The Journal of Laryngology & Otology (2017), ***131***, *298–302*.

doi:10.1017/S0022215116009786

MAIN ARTICLE

Enlarged vestibular aqueducts and other inner-ear abnormalities in patients with Down syndrome

C M CLARK[1], H H PATEL[1], S G KANEKAR[2], H ISILDAK[1]

Departments of [1]Surgery, Division of Otolaryngology – Head and Neck Surgery, and [2]Radiology, Pennsylvania State University College of Medicine, Hershey, PA, USA

Abstract

Background: Histopathological anomalies of inner-ear structures in individuals with Down syndrome have been well documented; however, few studies have examined the radiological features.

Methods: A retrospective study was conducted of temporal bone computed tomography images in 38 individuals (75 ears) with Down syndrome to evaluate the prevalence of inner-ear abnormalities and assess vestibular aqueduct widths.

Results: Inner-ear anomalies were identified in 20 of the 38 individuals (52.6 per cent). Seven of the 75 temporal bones (9.3 per cent) were found to have higher than previously reported. A dilated internal auditory canal and vestibule were more common among the present study group, while prior studies have demonstrated internal auditory canal stenosis and decreased vestibule size.

Conclusion: Down syndrome patients exhibit a high prevalence of dysplastic inner-ear features that confer substantial risk of sensorineural hearing loss. Computed tomography is a useful screening aid to detect inner-ear abnormalities, particularly enlarged vestibular aqueducts, which cause preventable sensorineural hearing loss in this population.

Key words: Down Syndrome; Hearing Loss; Vestibular Aqueduct; Inner Ear; Computed Tomography, X-Ray

Introduction

Down syndrome occurs as a consequence of trisomy at chromosome 21. It is one of the most common genetic disorders, affecting approximately 1 in every 700 live births.[1] Its incidence is related to advanced maternal age.[2] Individuals with Down syndrome demonstrate mild to moderate intellectual disability and exhibit significant phenotypic variance in associated health findings. Common sequelae include congenital heart disease, endocrine disorders, leukaemia, immunodeficiency, Alzheimer's disease and gastrointestinal abnormalities.[3]

With improved awareness and detection methods for Down syndrome and its related conditions, the life expectancy of affected individuals continues to increase. As a result, the prevalence of otolaryngological disease among this population is also on the rise. In fact, Down syndrome is the most commonly encountered genetic disorder by otolaryngologists. Persons with Down syndrome experience increased rates of craniofacial dysmorphism, pharyngolaryngeal abnormalities, and otic anomalies including impairments in hearing.[4]

Hearing loss has been reported in 40–90 per cent of individuals with Down syndrome,[5–9] which is markedly higher than the prevalence of 2.5 per cent among the general population.[10] The dysfunction in hearing encountered in this population often further exacerbates the acquisition and development of speech and language.[11] Hearing impairments in Down syndrome can be a consequence of conductive, sensorineural and mixed aetiologies.

Conductive hearing loss is the most commonly encountered type of hearing impairment in this population, and typically occurs secondary to abnormalities in the external and middle ear.[12] In particular, up to 40–50 per cent of newborns with Down syndrome exhibit stenotic ear canals that frequently lead to cerumen impaction and thus complicate the accuracy in diagnosis of middle-ear disease in this population.[13] Hypoplasia of the mid-face is also common among individuals with Down syndrome and can predispose them to Eustachian tube dysfunction.[14] These structural abnormalities lead to an increased prevalence of chronic otitis media and chronic middle-ear effusions among the Down syndrome population, which can

Accepted for publication 13 September 2016 First published online 28 December 2016

further exacerbate conductive hearing loss.[15] Sensorineural hearing loss in the Down syndrome population is believed to result from structural anomalies in inner-ear structures.[16]

Much attention has been paid to the histopathological abnormalities of the inner and middle ear in individuals with Down syndrome. A prior histological study of the Eustachian tubes in this population revealed a decrease in the density of cartilage cells, which is thought to be correlated with poor aeration of the middle-ear cavity.[17] Other studies of the temporal bones in Down syndrome patients have demonstrated dysplastic inner-ear structures, including small lateral semicircular canals, a reduction in the number of spiral ganglion cells, short cochlea and Mondini malformation.[18–21] Although the histological evaluation of inner-ear structures in this population has been relatively extensive, there remains a paucity of studies evaluating radiological imaging findings.

To the best of our knowledge, only three prior studies have investigated the radiological imaging findings of the inner ear in individuals with Down syndrome.[16,22,23] Two of these studies found that compared to matched controls and normative data, Down syndrome subjects had significantly larger vestibular aqueducts.[16,23] This has significant implications, as dilation of the vestibular aqueducts has been correlated with sensorineural hearing loss that is progressive in nature.[24] More importantly, the decline in hearing in persons with enlarged vestibular aqueducts is to some extent preventable, as patients can be instructed to avoid situations that lead to barotrauma.[25] Thus, the awareness and identification of this structural anomaly is imperative.

Accordingly, our study aimed to evaluate the prevalence of inner-ear abnormalities and measure the widths of the vestibular aqueducts on temporal bone computed tomography (CT) images of individuals with Down syndrome.

Materials and methods

Subjects

A total of 274 patients who had previously been seen in our otolaryngology clinic and had a clinical diagnosis of Down syndrome were identified in our electronic medical records. All prior imaging studies were reviewed for each patient to determine if the patient had ever undergone thin-cut, axial, high-resolution CT scanning (slice thickness of less than 1.0 mm) in which the temporal bones were visible. A total of 38 patients (75 ears, with 1 ear determined to be not assessable) were found to have CT scans meeting these criteria.

This study was reviewed and approved by the Institutional Review Board at the Penn State Milton S Hershey Medical Center. The Institutional Review Board determined this study to be exempt from informed consent and in compliance with Health Insurance Portability and Accountability Act ('HIPAA') regulations.

Radiological evaluation

A board-certified neuroradiologist reviewed the temporal bone CT images for each patient who met the inclusion criteria. The widths of the vestibular aqueducts for each patient were measured on axial views at the point of greatest middle anterior–posterior diameter using a measurement tool in Picture Archiving and Communication System software (GE Healthcare Imagecast™ PACS), and measurements were recorded. In accordance with previously established criteria, vestibular aqueduct enlargement was defined as a width measuring greater than 1.5 mm.[26]

Axial CT images were also evaluated for the presence of other inner-ear abnormalities, and findings were recorded for each patient. Additional abnormalities included cystic malformations of the lateral semicircular canals, and variations in internal auditory canal and vestibule widths. Normative data from Stimmer *et al*. were used as a reference for determinations in internal auditory canal width, with measurements greater than 7.8 mm on the right and 7.7 mm on the left in the axial plane signifying dilation.[27] Vestibule widths were assessed based on normative data established by Purcell *et al*.[28]

Mastoid air cell and middle-ear anomalies, if present, were also noted. Mastoid air cell abnormalities included under-pneumatisation, opacification, sclerosis and the presence of fluid. Middle-ear anomalies included decreased middle-ear cavity size and middle-ear cavity opacification.

Statistical analysis

Descriptive statistics, including means, standard deviations (SDs) and confidence intervals (CIs), were calculated for vestibular aqueduct widths. Proportions of study subjects exhibiting inner-ear abnormalities, including enlarged vestibular aqueducts, a dilated internal auditory canal, cystic malformations of lateral semicircular canals and dilated vestibules, were also calculated. In addition, proportions were determined for: mastoid air cell anomalies, including under-pneumatisation, opacification, sclerosis and fluid presence; and middle-ear anomalies, including decreased middle-ear cavity size and middle-ear cavity opacification. Microsoft Excel® was used to compute these values.

Results

A total of 38 patients (75 ears, with 1 ear found to be not assessable) with a diagnosis of Down syndrome who had undergone thin-cut, axial CT scanning (with a slice thickness of 1.0 mm), with visible temporal bones, were identified. Mean patient age was 24 ± 3 years.

Enlarged vestibular aqueducts (width of more than 1.5 mm) were observed in 9.3 per cent of ears (7 of

https://doi.org/10.1017/S0022215116009786 Published online by Cambridge University Press

TABLE I
PROPORTION OF EARS EXHIBITING EACH ANOMALY ON CT IN DOWN SYNDROME PARTICIPANTS

Anomaly	Ears affected* (*n* (%))
Inner-ear anomalies	
– Enlarged vestibular aqueduct†	7 (9.3)
– Dilated IAC‡	4 (5.3)
– Cystic malformations of LSCC	10 (13.3)
– Dilated vestibule	11 (14.7)
Mastoid air cell anomalies	
– Under-pneumatisation	14 (18.7)
– Opacification	12 (16.0)
– Sclerosis	1 (1.3)
– Fluid present	2 (2.7)
Middle-ear anomalies	
– Decreased MEC size	5 (6.7)
– MEC opacification	9 (12.0)

*Total $n = 75$. †Width of more than 1.5 mm; ‡width of more than 7.8 mm on right and 7.7 mm on left. CT = computed tomography; IAC = internal auditory canal; LSCC = lateral semicircular canal; MEC = middle-ear cavity

75 ears). The mean vestibular aqueduct width was 1.20 mm (95 per cent CI = 1.15–1.25 mm) with an SD of 0.23 mm.

Other abnormalities of the inner ear, including a dilated internal auditory canal, cystic malformations of the lateral semicircular canals, dilated vestibules and enlarged vestibular aqueducts, were identified in 52.6 per cent of patients (20 of 38 patients). A dilated internal auditory canal was identified in 5.3 per cent of ears (4 of 75 ears). Cystic malformations of the lateral semicircular canals were observed in 13.3 per cent of ears (10 of 75 ears). Dilated vestibules were seen in 14.7 per cent of ears (11 of 75 ears).

Mastoid air cell abnormalities, including under-pneumatisation, opacification, sclerosis and fluid, were observed in 44.7 per cent of patients (17 of 38 patients). Under-pneumatisation of the mastoid air cells was identified in 18.7 per cent of mastoid processes (14 out of 75). Opacification of the mastoid air cells was observed in 16.0 per cent of mastoid processes (12 out of 75). Sclerosis of the mastoid air cells was observed in 1.3 per cent of mastoid processes (1 out of 75). Fluid in the mastoid air cells was identified in 2.7 per cent of mastoid processes (2 out of 75).

Radiological anomalies of the middle ear were observed in 26.3 per cent of patients (10 of 38 patients). Decreases in middle-ear cavity size were observed in 6.7 per cent of ears (5 of 75 ears). Middle-ear cavity opacification was seen in 12.0 per cent of ears (9 of 75 ears). Table I highlights the percentage of ears exhibiting each inner-ear, mastoid air cell and middle-ear anomaly.

Discussion

Hearing dysfunction among individuals with Down syndrome has been well documented, and can occur as a consequence of conductive, sensorineural and mixed processes.[5–9,11] Conductive hearing loss in this population is believed to stem from structural abnormalities in the external and middle ear, midface, and Eustachian tubes, as well as chronic infection.[12–15] Aetiologies of sensorineural hearing loss in these patients are less well defined but are thought to occur secondary to anomalies in inner-ear structures.[16]

The histopathology of dysplastic inner-ear structures in persons with Down syndrome has been well described; however, little attention has been given to the associated imaging findings in the radiological literature.[16,22,23] In this study, we evaluated the prevalence of inner-ear anomalies and measured the vestibular aqueduct widths on temporal bone CT images in individuals with a clinical diagnosis of Down syndrome. We identified dysplastic inner-ear structures on the temporal bone CT scans of 52.6 per cent of these patients (20 of 38 patients). Observed structural anomalies included a dilated internal auditory canal, cystic malformations of the lateral semicircular canals, dilated vestibules and enlarged vestibular aqueducts.

Our study revealed abnormal inner-ear findings in 52.6 per cent of subjects (20 of 38 subjects), which differs slightly from previously reported prevalence rates. Saliba *et al*. recently detected inner-ear abnormalities on temporal bone CT images in 47 per cent of subjects with Down syndrome. The rate of sensorineural hearing loss among their study group was reported to be 41 per cent.[23] In 2012, Intrapiromkul *et al*. also evaluated the temporal bone CT images of individuals with Down syndrome, and found inner-ear anomalies in 74.5 per cent of subjects and sensorineural hearing loss in 33.3 per cent.[22]

Some of our other findings also vary from previous radiological assessments of the inner ear in the Down syndrome population. In particular, prior studies have demonstrated decreases in internal auditory canal and vestibule size in individuals with Down syndrome, as compared to normal subjects[16,23] and normative data.[22] However, we report increases in internal auditory canal and vestibule size among our study group, as determined by comparisons to previously established normative data.[27,28] Previous studies have demonstrated relationships between both narrow[23] and dilated[29,30] internal auditory canal widths and sensorineural hearing loss. It is possible that Down syndrome may predispose to aberrations in the development of these structures, resulting in both stenosis and dilation, both of which may lead to clinically significant hearing loss.

Individuals with enlarged vestibular aqueducts frequently exhibit progressive sensorineural hearing loss that can be exacerbated by barotrauma.[24] Prior radiological imaging studies have demonstrated that enlarged vestibular aqueducts occur at a higher rate among persons with Down syndrome, as compared to matched controls and normative data.[16,23] Intrapiromkul *et al*. detected enlarged vestibular aqueducts (defined as those with a width of more than

https://doi.org/10.1017/S0022215116009786 Published online by Cambridge University Press

1.5 mm) among 2.0 per cent of their Down syndrome subjects.[22,26] Using the same measurement criteria, we found a prevalence of 9.3 per cent (7 out of 75 ears) in our study population. The mean vestibular aqueduct width in our study subjects was 1.20 mm (95 per cent CI = 1.15–1.25 mm; SD = 0.23 mm). Saliba *et al*. reported a similar mean width of 1.18 mm (SD = 0.33 mm) in their Down syndrome subjects.[23] Blaser *et al*. identified a lower mean width of 0.60 mm (SD = 0.46 mm) among their Down syndrome subjects.[16]

As hearing dysfunction in patients with enlarged vestibular aqueducts is often progressive, and further decline can be prevented by the avoidance of barotrauma, it remains critical to identify and counsel individuals with this structural anomaly, particularly in this population, in which hearing loss can further exacerbate delays in development.[24,25]

- **Histopathological studies have shown increased rates of inner-ear dysplasia in Down syndrome**
- **Inner-ear anomalies, such as enlarged vestibular aqueducts, predispose to sensorineural hearing loss, which can be progressive**
- **Temporal bone computed tomography (CT) scans of 38 Down syndrome patients were evaluated for inner-ear abnormalities**
- **Dysplastic inner-ear features were identified in 52.6 per cent of patients; 9.3 per cent of ears had enlarged vestibular aqueducts**
- **Our findings underscore the utility of CT at detecting inner-ear dysplasia among Down syndrome individuals**
- **This imaging modality may be appropriate for sensorineural hearing loss early detection and intervention in this population**

Histopathological studies of the temporal bones can only be conducted post-mortem; thus, they remain impractical and of little clinical utility for evaluating the presence of inner-ear structural abnormalities, such as enlarged vestibular aqueducts, in patients with Down syndrome. We propose that CT is an appropriate screening method to allow for early detection in these individuals for whom early recognition of sensorineural hearing loss could allow for preventative measures that would greatly improve outcomes.

Conclusion

Individuals with Down syndrome exhibit a high prevalence of dysplastic inner-ear features, such as enlarged vestibular aqueducts, that confer significant risk of sensorineural hearing loss. Interestingly, our study also demonstrated the dilated internal auditory canal and vestibule as being common among our subjects, while prior studies have demonstrated internal auditory canal stenosis and decreased vestibule size in individuals with Down syndrome.[16,22,23] In our study of temporal bone CT images of patients with Down syndrome, enlarged vestibular aqueducts were identified in 9.3 per cent of subjects, which is significantly higher than the previously reported prevalence of only 2.0 per cent.[22] These findings underscore the utility of CT imaging at detecting inner-ear dysplasia among the Down syndrome population. Early detection of structural abnormalities such as enlarged vestibular aqueducts could prevent sensorineural hearing loss in this population by lifestyle and sport activity modification.

References

1 Parker SE, Mai CT, Canfield MA, Rickard R, Wang Y, Meyer RE *et al*. Updated national birth prevalence estimates for selected birth defects in the United States, 2004–2006. *Birth Defects Res A Clin Mol Teratol* 2010;**88**:1008–16
2 Vundinti BR, Ghosh K. Incidence of Down syndrome: hypotheses and reality. *Indian J Hum Genet* 2011;**17**:117–19
3 Asim A, Kumar A, Muthuswamy S, Jain S, Agarwal S. Down syndrome: an insight of the disease. *J Biomed Sci* 2015;**22**:41
4 Venail F, Gardiner Q, Mondain M. ENT and speech disorders in children with Down's syndrome: an overview of pathophysiology, clinical features, treatments, and current management. *Clin Pediatr* 2004;**43**:783–91
5 Fulton RT, Lloyd LL. Hearing impairment in a population of children with Down's syndrome. *Am J Ment Defic* 1968;**73**:298–302
6 Brooks DN, Wooley H, Kanjilal GC. Hearing loss and middle ear disorders in patients with Down's syndrome (mongolism). *J Ment Defic Res* 1972;**16**:21–9
7 Keiser H, Montague J, Wold D, Maune S, Pattison D. Hearing loss of Down syndrome adults. *Am J Ment Defic* 1981;**85**:467–72
8 Balkany TJ, Downs MP, Jafek BW, Krajiceck MJ. Hearing loss in Down's syndrome: a treatable handicap more common than generally recognized. *Clin Pediatr* 1979;**18**:116–18
9 McPherson B, Lai SP, Leung KK, Ng IH. Hearing loss in Chinese school children with Down syndrome. *Int J Pediatr Otorhinolaryngol* 2007;**71**:1905–15
10 Marttilla TI. Result of audiometrical screening in Finnish schoolchildren. *Int J Pediatr Otorhinolaryngol* 1986;**11**:39–46
11 Yoshinaga-Itano C, Sedey AL, Coulter DK, Mehl AL. Language of early and later-identified children with hearing loss. *Pediatrics* 1998;**102**:1161–71
12 Park AH, Wilson MA, Stevens PT, Harward R, Hohler N. Identification of hearing loss in pediatric patients with Down syndrome. *Otolaryngol Head Neck Surg* 2012;**146**:135–40
13 Strome M. Down's syndrome – a modern otorhinolaryngological perspective. *Laryngoscope* 1981;**41**:1581–94
14 Shibahara Y, Sando I. Congenital anomalies of the Eustachian tube in children with Down syndrome. *Ann Otol Rhinol Laryngol* 1989;**98**:543–7
15 Shott SR. Down syndrome: common otolaryngologic manifestations. *Am J Med Genet C Semin Med Genet* 2006;**142C**:131–40
16 Blaser S, Propst EJ, Martin D, Feigenbaum A, James AL, Shannon P *et al*. Inner ear dysplasia is common in children with Down syndrome (trisomy 21). *Laryngoscope* 2006;**116**:2113–19
17 Yamaguchi N, Sando I, Hashida Y, Takahashi H, Matsune S. Histologic study of eustachian tube cartilage with and without congenital anomalies: a preliminary study. *Ann Otol Rhinol Laryngol* 1990;**99**:984–7
18 Igarashi M, Takahashi M, Alford BR, Johnson PE. Inner ear morphology in Down's syndrome. *Acta Otolaryngol* 1977;**83**:175–81
19 Bilgin H, Kasemsuwan L, Schachern P, Paparella M, Le CT. Temporal bone study of Down's syndrome. *Arch Otolaryngol Head Neck Surg* 1996;**122**:271–5

https://doi.org/10.1017/S0022215116009786 Published online by Cambridge University Press

20 Walby AP, Schuknecht HF. Concomitant occurrence of cochleosaccular dysplasia and Down's syndrome. *Arch Otolaryngol* 1984;**110**:477–9
21 Harada T, Sando I. Temporal bone histopathologic findings in Down's syndrome. *Arch Otolaryngol* 1981;**107**:96–103
22 Intrapiromkul J, Aygun N, Tunkel DE, Carone M, Yousem DM. Inner ear anomalies seen on CT images in people with Down syndrome. *Pediatr Radiol* 2012;**42**:1449–55
23 Saliba I, Sbeity S, El-Zir E, Yammine FG, Noun CT, Haddad A. Down syndrome: an electrophysiological and radiological profile. *Laryngoscope* 2014;**124**:E141–7
24 Arcand P, Desrosiers M, Dube J, Abela A. The large vestibular aqueduct syndrome and sensorineural hearing loss in the pediatric population. *J Otolaryngol* 1991;**20**:247–50
25 Griffith AJ, Wangemann P. Hearing loss associated with enlargement of the vestibular aqueduct: mechanistic insights from clinical phenotypes, genotypes, and mouse models. *Hear Res* 2011;**281**:11–17
26 Valvassori GE, Clemis JD. The large vestibular aqueduct syndrome. *Laryngoscope* 1978;**88**:723–8
27 Stimmer H, Nidermeyer HP, Kehl V, Rummeny EJ. Nontumorous enlargement of the internal auditory canal: a risk factor for sensorineural hearing loss? A high resolution CT study. *Rofo* 2015;**187**:450–8
28 Purcell D, Johnson J, Fischbein N, Lalwani AK. Establishment of normative cochlear and vestibular measurements to aid in the diagnosis of inner ear malformations. *Otolaryngol Head Neck Surg* 2003;**128**:78–87
29 Jensen J. Congenital anomalies of the inner ear. *Radiol Clin North Am* 1974;**12**:473–82
30 Lin SR, Lee KF, Stein GN, Lee I. Asymmetrical internal auditory canals. *Arch Otolaryngol* 1973;**98**:164–9

Address for correspondence:
Dr Huseyin Isildak,
Department of Surgery,
Division of Otolaryngology – Head and Neck Surgery,
Pennsylvania State University,
College of Medicine,
500 University Drive, H091,
Hershey,
PA 17033-0850, USA

Fax: +01 717 531 4907
E-mail: hisildak@hmc.psu.edu

Dr H Isildak takes responsibility for the integrity of the content of the paper
Competing interests: None declared