Enlarged Vestibular Aqueduct in Congenital Non-Syndromic Sensorineural Hearing Loss in Egypt

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Abstract To estimate the frequency of isolated enlarged vestibular aqueduct (EVA) in patients with non-syndromic sensorineural hearing loss (SNHL) in an Egyptian population sample and to correlate its size with the degree of hearing loss. The study group comprised 16 patients (32 ears) suffering from non-syndromic SNHL since childhood. After a complete basic audiological evaluation, all patients were submitted to non contrast CT scan of the petrous bone in both axial & coronal planes. Vestibular aqueduct (VA) was measured at two points (midpoint & operculum) on right & left sides. The study group was divided according to VA size into three groups: group A, B and C. Group A included 6 ears (4 patients) with EVA, group B included 11 ears (7 patients) with borderline EVA and group C included 15 ears (9 patients) with normal VA size. There were no statistically significant differences between the three groups as regards laterality, degree of hearing loss and audiometric configuration. There was no correlation between VA midpoint & operculum and different variables (age and average pure tone thresholds). However, a significant correlation between VA midpoint & operculum was found. EVA was diagnosed in 6 out of 32 ears (18.75%) in the study sample. EVA size was not related to the degree of hearing loss or configuration. Despite the insignificant findings, moderate and high

frequency sloping SNHL were considered the most common findings seen in patients with EVA.

Keywords Enlarged vestibular aqueduct syndrome (EVAS) · Non-syndromic sensorineural hearing loss (SNHL) in children · Vestibular aqueduct midpoint (Mp) and operculum (Op)

Introduction

More than 200 years ago, temporal bone dissection by Carlo Mondini revealed wide vestibular aqueducts in patients with cochlear dysplasia (Mondini's dysplasia). In 1978, Valvassori and Clemis [1] were the first to use imaging, and to note an association between enlargement of the vestibular aqueduct and sensorineural hearing loss (SNHL). The association of this anatomic anomaly with SNHL led them to coin the term "large vestibular aqueduct syndrome" (LVAS) [2].

Enlarged Vestibular Aqueduct (EVA) is known to be the most common form of inner ear anomaly; the other common malformations are incomplete partition of the cochlea (Mondini dysplasia), aplasia of the posterior labyrinth (CHARGE association), large vestibule, and semicircular canal dysplasia. These anomalies are presented either isolated or in combination. Previous studies reported an incidence of isolated EVA ranging from 3.7 to 11.4% [3–8].

LVAS has been postulated to be inherited as an autosomal recessive trait with a number of mutations in the SLC26A4 gene in patients with syndromic and non-syndromic EVA [9, 10]. The SLC26A4 gene is considered as the second most frequent gene implicated in non-syndromic hearing loss (NSHL) after GJB2 in Caucasian population [10]. NSHL associated with EVA has been a source of interest because it

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is associated with clinical characteristics, including fluctuating, progressive sensorineural hearing loss, sometimes conductive or mixed hearing loss, which starts in childhood and may also be associated with vestibular symptoms. EVA is diagnosed radiologically by using two imaging modalities, temporal bone computerized tomography (CT scan) and inner ear Magnetic Resonance Imaging (MRI) [6, 11].

Although LVAS is considered to be the most frequent morphogenic cause of hearing loss in children, its frequency is probably underestimated as many children with hearing loss are not evaluated radiologically in developing countries. Besides, in Egypt consanguineous marriage is frequent and genetic HL is not uncommon. This study was conducted as a pilot study to estimate the frequency of isolated EVA in a limited number of patients with non-syndromic SNHL dating since childhood in Egyptian population. The second aim is to determine whether there is a correlation between the size of the vestibular aqueduct to the degree of hearing loss.

Methodology

Subjects

The study group comprised of 16 patients suffering from non-syndromic SNHL since childhood. Patients were selected from the Audiology clinic of Kasr Al-Eini Hospital, Cairo University; one of the main referral centers for hearing loss in Egypt in the period between September 2008 and January 2009. Ethical approval was obtained from the Otolaryngology Department council.

Methods

All patients included in the study were submitted to the following assessment protocol after obtaining an informed consent (from patients or guardians):

Full History Taking with General, Neurological and ENT Examination

The exclusion criteria were: thyroid dysfunction or enlargement, medical, otological or neurological diseases, and family history of a similar condition.

Audiological Evaluation

Pure tone audiometry (PTA) testing was performed in a sound treated room using Madsen orbiter 922 audiometer (calibrated according to ISO standards). The frequency range of 250–8,000 Hz and 500–4,000 Hz octave interval

was used for air and bone conduction respectively. The severity of hearing loss, as determined by air conduction PTA average (500–4,000 Hz), was considered as follows: mild for values > 25–40 dB, moderate from > 40 to 70 dB, severe > 70–90 dB and profound > 90 dB.

Computed Tomography Imaging (CT)

Using GE Light Speed Plus multislice machine (four slices), slice thickness was 1.25 mm, with interslice gap 0 mm and bone window setting with bone filter (edge enhancement $\pm$ reconstruction). Non contrast CT scan of the petrous temporal bone in axial planes was done to all patients included in the study. The reference data were the normal international anatomical findings of the High Resolution Computerized Tomography (HRCT) of the vestibular aqueduct.

The radiological dimensions of the vestibular aqueducts were measured at two sites; the operculum and the midpoint on both the right and the left sides. Diameter greater than or equal to 1.5 mm at the midpoint or greater than or equal to 2 mm at the operculum was defined as an EVA. A midpoint measurement of 1.0–1.4 mm and an operculum measurement of 1.5–1.9 mm were considered borderline EVA. Less than 1.0 mm for the midpoint and 1.5 mm for the operculum were reported as normal vestibular aqueduct (VA) [12]. CT scans were also checked as a whole for any other congenital anomalies or pathologies.

The Statistical Analysis

The data collected were saved in excel software in PC. Data were tabulated and statistically analyzed to evaluate the differences between the groups under study as regards the various parameters. Calculations were done by means of statistical software package SPSS version 10. The statistical analysis included; the arithmetic mean and standard deviation for quantitative variables. Qualitative variables were expressed as numbers and percentage. Comparisons were made in different groups using the corrected χ^2 test. Pearson correlation coefficient was tried in between the essential studied parameters. A difference was considered statistically significant when the probability (*P*-value) was < 0.05.

Results

Study Groups

This study was carried out on 16 patients suffering from non-syndromic SNHL since childhood. Their age ranged from 6 to 20 years with a mean age of 11.75 ± 4.42 years (Table 1). The study comprised 11 (69%) males and 5

Table 1 The mean and standard deviation (*SD*) of age in the three study groups. Group A: enlarged vestibular aqueduct (*EVA*), Group B: borderline *EVA*, Group C: Normal vestibular aqueduct (*VA*)

Group	No of ears	Age Mean ($\pm$ <i>SD</i>)	Age at onset of HL Mean ($\pm$ <i>SD</i>)
Group A	6	10 $\pm$ 2.68	6.67 $\pm$ 2.99
Group B	11	11.82 $\pm$ 5.15	7.77 $\pm$ 4.8
Group C	15	12.4 $\pm$ 4.47	6.09 $\pm$ 4.89
Total	32	11.75 $\pm$ 4.42	6.88 $\pm$ 4.42

Table 2 The mean, standard deviation (*SD*) and range of the vestibular aqueduct dimensions at both the midpoint (*Mp*) and the operculum (*Op*) in millimeters (mm) in the three study groups. Group A: enlarged vestibular aqueduct (*EVA*), Group B: Borderline *EVA*, Group C: Normal vestibular aqueduct (*VA*)

	VA Mp		VA Op	
	Mean $\pm$ <i>SD</i>	Range	Mean $\pm$ <i>SD</i>	Range
Group A (<i>n</i> = 6)	2.65 $\pm$ 1.11	1.5–3.8	4.2 $\pm$ 1.49	2.4–6
Group B (<i>n</i> = 11)	0.85 $\pm$ 0.23	0.5–1.2	1.7 $\pm$ 0.17	1.5–1.9
Group C (<i>n</i> = 15)	0.65 $\pm$ 0.12	0.4–0.9	1 $\pm$ 0.19	0.7–1.3

(31%) females. The duration of hearing loss ranged from 0.5 to 15 years with a mean of 5.09 ± 5.44 years.

The study group (32 ears) was divided according to the size of the vestibular aqueduct as measured at two points (the midpoint and the operculum) into:

- Enlarged vestibular aqueduct (*EVA*) → group A: It included 6 ears (18.8%)
- Borderline *EVA* → group B: Included 11 ears (34.4%)
- Normal vestibular aqueduct (*VA*) dimensions → group C: Included 15 ears (46.8%)

There was no statistically significant difference between the three study groups as regard laterality ($P = 0.924$) neither between size of the *VA Op* or the *Mp* with age ($P = 0.123$ and 0.118 respectively).

Radiographic Findings

The width of the *VA* was measured at two points: the midpoint (*Mp*) and the operculum (*Op*). These dimensions are shown in Table (2) in the three study groups. According to the *VA* size, 4 patients had *EVA* in one or both ears (6 ears: 2 patients had bilateral *EVA* and 2 patients had unilateral *EVA*). An example of bilateral *EVA* is demonstrated in Fig. (1). Seven patients had borderline *EVA* (11 ears: 4 patients had bilateral and 3 patients had unilateral borderline *EVA*) and 9 patients had within normal *VA* dimensions (15 ears: 6 patients had bilateral normal *VA* and the other 3 had unilateral normal *VA*) (Fig. 2). Pearson correlation revealed a highly significant positive correlation between the width of the *VA Op* and that of the *Mp* (Fig. 3) i.e. both dimensions of the *VA* were significantly

Fig. 1 CT scan of a female child aged 7 years with bilateral *EVA*: Right *VA* operculum = 6.0 mm and mid point = 3.8 mm. Left *VA* operculum = 5.2 mm and midpoint = 3.8 mm

Fig. 2 A Schematic diagram showing enlarged vestibular aqueduct (*EVA*), Borderline *EVA* and normal vestibular aqueduct (*VA*) presence in the study group according to laterality: (*Pt* patient)

correlated to each other ($r = 0.967$; $P < 0.001$). No other inner ear malformation was encountered. Eight patients were diagnosed with adenoidal hypertrophy, 4 patients with sinusitis, 1 patient with left maxillary antral polyp and 1 patient with bilateral high arched jugular bulb.

Audiological Findings

Hearing Loss Severity

All patients included in the study were diagnosed with SNHL. The severity of hearing loss (HL) as determined by pure tone averages were; 5/32 ears (15.6%) presented mild

Fig. 3 A scatter plot showing the correlation between the vestibular aqueduct (VA) midpoint and operculum measurements in the 32 ears

Fig. 4 The number of ears included in each degree of hearing loss in the three study groups (Group A: enlarged vestibular aqueduct (EVA), Group B: Borderline EVA, Group C: Normal vestibular aqueduct, VA)

Fig. 5 Pure tone audiometry thresholds of the three study groups by obtaining the mean at each frequency (Group A: enlarged vestibular aqueduct (EVA), Group B: Borderline EVA, Group C: Normal vestibular aqueduct, VA)

SNHL, 17/32 ears (53.1%) had moderate SNHL (9 ears: moderate and 8 ears: moderately severe SNHL), 3/32 ears (9.4%) had severe SNHL, and 7/32 ears (21.9%) showed profound SNHL. The severity of HL with its distribution in

Table 3 Pearson correlation coefficient (r) of the vestibular aqueduct (VA) operculum and midpoint with the mean pure tone thresholds at different frequencies

Frequency	Pearson correlation	VA Operculum (in mm)	VA Midpoint (in mm)
250 Hz	r	0.039	0.078
	P -value	0.83	0.672
500 Hz	r	0.31	0.072
	P -value	0.864	0.696
1,000 Hz	r	0.035	0.067
	P -value	0.851	0.716
2,000 Hz	r	−0.04	0.001
	P -value	0.829	0.997
4,000 Hz	r	−0.121	−0.068
	P -value	0.509	0.71
8,000 Hz	r	−0.038	−0.032
	P -value	0.838	0.864

the three study groups is demonstrated in Fig. 4. Comparing the dimensions of the VA in the three study groups with the degree of hearing loss revealed no statistically significant difference ($P = 0.263$) between the three groups. The mean PTA thresholds at each frequency of the three groups are demonstrated in Fig. 5. There was no statistically significant correlation between size of the VA Op or the Mp and the mean PTA thresholds at different frequencies ($P > 0.05$) (Table 3).

Audiometric Configuration

In the 32 ears included in this study, there were 4 ears (12.5%) with rising configuration, 3 ears (9.4%) with flat configuration, 2 ears (6.2%) with reversed cookie bite audiogram (RCB) (both rising and high frequency sloping), 4 ears (12.5%) with total hearing loss (THL), and 19 ears (59.4%) whose audiograms were of sloping or high frequency configuration. Distribution of the different configurations in the three study groups is demonstrated in Fig. 6. Comparing the VA Op and Mp and these different configurations in the three study groups revealed no statistically significant difference ($P = 0.654$ and 0.444 respectively) (Table 4).

Discussion

EVA was diagnosed in 6 out of 32 ears (18.75%) in the study sample according to the preset criteria of an EVA (VA diameter > 1.5 mm at the Mp or an Op measurement of > 2 mm). This is a relatively high incidence when compared with that reported in the literature [3–8, 12] and

Fig. 6 The number of ears included in each audiometric configuration in the different study groups (*RCB* reversed cookie bite, *Sloping HF* sloping high frequency, *THL* total hearing loss, Group A: enlarged vestibular aqueduct or EVA, Group B: Borderline EVA, Group C: Normal vestibular aqueduct, VA)

Table 4 The Mean and standard deviation (*SD*) of both vestibular aqueduct (VA) operculum and midpoint in the different audiometric configurations (*RCB* reversed cookie bite, *HF* high frequency, *THL* total hearing loss)

Audiometric configurations	VA operculum (in mm)		VA Midpoint (in mm)	
	Mean	SD	Mean	SD
Rising (<i>n</i> = 4)	1.53	± 0.76	1	± 0.42
Flat (<i>n</i> = 3)	2.93	± 2.69	1.83	± 1.72
RCB (<i>n</i> = 2)	1.4	± 0.28	0.85	± 0.35
HF sloping (<i>n</i> = 19)	1.62	±1.11	0.98	±0.78
THL (<i>n</i> = 4)	1.85	± 0.7	1.25	± 0.31
<i>P</i> -value	0.654		0.444	

might be accepted in a pilot study with a limited number of patients.

Developmental growth of the VA throughout infancy and early childhood has been described, indicating that EVA may result from abnormal postnatal and pre-adolescent development and reaches the adult size at 3–4 years [13, 14]. In the present study, the youngest child was 6 years old. There was no correlation between the size of the VA operculum or midpoint with age. This is in accordance with the study of Legeais et al. [15] who found that there was no statistically significant variability in VA diameter as a function of age. The onset of SNHL as a presentation of EVA may be early after birth to adulthood with the highest frequency in childhood [16–22]. In the current study, the age of onset of SNHL was 6.67 ± 2.99 years in patients with EVA.

The EVA syndrome has been reported to be bilateral in 55 to 94% of cases [20, 23–25] and is generally reported to be asymmetrical [8, 19]. Some authors claimed slight female preponderance [23, 24] whereas others reported the inverse [25]. In this study, there was no statistically significant difference between the three study groups as regards to laterality. Vijayasekaran et al. [26] compared the

median measurement of the VA at the Mp and at the Op for the left and the right ears of the 73 normal hearing subjects. They noted no statistically significant difference as regards the VA size of both sides.

Audiological Features of the SNHL

SNHL in patients with EVA has been reported to be fluctuating, stable or progressive [4, 6] following trigger activities such as minor head trauma, jogging, or common colds [2, 7, 19, 24, 27, 28]. Because of lack of serial audiometric data in our patients, we could not examine the progression of SNHL.

The degree of SNHL in patients with EVA has been described by many authors to range from mild to profound and even patients with EVA without any hearing impairment has also been reported [19, 20, 28–31]. In our patients with EVA: 4 ears had moderate SNHL and 2 ears had profound SNHL. In patients with borderline EVA, the majority also had moderate SNHL (5/11). However, there was no statistically significant difference between the three groups as regards the severity of HL or the average PTA threshold at each frequency. Moreover, there was no correlation between the size of the VA Op and Mp and the audiometric threshold at different frequencies. Many studies [3, 11, 20, 22, 32, 33] reported similar results. Contrary to these reports, Antonelli et al. [34] reported a significant correlation between the VA size and severity of hearing impairment in patients with EVA and cochlear dysplasia. Others [21, 35–37] described a correlation between the side of the more enlarged VA and endolymphatic sac (ES), and the side of the more marked SNHL. They also concluded that a markedly widened VA is usually associated with profound hearing loss. We can explain this controversy by the fact that the severity of SNHL varies over time as it is usually progressive. Accordingly, this correlation may not be found while evaluating hearing in children and young adults shortly after diagnosis of EVA but could be evident later in life.

Regarding the PTA configuration, the high frequency sloping curve audiogram was the more frequent configuration in our patients with EVA and borderline EVA (50 and 45.44% respectively). There was no significant difference between VA operculum or midpoint and the PTA configuration in the three groups. Similar findings were reported in the literature [1, 8, 12, 19, 22, 29].

Several authors [2, 3, 19, 22, 29] suggested the potential causes of SNHL in patients with isolated EVA including hydro-electrolyte imbalance of inner ear fluids resulting in accumulation of excess endolymph. The resulting volume or pressure effect participates in an enlarged endolymphatic duct and sac. The reflux of hyperosmotic endolymphatic sac contents, infused through a wide patent

endolymphatic duct, into the basal end of the cochlear duct under sudden fluctuation in cerebrospinal fluid (CSF) changes or minor head injury produces the high frequency HL found in patients with EVA. Another speculation was proposed that abnormalities of the inner ear membrane with a dilated communication between the CSF and the vestibule form a fistula damaging the membranous labyrinth [27, 38–40]. Further histopathologic studies of confirmed cases are needed before definitive conclusions can be established.

In conclusion, EVA was frequent in patients with non-syndromic SNHL especially if dating back to infancy or childhood. With the present measurements, EVA is not related to the level of hearing loss or its configuration although further studies with a larger sample group are needed to make this finding conclusive. Despite the insignificant findings, moderate and high frequency sloping SNHL were considered the most common findings seen in patients with EVA. Each patient with non-syndromic SNHL should have a high resolution CT with measurement of the VA Op and Mp to exclude EVA or borderline EVA. The radiological evaluation should be part of an investigation battery, including genetic mapping and full audiological evaluation. Measurement of the VA thickness and morphology is another method of CT scan measurements recommended for further application. MRI technology and 3D reconstruction enables better visualization of the extra-osseous portion of the ES. Early detection and intervention is essential. Vestibular dysfunction accompanying EVA should be investigated thoroughly as it is difficult to be diagnosed in infancy and is generally rapidly compensated early in life.

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