

## X-linked deafness: A review of clinical and radiological findings and current management strategies

Sonia Kumar, Thomas Mawby, Vanaja Sivapathasingam, Jane Humphries, James Ramsden

Sonia Kumar, Thomas Mawby, Vanaja Sivapathasingam, Jane Humphries, James Ramsden, ENT Department, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom

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**Correspondence to:** Sonia Kumar, PhD, SpR Otolaryngology, ENT Department, John Radcliffe Hospital, Headley Road, Oxford OX3 9DU, United Kingdom. [soniakumar111@googlemail.com](mailto:soniakumar111@googlemail.com)  
Telephone: +44-1865-741166

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### Abstract

X-linked deafness is a rare genetic disorder causing a severe mixed hearing loss. This is due to an abnormal connection between the internal auditory meatus (IAM) and the basal turn of the cochlear leading to a "3<sup>rd</sup> window effect" and cochlear conductive hearing loss. Patients are traditionally treated with conventional

hearing aids however these are often unsatisfactory. Cochlear implantation is a high-risk procedure in such cases due to the risk of inadvertent electrode placement in the IAM. We present three paediatric cases where the hearing loss was managed with a combination of a bone anchored hearing aid in combination with a conventional behind the ear hearing aid. We also present a review of the current literature regarding the management of X-linked deafness.

**Key words:** X-linked deafness; Bone anchored hearing aid; 3<sup>rd</sup> window; Cochlear implantation; Paediatric; Conductive hearing loss; Sensori-neural hearing loss

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**Core tip:** X-linked deafness is a rare genetic disorder causing a severe mixed hearing loss. This is due to an abnormal connection between the internal auditory meatus (IAM) and the basal turn of the cochlear leading to a "3<sup>rd</sup> window effect" and cochlear conductive hearing loss. Patients are traditionally treated with conventional hearing aids however these are often unsatisfactory. Cochlear implantation is a high-risk procedure in such cases due to the risk of inadvertent electrode placement in the IAM.

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### INTRODUCTION

X linked deafness (DFXN3) is a rare genetic disorder associated with a mutation on the *POU3F4* gene on the

Xq21 chromosome. Due to its X-linked recessive pattern of inheritance, male patients present with a severe hearing loss whilst female patients may present with normal to mild hearing loss<sup>[1]</sup>. Patients present with a mixed progressive hearing loss at a young age, delayed speech and subsequent educational difficulties. They are traditionally treated with conventional hearing aids.

The hearing loss associated with X-linked deafness can be explained by the well-recognised inner ear abnormalities identified. Most notably there is widening of the fundus of the internal auditory meatus (IAM) bilaterally with dilatation of the internal auditory canal. This was first described in the early 1990s across seven pedigrees of patients<sup>[2]</sup>. In addition there is also an absence of the bony partition between the fundus of the IAM and the basal turn of the cochlear. Abnormalities of the bony modioli, vestibular aqueduct and facial nerve canals have also been described with female patients displaying milder abnormalities compared with the males.

The abnormal connection between the IAM and the basal turn of cochlear acts as a 3<sup>rd</sup> window and therefore causes both a cochlear conductive loss as well as a progressive profound sensorineural hearing loss. Clinically there is also an association with stapes fixation adding to the conductive component of the hearing loss<sup>[1]</sup>.

The abnormal connection between the CSF filled subarachnoid spaces and the perilymphatic space of the cochlear represents a high risk for surgery such as stapedectomy. This abnormal communication leads to an increased perilymphatic pressure which in turn leads to perilymph gushing or a "stapes gusher" which is well documented during mobilization of the stapedial footplate<sup>[3]</sup>. It was suggested therefore that X-linked deafness was an absolute contraindication to stapes surgery due to the risk of gushing<sup>[4]</sup>. The increased perilymphatic pressure also causes progressive cochlear damage and therefore a progressive sensorineural hearing loss.

Cochlear implantation is a recognized treatment for patients with profound X-linked sensorineural deafness. However there is a risk in such patients of inadvertent electrode placement within the IAM due to the abnormal connection between the basal turn and the IAM. There are several reports of CSF leak during cochleostomy and in some cases minimal auditory benefit<sup>[5]</sup>. Repeat implantation following wrongful electrode insertion, although possible, is a difficult procedure with many risks including injury to the labyrinthine artery<sup>[6]</sup> and image guided insertion may be useful tool in the future<sup>[7]</sup>.

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## CASE REPORT

### Case 1

An 11-year-old boy from Bulgaria was referred for a cochlear implant assessment when he moved to the United Kingdom. He became deaf as a baby shortly after gentamicin treatment for meningitis at the age of 1. His parents declined a cochlear implant aged 3 and he

subsequently learnt to sign, attended mainstream school and wore bilateral behind-the-ear (BTE) hearing aids. As he grew older his communication became more limited and he was only able to repeat 9% of the AB word list when he used both hearing aids. His audiogram is presented below (Figure 1). His air conduction threshold demonstrated a severe to profound loss whilst his bone conduction threshold confirmed a moderate hearing loss. A CT scan showed a wide connection between the IAM and the basal turn of the cochlear and genetic testing confirmed a mutation in the *POU3F4* gene. The patient was fitted with a right bone anchored hearing aid (BAHA), which he wears alongside his BTE hearing aids.

### Case 2

TB was referred to the cochlear implant clinic aged 2 years and 10 mo. His hearing loss was identified through the newborn hearing screen and he had been managed with hearing aids. However his thresholds had deteriorated significantly over the last few months. His speech was significantly delayed. There was no family history of hearing loss. His audiogram demonstrated a down-sloping mild to moderate sensorineural loss and an up-sloping conductive loss (Figure 1). The CT scan showed an outpouching in the area of the vestibular aqueduct and a wide connection between the IAM and the basal turn of the cochlear. There was also evidence of fixation of the malleus hear to the anterior attic wall bilaterally. An examination under anaesthetic of the right ear revealed mobile ossicles and therefore TB was fitted with a left BAHA. The BAHA in combination with bilateral BTE hearing aids allowed TB's speech and conversational language to progress.

### Case 3

AP is a 7-year-old boy whose hearing loss was identified aged 2 when he lived in India. He was initially treated with conventional hearing aids and a diagnosis of Mondinis malformation of the cochlear was made. Over time he was noted to have a mixed hearing loss and a drop in his low frequency air conduction thresholds (Figure 1). A review of the imaging he underwent in India as a baby has shown the typical appearances of X-linked deafness and he is currently undergoing genetic testing confirmed mutations in *POU3F4* gene alongside his younger brother who also has a hearing loss. He was fitted with a BAHA to use with his conventional hearing aids.

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## DISCUSSION

In our three cases we have successfully managed the hearing in these patients with a combination of a BAHA alongside a conventional BTE avoiding the complications of implant surgery (Figure 2). Our series of patients all demonstrated a progressive drop in low frequency air conduction thresholds. BAHAs have the advantage of aiding the low frequency thresholds where conventional air conduction aids may fail. In conjunction

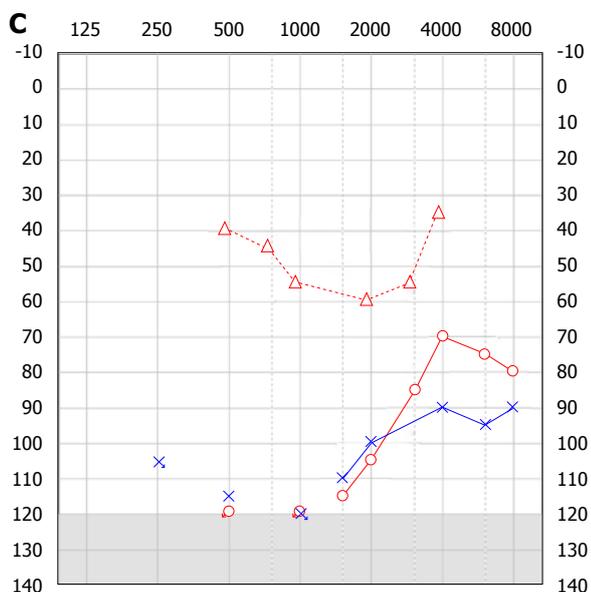
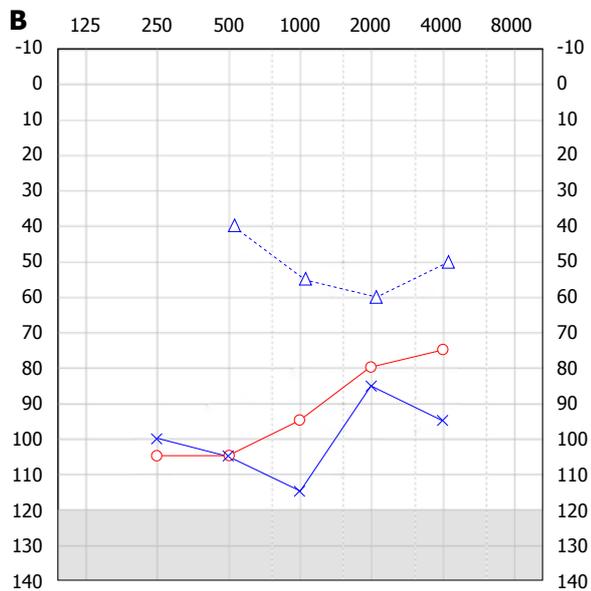
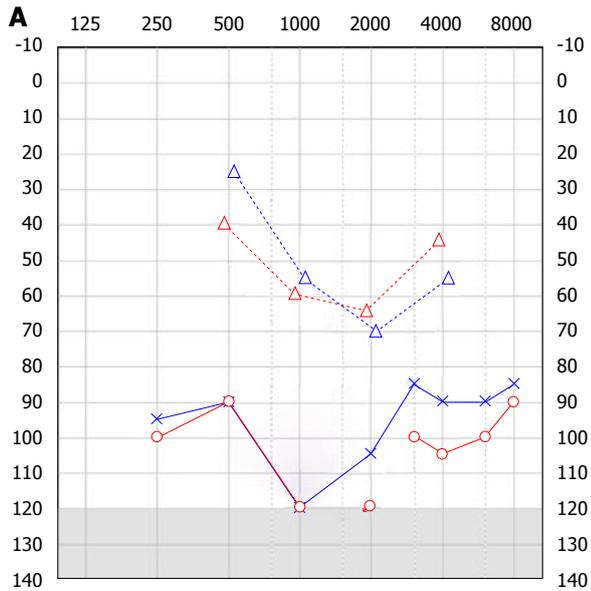


Figure 1 Pure tone audiograms of patients with X-linked deafness pre-operatively.

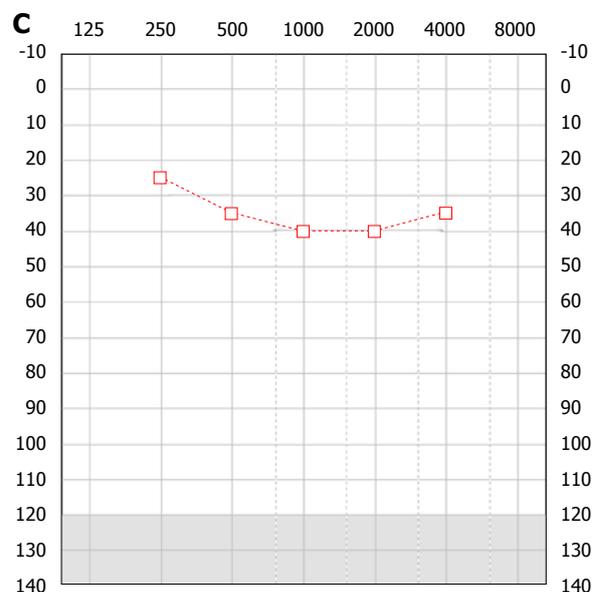
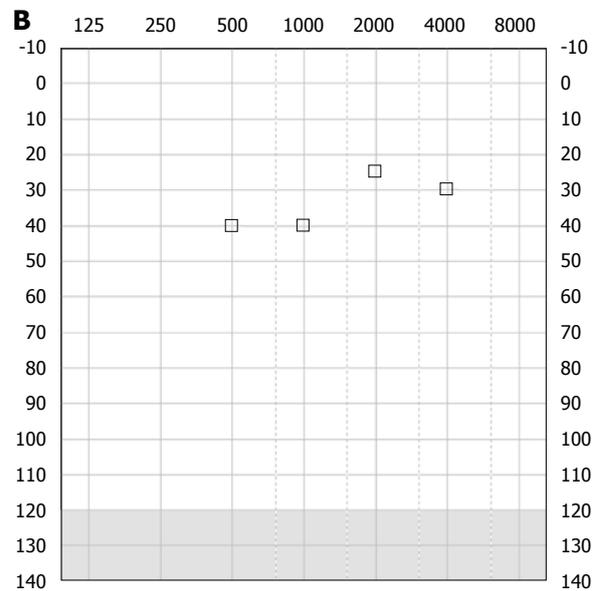
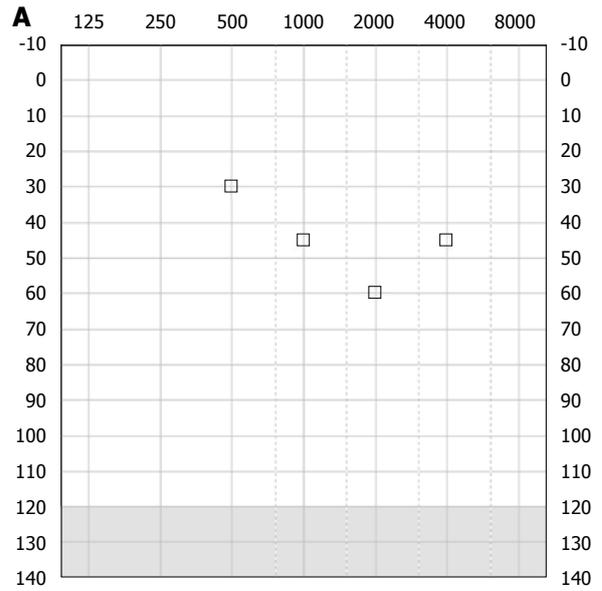


Figure 2 Aided audiograms of patients (bone anchored hearing aid and behind the ear hearing aids in combination).

with a conventional aid for the high frequency loss our patients have reported good outcomes as stated by parents and school. The bone conduction thresholds in our patients were within the limits at which a BAHA is considered beneficial and even our third patients, AP, whose threshold were borderline, had some perceived auditory benefit. BAHA is a safe, quick and well-tolerated procedure and is licensed in the United Kingdom in children aged 5 and over. Those patients that are younger may use the device on a softband.

## COMMENTS

### Case characteristics

An 11-year-old boy from Bulgaria was referred for a cochlear implant assessment when he moved to the United Kingdom; AP is a 7-year-old boy whose hearing loss was identified aged 2 when he lived in India.

### Clinical diagnosis

As he grew older his communication became more limited and he was only able to repeat 9% of the AB word list when he used both hearing aids; over time he was noted to have a mixed hearing loss and a drop in his low frequency air conduction thresholds.

### Differential diagnosis

The hearing loss associated with X-linked deafness can be explained by the well-recognised inner ear abnormalities identified.

### Laboratory diagnosis

All labs were within normal limits.

### Imaging diagnosis

The computed tomography scan showed an outpouching in the area of the vestibular aqueduct and a wide connection between the internal auditory meatus and the basal turn of the cochlear.

### Pathological diagnosis

Bone anchored hearing aids have the advantage of aiding the low frequency thresholds where conventional air conduction aids may fail. In conjunction with a conventional aid for the high frequency loss the patients have reported good outcomes as stated by parents and school.

### Treatment

Cochlear implantation is a recognized treatment for patients with profound

X-linked sensorineural deafness.

### Related reports

There are several reports of CSF leak during cochleostomy<sup>[5]</sup> and in some cases minimal auditory benefit<sup>[5]</sup>.

### Experiences and lessons

Repeat implantation following wrongful electrode insertion, although possible, is a difficult procedure with many risks including injury to the labarynthine artery<sup>[6]</sup> and image guided insertion may be useful tool in the future<sup>[7]</sup>.

### Peer-review

The paper is well written.

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