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Hearing impairment in 18q deletion syndrome

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Abstract
The 18q- syndrome is associated with hearing impairment in 50–80 per cent of cases. The hearing loss may be sensorineural or conductive. A high proportion of cases are associated with narrow or stenosed external auditory canals. This may be a useful clinical pointer to the syndrome. Two cases with impaired hearing are presented in this paper including one case with complex external ear and middle ear malformations. The clinical and audiological features in each case are described.

Key words: Deafness; Chromosome, Human, Pair 18; Chromosome Deletion; Ear Canal

Introduction

Deletions of the terminal portion of the long arm of chromosome 18 (18q- syndrome) is well recognized. This is one of the more frequent chromosome deletion syndromes. It is estimated to occur at a frequency of around 1 in 40 000 births.[1] The clinical features include mental retardation, growth deficiency, facial dysmorphism and neurological abnormalities. The craniofacial features include deep set eyes, midfacial hypoplasia, upwardly slanting palpebral fissures and a 'carp shaped' mouth. In some cases of growth retardation there may be a deficiency of growth hormone.[2] The neurological abnormalities have been reviewed by Miller *et al.*[3] and Kline *et al.*[4] These include hypotonia, seizures, chorea, ophthalmological abnormalities and structural brain abnormalities (dilated ventricles, hydrocephalus, porencephaly, cerebellar hypoplasia, migration defects and abnormal myelination). The degree of mental retardation is variable and may be relatively mild in those with small deletions. Unlike many chromosomal syndromes life expectancy is thought to be normal and many affected adults have been described. Although deafness has been frequently mentioned in case reports, there has been no specific study of deafness in this syndrome.

In this paper the otological and audiological findings in two individuals with 18q- syndrome are presented and the literature reviewed. In the second case the details of operations carried out on the malformed ears have been described.

Case reports

Case 1

This boy was noted to have hypospadias at birth and showed slight delay in his early motor milestones. He had a prominent over-riding lower jaw and rather deep set eyes. There was bilateral fifth finger clinodactyly. There were concerns about his speech development and hearing in early childhood. He was found to have bilateral otitis media with effusion, which was thought to be responsible for his hearing impairment. Grommets were inserted at three years of age which resulted in a temporary improvement of hearing. The pinnae, external auditory canals and tympanic membranes appeared normal. Pure tone audiometry carried out at the age of seven years showed bilateral mild sensorineural hearing losses (Figure 1). Brain stem electric response audiometry (BSER) elicited normal responses on both sides. However, evoked otoacoustic emission (EOAE) testing showed abnormal responses on both sides. A magnetic resonance image (MRI) brain scan and a computed tomography (CT) scan of the petrous temporal bones were both found to be normal. Chromosomal analysis at the age of four years showed a deletion 18q. 22-qter in all cells. Examination of the parental blood showed normal chromosomal patterns.

Case 2

A 15-year-old girl was found to have bilateral mixed hearing losses on pure tone audiometry (Figure 2). A diagnosis of a *de novo* 18q deletion had been made at six years of age. Clinical examination showed that both pinnae appeared normal but the external auditory canals were very narrow. She had great difficulty using hearing aids because of the narrow canals. CT scans of the ears were found to be normal. She underwent surgery in an attempt to improve the hearing. Exploration of the right ear was performed initially, at 15 years. Anteriorly, there was a large bony defect opening into the temporo-mandibular joint. The bony canal was very narrow, and the tympanic membrane was absent. The periosteum medial to the bony canal was attached to the malleus and the ossicular chain was mobile. Split skin grafts were placed over the periosteum in contact with the malleus and the exposed bony area of the external auditory canal. Although there was an initial improvement of the hearing in the right ear after surgery, the canal has narrowed again and the hearing has subsequently deteriorated (Figure 3(a) and (b)).

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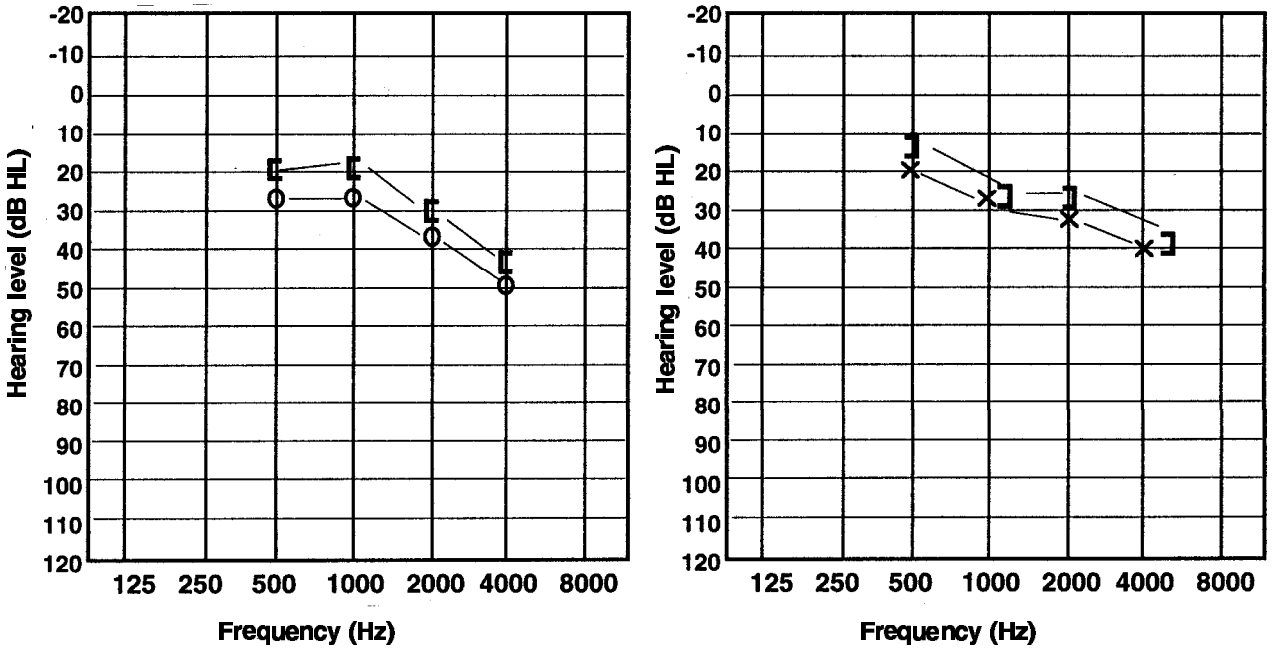

FIG. 1

Pure tone audiogram in Case 1, showing bilateral mild sensorineural hearing losses. Air conduction: right = 0, left = X. Bone conduction: masked right = [; left =].

Exploration of the left ear was carried out 18 months after the first operation. The bony external auditory canal was narrow and had a blind ending. There was no tympanic membrane on this side. The ossicular chain was intact but the malleus was deformed. There was a fibrous connection between the tip of the handle of the malleus and the meatal skin. The bony external auditory canal was enlarged. An underlay graft of temporalis fascia was placed underneath the handle of the malleus covering the bone of the external auditory canal. Post-operatively the left ear healed well, but the hearing did not improve. With the widening of the external auditory canal the patient was able to use a hearing aid in the left ear.

Discussion

It is difficult to obtain an accurate estimate of the frequency of deafness in the 18q- syndrome since hearing impairment has not been stated in many reports on the condition. This may be because of difficulties in hearing assessments – the syndrome is associated with mental handicap that could have caused difficulties with hearing tests. Keppler-Noreuil *et al.*,[1] reported an incidence of 50–80 per cent with hearing impairment in the syndrome in their review of the literature. Gay *et al.*,[5] found hearing losses in 25 per cent of patients on an 18q- register in Texas. In a detailed genetic study of seven patients by

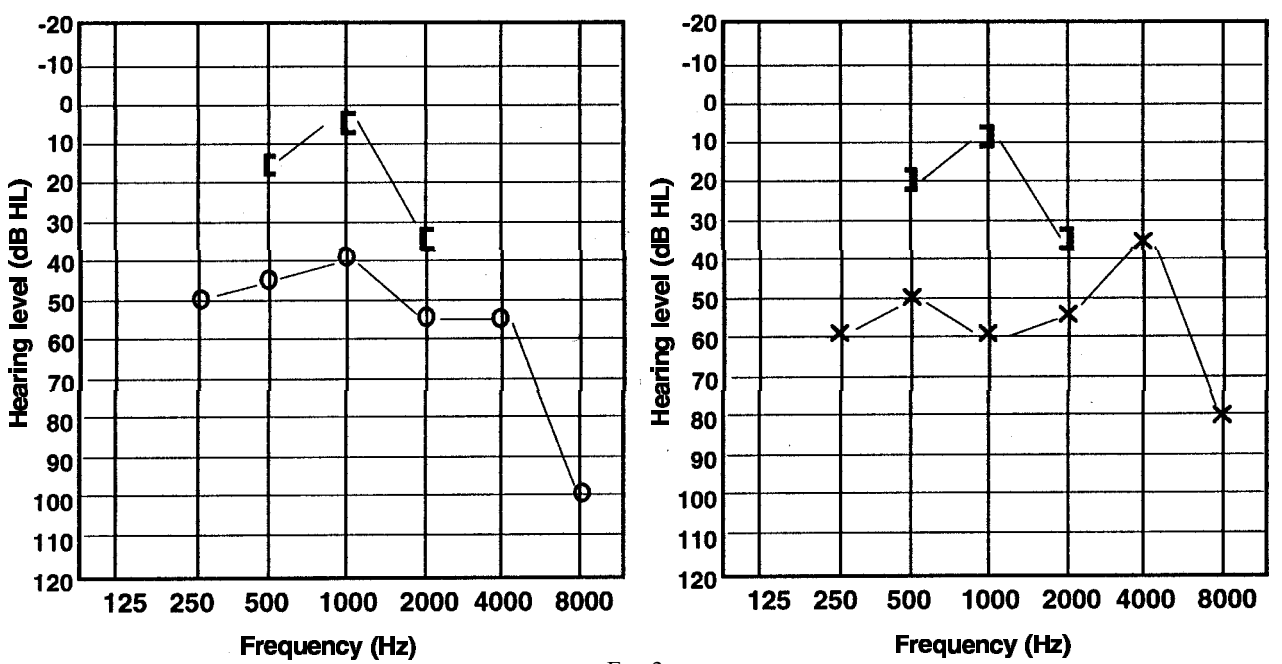

FIG. 2

Pure tone audiogram in Case 2 before surgery. Note the bilateral conductive hearing losses, with dips at 8 kHz indicating a sensorineural component of the deafness.

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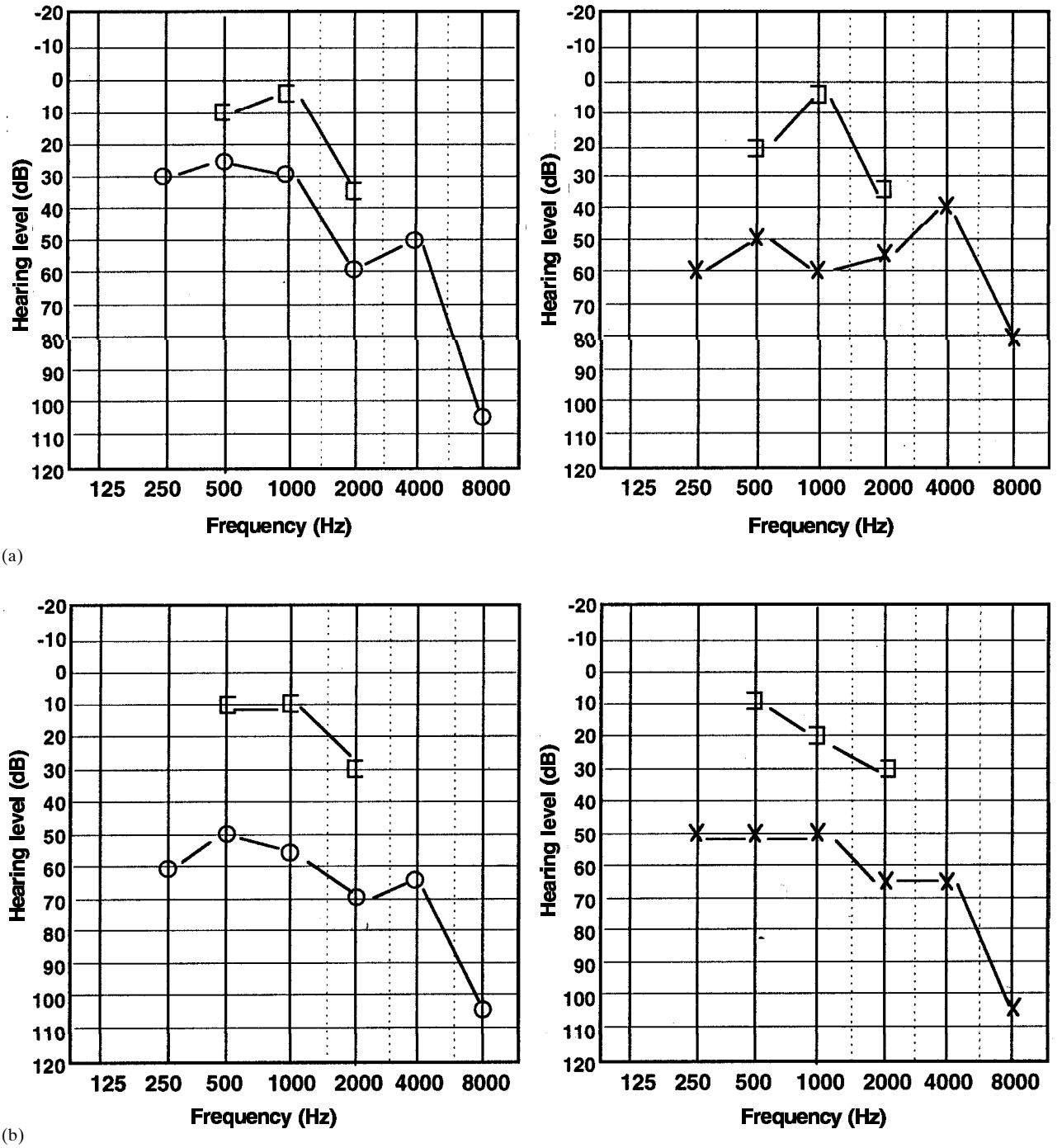

FIG. 3

(a) Improvement in air conduction thresholds in the right ear shown in an audiogram carried out six weeks after surgery. (b) The air conduction thresholds in the right ear deteriorated markedly 12 months after surgery.

Kline *et al.*,[4] there were five with either sensorineural or conductive hearing loss. In an earlier study Wertelecki and Gerald[6] found hearing losses in five out of six patients. They also made reference to seven cases of deafness in the preceding literature. It would seem, therefore, that hearing impairment is one of the commonest features of the syndrome. As many of these children may also have learning difficulties, it is of vital importance to recognize a hearing impairment, in order that appropriate rehabilitative measures and educational input could be arranged.

One of the striking features in our second case and in many of the cases in the literature was the narrowing of the external auditory canal.[5–8] In our patient the tympanic membrane was absent on both sides. The narrowing of the external auditory canal may cause difficulties with the fitting of hearing aids. This problem was overcome by the operation performed on the patient's left ear *(Case 2)*. It appears that the narrowing of the external auditory canal is not always associated with the deafness and vice versa. Loss of hearing with narrowing of the external auditory canal may be due to abnormal development of the ear. There are a number of genetic syndromes in which malformations of the outer ear and middle ear are associated with conductive deafness e.g. Treacher-Collins syndrome. The structural defects in Treacher-Collins syndrome have been delineated.[9] The gene responsible for this disorder was identified on chromosome 5.[10] It is rare to have a stenosed external auditory canal in the

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absence of other malformations of the pinna. This combination may be useful in making a clinical diagnosis of the 18q- syndrome.

The normal BSER and MRI brain scan findings in *Case 1* show that the hearing impairment is not due to a neural lesion (although there is evidence of decreased myelination in the 18q- syndrome).[1,5] The abnormal EOAE results in this case clearly show that the sensorineural component of the deafness in the 18q- syndrome is due to a cochlear disorder.[1] In *Case 2* abnormalities of the external and middle ears were responsible for the conductive component of the deafness.

The genotype phenotype analysis provided by Kline *et al*.,[4] suggests there is no chromosomal region within the deletion that can be implicated in the aetiology of deafness in 18q-syndrome. However the two cases presented here indicate two separate causes of deafness and the literature also supports this by suggesting that both sensorineural and conductive deafness can occur. In genetic terms this indicates that there are two or more genes in this region of chromosome 18 which have an effect on the function of the auditory system. On account of the chromosomal abnormalities detected (18q deletion), no further molecular studies were carried out in the cases reported here. Chromosome rearrangements have often helped to map single gene disorders and further analysis of other cases may prove beneficial. At present there are no non-syndromic deafness genes mapped to this area and no genes in the homologous region in the mouse genome responsible for deafness.

Conclusions

The audiological and otological findings of two 18q- subjects with impaired hearing have been described. In the first case it was shown that the underlying sensorineural deafness was due to a cochlear disorder. The malformation of the external and middle ears in the second case is described in detail. It is a complex abnormality in which surgery did not improve the hearing. The results of surgery on a larger series of patients and evaluation of surgical outcomes in relation to the underlying pattern of malformations would be essential to determine the role of surgery in the rehabilitation of hearing in the 18q- syndrome.

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