Ear health and hearing surveillance in girls and women with Turner's syndrome: recommendations from the Turner's Syndrome Support Society

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Background: Turner's syndrome (TS) is a common chromosomal disorder, affecting one in 2000 newborn girls, in which part or all of one X chromosome is missing. Ear and hearing problems are very common in girls and women with TS. The aim of this review was to review the published literature to suggest recommendations for otological health surveillance.

Method: A keyword search of Ovid Medline was performed for published literature on the subject and evidence rated according to the GRADE criteria.

Results: Middle ear disorders are very common and persistent in girls and women with TS as are progressive sensorineural hearing loss and balance disorders.

Conclusions: Otolaryngologists should be aware of the high prevalence and challenging nature of all forms of ear disease in individuals with TS. Early intervention may offer benefits to health and education, and we advocate routine lifelong annual hearing screening in this group.

Turner's syndrome (TS) is a common chromosomal disorder, affecting one in 2000 newborn girls, in which part or all of one X chromosome is missing. Characteristic features include a low hairline at the back of the neck, a wide or webbed neck, swollen hands and feet, a high arched palate and short stature. These features may be subtle and not all affected individuals are diagnosed at birth. Almost a quarter are not diagnosed until adolescence presenting with short stature and failure to enter puberty.[1] Timely treatment with growth hormone and oestrogen can lead to favourable growth outcome. Early diagnosis is important as affected individuals may suffer from a range of health issues such as hypothyroidism, coeliac disease and heart problems such as aortic valve problems, coarctation of the aorta and aortic dissection. Most individuals with TS are of normal intelligence but may have specific learning difficulties and problems with spatial visualisation affecting tasks such as driving.

Ear and hearing problems are very common in girls and women with TS. Conductive hearing loss may be preventable by appropriate treatment of middle ear disease. Early identification of sensorineural hearing loss may be important for schooling and vocation. The aim of this review was to review the published literature to suggest recommendations for otological health surveillance.

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Method

Ethical considerations

As no patient data were used, there was no requirement for us to register this study with our local research ethics committee.

Review method

A keyword search of the English-language literature was performed on the 20th of November 2015 using Ovid Medline with the following keywords:

- Turner syndrome (subject heading)
- ear
- oto$
- otitis
- hearing
- deaf$
- cholesteatoma
- tympan$

Abstracts and full text articles were reviewed and collated. The strength of the evidence behind each recommendation was rated A–D according to the grading system of the GRADE Working Group.[2]

Results

Middle ear

Recurrent acute otitis media is very common in girls with TS, with the reported prevalence in large cross-sectional studies being 61–88%.[3–8] In many cases, girls are treated for many years for ear infections before their diagnosis of TS is known.[9] Girls with monosomy X (45 X, 0 karyotype) are more prone to middle ear problems than those with deletions or mosaicism.[3,6,10–14]

Otitis media with effusion is very common in childhood, with middle ear fluid present in 55–78% of girls under 16 with TS.[10,15] Conductive hearing loss is found in 39–43% of girls under 16,[10,15] and it persists beyond the age of 20 in around 20%.[4,16] Ventilation tube (grommet) insertion is required in around a third of girls.[6]

Tympanic membrane pathology is very common with chronic perforations noted in 10% and retraction pockets in 19%.[6,10] Cholesteatoma is also very common, almost always in girls with a prior history of recurrent acute otitis media. Prevalence figures of 3–15% have been reported in large cross-sectional studies.[3,10,15,17] Cholesteatoma is often extensive and recurrence rates after mastoid surgery are high.[15,17] Cholesteatoma surgery is further complicated by a high rate of dehiscent or abnormally placed facial nerves and stapes abnormalities.[17,18]

Two large cross-sectional studies (each more than a hundred subjects; one study in girls[10] and one in women[16]) have shown no association between conductive hearing loss and prior treatment with oestrogen or growth hormone. One randomised controlled trial of 2 years of growth hormone treatment in girls with TS (88 girls aged 9 months to 4 years) showed no difference in the incidence of middle ear disease.[19] There is evidence, therefore, that growth hormone and oestrogen therapy are unhelpful in preventing the development of middle ear disease, but equally there is nothing to suggest they worsen those problems.

There is one paper that suggests that early, aggressive surgical intervention in the form of ventilation tubes can reduce the incidence of chronic otitis media in later life but the evidence is weak: in a retrospective study of 178 patients with TS, older age at first insertion of ventilation tubes was associated with a higher risk of subsequent need for tympanoplasty or mastoid surgery.[15] There is no evidence regarding the role of adenoidectomy in modifying the course of middle ear disease in TS. Nonetheless, even in the absence of good evidence either way, it is hard to argue against the suggestion that middle ear disease should be diagnosed and treated as early as possible.

Recommendations

- Otolaryngologists should be aware that girls presenting with middle ear disease and short stature may have an underlying diagnosis of TS and should be prepared to refer to paediatric endocrinology services for investigation [strength of recommendation A].
- Growth hormone and oestrogen treatment do not prevent the development of middle ear disease in girls and women with TS [B].
- Otitis media with effusion, chronic perforation of the tympanic membrane and retraction pockets are all very common in girls and women with TS. Persistent otorrhoea should lead to prompt referral to an otolaryngologist [A].
- Otitis media with effusion, chronic perforation of the tympanic membrane and retraction pockets should be managed by conventional means, including surgery as required. There is no evidence to support treating girls and women with TS more or less aggressively than other individuals but prolonged follow-up will be required as middle ear disease often persists into the third decade of life [C].
- Cholesteatoma surgery in girls and women with TS can be challenging. Such surgery should be undertaken by experienced otologists who are prepared to encounter abnormalities of the facial nerve and stapes [A].

Inner ear

It is very common for girls and women with TS to develop a progressive, high-tone sensorineural hearing loss that resembles presbyacusis but which comes on at a much younger age and which progresses much faster.[7,14] There is a characteristic audiometric pattern with a dip or notch around 1.5–2 kHz. This has been detected in girls as young as six years of age[6] and is found in 58% of girls under 16[6] and 78% of women aged 16–34.[13] This progressive hearing loss seems to be more common in those with a history of recurrent ear infections earlier in life.[13] More usefully, a number of large cross-sectional studies and one longitudinal study suggest that the presence of a dip or notch at 1.5–2 kHz is a good predictor of those who will go on to develop a progressive sensorineural loss.[5,6,10,13,14,20] Absence of a dip is a reassuring sign.

Above the age of 40, 27% of women with TS will have hearing thresholds greater than 20 dB and 27% will be wearing hearing aids.[14] Not all women with TS who have a

significant hearing impairment have been identified and given hearing aids; many authors have suggested that regular hearing surveillance in this population would be of benefit[4–6,8,10,11,13,14,19,21,22] although there are no reports of the effectiveness of such a screening programme in the literature to date. A 2007 report from an American expert panel suggested annual hearing screening for those with a history of middle ear disease, and hearing screening every 2–3 years for those with no such history.[23] Again, there is no published report of the effectiveness of such a programme.

Two large cross-sectional studies (each with more than 100 subjects) have failed to show any association between hearing thresholds and a history of prior treatment with growth hormone or oestrogen therapy.[10,16] Thus, there is no evidence at present to support either growth hormone or oestrogen as specific therapy to prevent progressive hearing impairment in girls and women with TS.

A study of 30 women with TS, aged 40–67 years and with mild to moderate sensorineural hearing loss, showed significant deficiencies in sound localisation compared to controls.[20] Girls and women with TS are well known to have problems with visuospatial processing affecting their ability to work in three dimensions, so this problem with sound localisation probably reflects a wider underlying problem with spatial awareness. This may result in girls and women with TS reporting greater hearing difficulties in day-to-day life than their pure-tone thresholds would suggest.

Women ($n = 75$, age 16–59)[24] and girls (mean age 9 years, $n = 105$)[25] with TS have been shown to have deficiencies in tests of balance (Romberg and heel-toe) and fine motor skills compared with controls, and the balance problems are associated with the severity of hearing loss present. Complaints of vertigo are rare, but poor balance leads to falls and therefore injuries. Interestingly, a study of 177 consecutive women with TS aged 19–60 years showed that there was a history of fractures in 32% and that in those with low bone mineral density (which is very common in TS), hearing loss is an independent predictor of their risk of fractures.[26] This suggests that there may be a loss of vestibular function in parallel with the loss of cochlear function. The balance problems seem to be due to a combination of peripheral vestibular and central processing issues, but published research in this area is limited.

Recommendations

- Progressive sensorineural hearing loss is very common and is not always diagnosed promptly. Annual hearing screening in girls and women with TS should be recommended, beginning in infancy and extending lifelong [B].
- Growth hormone and oestrogen treatment do not prevent the development of sensorineural hearing loss in girls and women with TS [B].
- Where a hearing loss is diagnosed, rehabilitation with hearing aids (including implanted bone conduction devices) and cochlear implants should proceed as normal with no evidence that girls and women with TS should be treated any differently than other individuals [B].
- Professionals should be aware that girls and women with TS may have difficulties with sound localisation giving rise to a hearing disability greater than pure-tone thresholds might suggest [B].
- Professionals and families should be made aware that girls and women with TS may have issues with balance and motor skills that put them at increased risk for falls and fractures, particularly if there is a hearing impairment [B].

Discussion

Middle ear disease and sensorineural hearing loss are very common in girls and women with TS, and they present particular challenges. Increased awareness of the condition among otolaryngologists may lead to earlier diagnosis of TS in girls presenting with ear infections.

Otolaryngologists should be aware that middle ear disease in girls with TS can be persistent and challenging to deal with. Prolonged clinical follow-up is advisable for girls with otitis media as it does not behave in the same benign, self-limiting fashion as in other children. Cholesteatoma in particular is both common and recalcitrant. Surgeons undertaking cholesteatoma surgery in individuals with TS should be prepared to deal with abnormalities of the stapes and facial nerve.

Sensorineural hearing loss is sufficiently common that we feel that regular hearing screening should be mandatory, as it already is in other conditions such as Down's syndrome:[27] indeed, the prevalence of sensorineural hearing impairment in TS is higher than that in Down's syndrome. Not all women with TS are having their hearing loss diagnosed and treated promptly, and it is very likely that undiagnosed hearing impairment in this group is causing an unnecessary burden of difficulty. Whether hearing screening should be at annual intervals or less frequent is currently unclear, but it is often logistically easiest to arrange a screening programme with testing at annual intervals; so, in the absence of any evidence to the contrary, that is our recommendation.

Balance problems put girls and women with TS at increased risk of falls and fractures, and these tend to be worst in those with hearing loss. Those with a hearing loss should be monitored closely for balance problems and investigated appropriately.

Recommendations for future research

- Is routine measurement of height and weight for children presenting to otolaryngology clinics with middle ear disease effective in detecting those girls who merit further investigation such as karyotyping?
- Is early adenoidectomy effective in preventing middle ear disease in girls with TS?
- Are routine otolaryngological interventions such as grommets (ventilation tubes) and myringoplasty as effective in girls and women with TS as in others?
- Is annual hearing screening for the TS population effective in achieving early diagnosis and aiding for those with sensorineural hearing loss?
- What is the role of bone-anchored hearing aids in girls and women with TS? Are they more prone to fixture loss or skin complications?
- Are interventions to improve balance effective in reducing the incidence of fractures in women with TS?

Keypoints

- Turner's Syndrome should be considered in any girl with short stature presenting to otolaryngology clinics with recurrent ear infections.
- All forms of chronic otitis media are common in girls with Turner's Syndrome, and they often run a more protracted course than in other people.
- Cholesteatoma in particular is more common and more challenging than in other people.
- Progressive sensorineural hearing impairment is common and a substantial proportion of women with Turner's Syndrome require hearing aids.
- We recommend lifelong annual hearing screening for girls and women with Turner's Syndrome.
- Balance issues are also common and may lead to falls and injuries.

Conflict of interest

None to declare.

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