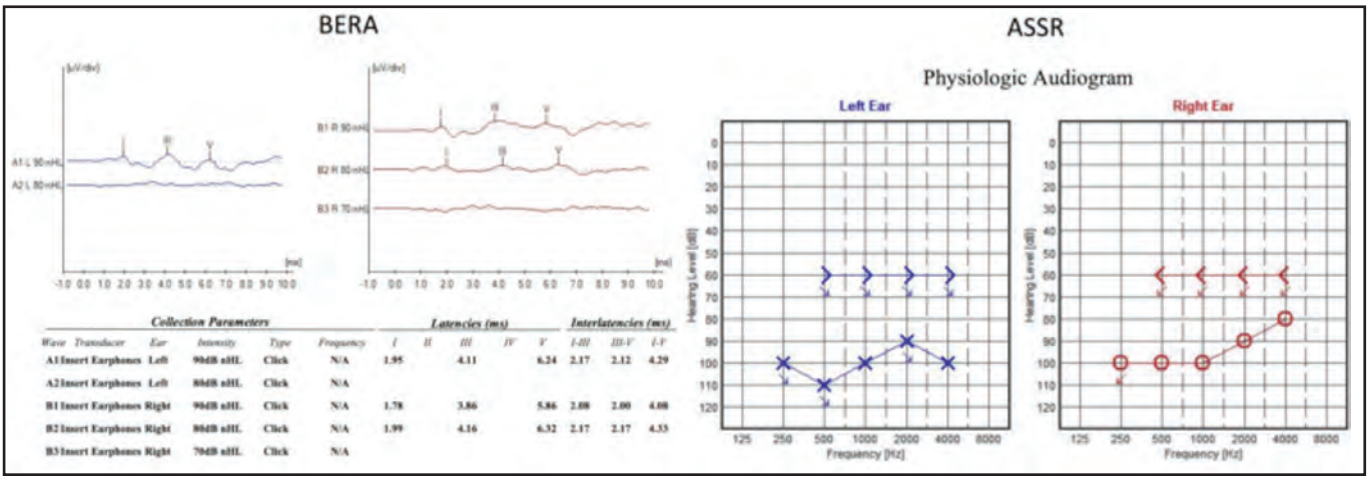

Fig. 2: Results of brainstem evoked response audiometry (BERA) and auditory steady state response (ASSR) tests of the first patient.

tympanic membrane in both ears. Non-contrast CT scan revealed diameter of internal auditory canal (IAC) were 2.08 to 2.93 mm in the right ear and 2.68 to 3.01 mm in the left ear and bilateral high jugular bulb.

Tympanometry showed type A tympanogram in both the ears. A BERA with click stimuli (2000 to 4000 Hz) showed that wave V was detected at 80 dBnHL on the right ear and at 90 dBnHL on the left ear. ASSR test (500 to 4000 Hz) revealed right and left AC >90dB and BC undetected more than 60 dB (Figure 2).

The patient was diagnosed with Apert syndrome with type III syndactyly (rosebud) based on the clinical findings, bilateral profound sensory neural hearing loss (SNHL), delayed speech, global developmental delay, bifid uvula and adenotonsillar hypertrophy. Based on the examinations, the patient was suggested to use hearing aids, undergo tonsiloadenoidectomy and consult to speech therapy.

Second Case

A 27-months-old girl with Apert syndrome presented to the ENT clinic for hearing examination. The patient also had delayed speech in which she was only able to say four simple words ("mama", "papa", "num" and "mam") and had type II syndactyly (mitten) in both hands and feet. She was able to respond when called and show signs of interest to the environment by pulling the mother's hands. The patient was born to an uneventful pregnancy by normal vaginal birth at term with a birth weight of 3500 gm. The patient was born

with flat head syndrome, cleft palate and syndactyly. The child underwent palatoplasty at the age of 9 months, FOA surgery at the age of 20 months, and syndactyly repair at the age of 23 months.

The patient had normal motor development with craniosynostosis, midfacial retrusion, hypertelorism, proptosis, downslanting palpebral fissures, low-set ears and repaired cleft palate. Patient had normal ear canal with intact dull tympanic membrane in the both ears.

Non-contrast CT scan showed dysplasia of the lateral semicircular canal of the right ear. Diameter of IAC were 4.38 to 5.59 mm in the right ear and 3.98 to 5.74 mm in the left ear. Tympanometry revealed type B tympanogram in both ears, suggesting the presence of OME. A BERA with click stimuli revealed that wave V was detected at 30 dBnHL in both the ears, while with tone burst stimuli at 500 Hz showed that wave V was detected at 20 dB in both ears. The patient was diagnosed with Apert syndrome with type II syndactyly (mitten) based on clinical findings, otitis media effusion (OME) and mild conductive hearing loss (CHL). The patient advised to visit outpatient clinic regularly to evaluate middle ear condition and hearing function.

Third Case

A 4-month-old Apert syndrome boy presented to the ENT clinic for hearing evaluation. The parents complained that the patient had brachycephaly, proptosis, lagophthalmos and syndactyly in both hands and feet. The child was born to an uneventful pregnancy by a caesarean section after 36 weeks of gestation with a birth weight of 2875 gm. The patient had uneventful postnatal period, had no history of ear discharge, could respond to sound and could raise his head at the age of 3 months. The patient was diagnosed with Apert syndrome with bilateral type II syndactyly (mitten) in both hands and feet, tetralogy of Fallot, right undescended testis and spina bifida.

Physical examination revealed brachycephaly, wide fontanelle, high forehead, midfacial retrusion, exophthalmos, hypertelorism, downslanting palpebral fissures and low-set ears, while oropharyngeal examination revealed pseudo cleft. Patient had normal ear canal with intact tympanic membrane in both the ears. Non-contrast CT scan showed dilated endolymphatic space in the ampulla of semicircular canal in both ears.

Tympanometry test revealed a bilateral type A tympanogram and OAE test showed normal findings. A BERA with click stimuli revealed that wave V was detected at 30 dBnHL and with tone burst stimuli at 500 Hz showed that wave V was detected at 20 dBnHL in both ears. We found the latency of wave I-III at 60 dBnHL was lengthened in the right ear (2.91 ms). The patient was diagnosed with Apert syndrome with type II syndactyly (mitten) based on the clinical findings. The patient was advised to visit ENT outpatient clinic regularly to evaluate hearing function.

DISCUSSION

The clinical features found in our three patients, including craniosynostosis, midfacial retrusion, down slanting palpebral fissures and syndactyly, are consistent with the diagnosis of Apert syndrome. In addition, all three cases also exhibited ear malformations such as bilateral high riding jugular bulb, dysplasia and dilatation of semicircular canal and low-set ears. This is consistent with previous literature stating that ear malformations in patients with Apert syndrome may involve the outer ears (low-set ears, posteriorly rotated ears, micro or macrotia, abnormal pinna morphology and narrowing of external auditory canal, the middle ear (Eustachian tube dysfunction, CHL, chronic recurrent OME, stapes fixation and ossicular malformations), and/or the inner ear (dilated cochlear aqueduct, dilated vestibulum, cochlear hypoplasia, high-riding jugular bulb, superior and posterior semicircular canal dehiscence, and mastoid cell opacification).[2,3,6]

With the involvement of ear organs in the pathophysiology of Apert syndrome, patients with Apert syndrome may suffer from hearing loss, of which the most common type of hearing loss is CHL. However, cases with mixed-type hearing loss or SNHL have also been described in Apert syndrome. This is proven by findings from a case series involving 125 patients with Apert syndrome which found that about 80% of these patients suffered from hearing loss, 93% of which suffered from CHL, 5% from mixed-type hearing loss, and 2% from SNHL.[7] Our second case had mild CHL with OME from the tympanometry, BERA. It is consistent with literature that found CHL in Apert syndrome may be attributed to chronic persistent OME, tympanic membrane ossification, congenital ossicular anomalies (e.g., stapes fixation, ossicular erosions).[1,2,6,7] As stated by Rajenderkumar et al.[2], chronic persistent OME, which happens in nearly all patients with Apert syndrome (93%), is responsible for mild-to-moderate CHL in more than 56% cases. On the other hand, the stapes fixation observed in Apert syndrome patients may be elaborated by the fact that the syndrome is characterised by the disturbance of the development of the branchial arches, which are the precursors of the ossicles.[2]

While CHL is commonly found in patients with Apert syndrome, SNHL is rarely reported in this syndrome. Our first case showed profound sensorineural hearing loss without any cofounding factors related to SNHL in pre-postnatal history. Zanetti et al.[1] postulated that SNHL in Apert syndrome may arise from auditory nerve compression due to skull base defect or narrow internal auditory canal, while Church et al.[8] added that the hearing loss may be caused by brainstem compression, Alnord-Chiari malformation, or auditory nerve stretch. This is based on the finding that, according to BERA with click stimuli, wave II was either absent or abnormal in all cases, while the interpeak latency of wave I-III was lengthened in 91% of the patients and those of wave III-V was lengthened in 27% of the study's patients – suggesting a decrease in nerve conduction velocity when the impulse passes through internal auditory canal and posterior fossa.[8] We found prolonged interpeak latency of wave I-III in our third case, which suggesting a possibility of decrease in nerve conduction velocity. The normal diameter of IAC varies from 4 to 8 mm based on several publications, although it is

considered stenotic if smaller than 2 mm.[9] First and third case has smaller diameter than normal IAC variation (< 4 mm). Other possibility of this prolonged interpeak latency of wave I-III is delayed maturation of auditory nerve pathways.

All in all, these findings highlight that hearing loss is common in Apert syndrome, thus emphasizing the importance to perform hearing screening and evaluation in Apert syndrome patients to promptly detect abnormalities that are overlooked with radiological imaging.[8] This is saliently important to enable prompt intervention and early speech-language therapy to prevent progressive hearing loss and cognitive and developmental delay in these patients.

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