Clinical analysis based on 208 patients with microtia (especially reviewed oculo-auriculo-vertebral spectrum, hearing test, CT scan)

Lei Jin, Shaojuan Hao, Yaoyao Fu, Tianyu Zhang, Zhengmin Wang

Department of Otorhinolaryngology, Head and Neck Surgery, Eye and ENT Hospital of Fudan University, Shanghai, China

SUMMARY: Jin L, Hao SJ, Fu YY, Zhang TY, Wang ZM. Clinical analysis based on 208 patients with microtia (especially reviewed oculo-auriculo-vertebral spectrum, hearing test, CT scan). Turk J Pediatr 2010; 52: 582-587.

Microtia is a common birth defect and characteristic of abnormal auricle. It can be isolated or occur as a part of syndromes involving the first and second bronchial arch structures, such as oculo-auriculo-vertebral spectrum. We conducted a careful review of the literature regarding the clinical features of patients with microtia, but found few studies with respect to the Chinese population. In this study, we explored the clinical features of a single clinic population of 208 Chinese individuals with microtia. It showed that 15 cases (7.2%) had been afflicted with middle ear cholesteatoma, which would have brought about risky complications without an immediate removal; that 12 of 68 contralateral, normal-appearing ears had presented mild to moderate conductive or combined hearing loss (21-70 dB); that the degree of hearing loss deteriorated as the grade of microtia increased, with significant differences between grades I and III ($p<0.05$); and that there was a male predominance, with the right side more likely to be affected.

Key words: microtia, oculoauriculovertebral spectrum, cholesteatoma, hearing loss, China.

Microtia is a common birth defect and characteristic of an abnormal auricle. It can be isolated or occur as a part of syndromes involving the first and second bronchial arch structures, such as the oculo-auriculo-vertebral spectrum (OAVS) (Fig. 1). The prevalence of microtia is reported to be 0.83/10000-17.4/10000[1-7], with 1/5600 thought to be the best estimate. Most of the cases are sporadic, and approximately 2% of patients carry a positive family history[8]. Reported risk factors of microtia include maternal diabetes[9], medication use during the first two months of gestation[10], exposure to chemical agents[11], intracytoplasmic sperm injection (ICSI) pregnancy[11-13], twin pregnancy[12, 13], and high parity[5]. Furthermore, genetic factors are likely to be responsible for some cases[14-16]. However, the molecular basis of this condition remains unknown.

Temporal computed tomography (CT) scan is performed to detect middle ear anomalies in microtia patients, and mastoid bone sclerosis, deformed ossicles and atresia of the external auditory canal are the most common findings[11]. In addition, pure tone audiometry or brainstem-evoked response audiometry can not be ignored because conductive hearing loss is frequent[17]. However, the relationship between the degree of microtia and auditory function is seldom considered.

We performed a careful review of the literature regarding the clinical features of those with microtia. Unfortunately, we found few studies with respect to Asians and particularly to the Chinese population. Considering racial differences, we hypothesized that its clinical features in Chinese cases might differ from those in other populations. Thus, we explored the clinical features of a single clinic population of 208 Chinese individuals with microtia, and made a comparison against those of previous studies. We also investigated the frequency of

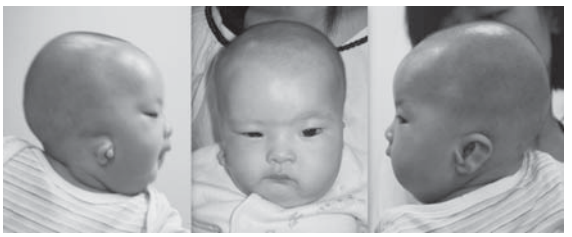

Fig. 1. Photographs of case No. 154 (female, 8 months old). **Left ear:** one preauricular tag, microtia grade I. Right **ear:** microtia grade III. Right-sided hemifacial microsomia with smaller right eye, left epibulbar lipoma and cervical scoliosis.

middle ear cholesteatoma in microtia patients as well as the relationship between the degree of microtia and auditory function.

The study was approved by the Ethics Committee of the Eye and Ear, Nose and Throat (E&ENT) Hospital of Fudan University in the city of Shanghai.

Material and Methods

Patients

We evaluated the clinical data of 211 patients who were admitted between September 2007 and July 2009 for auricle reconstruction or hearing problem in the Department of Otorhinolaryngology, E&ENT Hospital of Fudan University. Of these cases, three were excluded for their diagnoses of Treacher Collins syndrome (TCS), and the rest, of Han ethnicity, who presented either microtia or preauricular tags with hemifacial microsomia, were included. The subjects whose relatives had microtia or preauricular tags/sinuses were categorized as familial microtia. For a comparative analysis, we defined bilateral involvement as presence of such signs as microtia or preauricular tags/sinuses on both sides. The data available for our analyses were the records of 208 (100%) patients from the Hospital, the facial photographs of 156 (75%), the results of pure tone audiometry of 103 (49.5%) (206 ears), and temporal CT scan results of 107 (51.4%).

Classification

We classified all the patients (516 ears) into three grades against Marx's widely used classification system as: grade I, an abnormally small auricle with most anatomical structures recognizable; grade II, some still recognizable; and grade III (the peanut-shell type), only a rudiment of soft tissues present. Those with preauricular tags accompanied by hemifacial microsomia were regarded as microtia grade I, and the contralateral ears of unilaterally affected cases were classified as grade 0.

Results of Pure Tone Audiometry

Pure tone averages were calculated for each ear using air conduction decibels at 0.5, 1 and 2 kHz.

Statistical Analysis

To verify the hypothesis that the severities of the outer ear malformations and conductive hearing loss were parallel, we performed one way ANOVA to compare the mean values of audiometry between different microtia grades. We also conducted a T-test to compare the mean values of audiometry in contralateral ears with 20 dB, the low limit of normal hearing.

Results

Clinical Data

The age of the 208 patients ranged from 3 months to 31 years, and 69.7% of them were male. Regarding the laterality, 56.6% of the unilaterally affected ears were right-sided. A total of 141 (67.8%) of 208 patients were isolated cases and the others occurred with hemifacial microsomia or other malformations, such as eye and vertebral defects. The main clinical features were classified into six categories (Fig. 2).

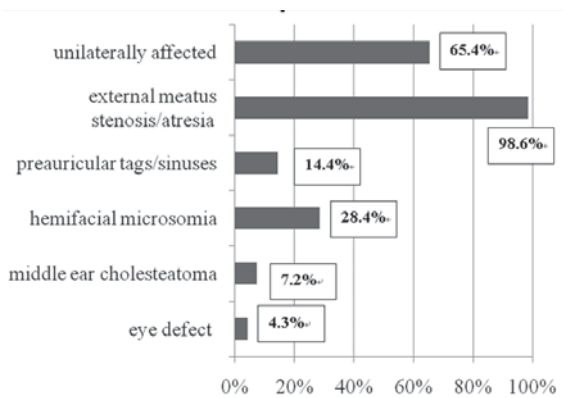

Fig. 2. Clinical features of 208 patients.

Table I. Characteristics of Microtia/OAVS in Different Populations (1)

Patient-based study					
Publication year		2007	1999	1996	1995
Population	China	Finland	Mexico	Japan	USA
N	208	190	145	592	92
Male	69.7%	58%	60%	64.7%	59.8%
Bilateral	34.6%	11.5%	25%	9.1%	16.5%
Laterality	56.6% right	59.5% right	69.% right	58.4% right	68.4% right
Aural stenosis	98.6%	93%	54.9%	92%	
Preauricular sinuses/tags	14.4%	33.5%	17.9%	13%	25%
Mandibular dysplasia	28.4%		40%	4.6%	10.9%
Vertebral defects	2/208		22.4%		
Eye defects	9/208		0%	2/592	
Cardiac defects	1/208	11%	4.1%		
Familial cases	10.1%	14.4%	33.8%	2.5-3.5%	9.8%
Reference		1	18	22	20

OAVS: Oculo-auriculo-vertebral spectrum.

Eye defects included epibulbar lipoma (3/9), nystagmus (2/9) and tropia (4/9). Only 2 cases were diagnosed as cervical scoliosis and 1 case as congenital ventricular septal defects. We also found such clinical malformations as facial paralysis in 4 cases, cleft lip and palate in 2, lip hemangioma in 1 and renal hypoplasia in 1. None of our patients was conceived by ICSI and there were 2 dizygotic twin pairs. We compared our data with those of the previous studies (Tables I, II).

Familial Data

Of 208 patients, 186 were sporadic and 21 carried a family history. Most affected relatives showed preauricular tags/sinuses as the only manifestation, and 2 mothers presented the same grade of microtia as their daughters, suggesting that genetic factors were responsible for some microtia cases.

Hearing Function

Air conduction results of pure tone audiometry were available for analysis in 103 patients (206

Table II. Characteristics of Microtia/OAVS in Different Populations (2)

Population-based study								
Publication year	2009	2005	2004	2000	1997	1996	1995	1986
Population	Columbia	Hawaii	USA	China	Venezuela	France/ Sweden/ California	Italy	South America
N	27	120	549	453	38	954	156	184
Male	63%		56.5%	No sex difference	63%	Male excess	No sex difference	
Bilateral		20.2%	18%		18.5%		14.7%%	9.3%
Laterality		64% right				61% right	57.1% right	62.7% right
Aural atresia/ stenosis								75.5% (atresia)
Vertebral defects			14.9%				12.5%	
Eye defects		3.6%	46.8%			5.6%		
Cardiac defects		20.7%	32.4%	3.5%		12.1%	31.3%	
Reference	21	2	3	4	23	5	6	7

OAVS: Oculo-auriculo-vertebral spectrum.

ears). Mixed hearing loss was detected in 55 (53.4%) patients and conductive hearing loss in the rest. Two hundred and six ears were categorized into four groups (grade 0-III) as follows: 68 grade 0, 32 grade I, 24 grade II, and 82 grade III. We used one way ANOVA to compare means of audiometry between different microtia grades, and the statistical results showed that hearing loss deteriorated as the grade of microtia increased, with significant differences between the means of grade I and grade III ($p<0.05$). Interestingly, 12 of 68 contralateral, normal-appearing ears showed mild to moderate conductive or mixed hearing loss (21-70 dB). However, T-test showed no significant differences between the mean decibels of grade 0 and 20 dB ($p>0.05$).

CT Scan Results

We evaluated temporal CT scan results of 107 (51.4%) patients, finding such abnormalities as atresia of the external auditory canal, middle cavity anomaly, deformed ossicles, loss of pneumatization of mastoid cell, and middle ear cholesteatoma (Fig. 3).

Discussion

Microtia and OAVS share similar clinical expressions and the relationship between them remains unclear. Although the term OAVS was originally used to describe those with microtia, mandibular hypoplasia, vertebral defects, and ocular abnormalities, many previous studies suggested using isolated microtia[8,17,18], preauricular tags in association with hemifacial microsomia[8] or multiple accessory tragi[19] as the mildest expression of OAVS. In our opinion, as the external ear, middle ear, mandible, and cervical spine are all derived from the first and second branchial arches, teratogenesis of these structures is naturally interrelated, and thus OAVS should be a broad spectrum of anomalies, ranging from isolated microtia to Goldenhar syndrome (OMIM 164210). All the patients in this study presented either microtia or preauricular tags with hemifacial microsomia, fulfilling the minimal diagnostic criteria of OAVS above. The infant shown in Fig. 1 represents a typical patient with OAVS.

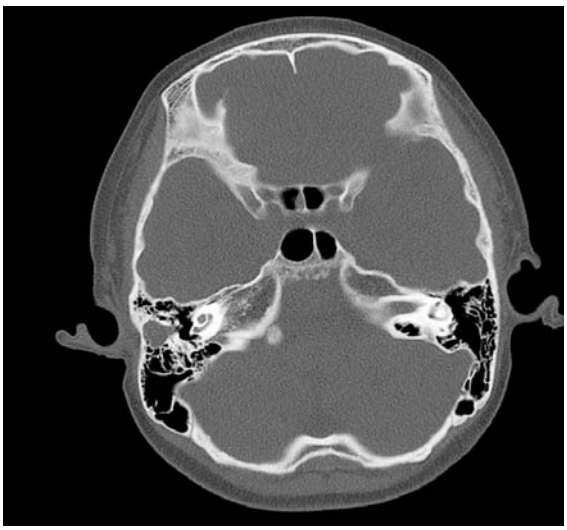

Fig. 3. CT scan result of case No. 66 (male, 11 years old). **Right side:** microtia grade I with external meatus stenosis. Left side: normal. CT scan showed right-sided middle ear cholesteatoma and deformed ossicles.

There have been quite a few patient-based studies as well as population register reports on the characteristics of microtia patients. Male predominance has been reported except in three studies[4, 6, 11]. In our study, the male cases accounted for 69.7%, which was consistent with the phenomenon of male preponderance[1,3,5,18,20-23]. Right-side predominance as the laterality of microtia has also been reported to range between 57.1%[6] and 69%[18]. In our study, the right ear was affected in 56.6% of cases. The prevalence of bilateral disease varies from 9.1%[22] to 25%[18] in other reports. Aural atresia or stenosis was present in 98.6% of our patients, which was higher than any other ratios reported. Since we investigated a single clinic population in the E&ENT hospital, sample bias was inevitable. Therefore, it was reasonable for the ratio of aural atresia to be high in a group of patients who came for hearing reconstruction. Only 14.4% of the cases presented preauricular tags/sinuses, which was similar to the percentage reported by Okajima et al.[22], but much lower than that by Suutarla et al.[1] (33.5%), which could be explained in terms of racial variability. It was not possible to conduct a cervical radiological examination and echocardiography in every patient, thus only two cases were diagnosed as cervical scoliosis and one case as congenital ventricular septal defects. Vertebral and cardiac anomalies were found in over 10% of cases in other populations[3,6]. Therefore, we

most likely would have found more vertebral and cardiac deformities in our patients if proper examinations could have been done. Reproductive technology and twin pregnancies were reported to be associated with OAVS[12, 13]. None of our patients was conceived by ICSI, while two male sporadic patients had dizygotic twin sisters, both normal and healthy.

Temporal CT scan is useful in detecting middle ear malformations. Engiz et al.[11] evaluated 11 patients with a phenotypic appearance characteristic for Goldenhar syndrome, and radiological findings included mandibular hypoplasia, middle cavity anomaly, hypoplasia of internal auditory canals, loss of pneumatization of mastoid cell, deformed ossicles, atresia of the external auditory canal, and absent temporomandibular joint. In our study, temporal CT scan found similar abnormalities: atresia of external auditory canal, middle cavity anomaly, deformed ossicles, and loss of pneumatization of mastoid cells. Intriguingly, 15 cases (7.2%) had middle ear cholesteatoma, which necessitated an immediate surgical removal. Therefore, we suggest that every patient with microtia undergo a temporal CT scan examination at an early age to exclude middle ear cholesteatoma, which otherwise would lead to risky complications. No data on such frequency of the clinical manifestation have been reported previously.

Much of the literature has argued that there was a close correlation between the degree of microtia and severity of middle ear dysplasia[24] and that middle ear dysplasia and ossicle deformations could lead to conductive hearing loss. In this study, we hypothesized that the poorer the condition of the external ear, the greater the hearing loss. Okajima et al.[22] concluded that the conductive hearing loss did not deteriorate as the grade of microtia increased. In this study, we used one way ANOVA to compare the mean decibels of pure tone audiometry of different microtia grades. Our results via a statistical analysis showed the opposite, with significant differences between grade I and grade III ($p<0.05$), which partially verified our hypothesis, although there were no statistical differences between grade I and II or between grade II and III, which could be explained in terms of the limitation of the sample size.

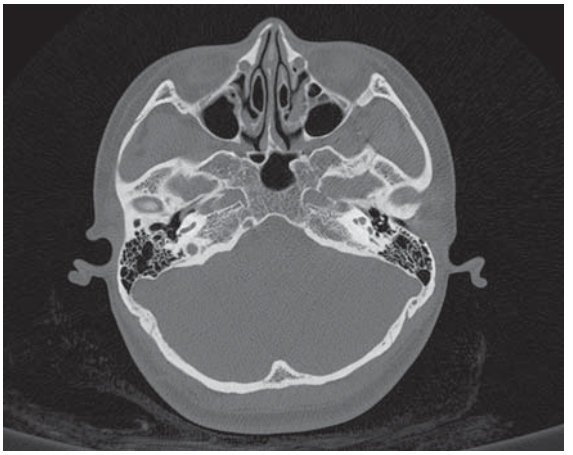

Fig. 4. CT scan results of case No. 208 (female, 16 years old).
Right side: microtia grade II and one preauricular tag with external meatus stenosis. Left side: normal outer ear and external meatus, but CT scan showed deformed ossicles.

Furthermore, 12 of 68 contralateral, normal-appearing ears had mild to moderate conductive or mixed hearing loss (21-70 dB). Eavey[20] reported additional conductive hearing loss caused by otitis media with effusion, which developed in the normal ears. Otitis media could be a factor, but was unlikely to explain all the cases of hearing loss. Our temporal CT scan results showed middle ear deformities in some contralateral ears (Fig. 4), and thus we strongly suggest that hearing function tests be performed in every patient with unilateral or bilateral microtia. It is likely that the parents of unilaterally affected kids would mistakenly accept the hearing of the "unaffected" ear as normal. The delay in the clinical diagnosis could impose a great impact on their speech development, or even result in mental retardation.

In conclusion, as concerns children with microtia, especially non-isolated microtia, parents should be provided with enough guidance and proper advice in handling expected and unexpected hearing loss, middle ear cholesteatoma and other associated medical conditions, so as to ensure that temporal CT scan examinations plus hearing function tests be performed in every patient as early as possible.

REFERENCES

1. Suutarla S, Rautio J, Ritvanen, et al. Microtia in Finland: comparison of characteristics in different populations. Int J Pediatr Otorhinolaryngol 2007; 71: 1211-1217.

2. Forrester MB, Merz RD. Descriptive epidemiology of anotia and microtia, Hawaii, 1986–2002. Congenit Anom (Kyoto) 2005; 45: 119-124.
3. Shaw GM, Carmichael SL, Kaidarova Z, et al. Epidemiologic characteristics of anotia and microtia in California, 1989–1997. Birth Defects Res A Clin Mol Teratol 2004; 70: 472-475.
4. Zhu J, Wang Y, Liang J, et al. An epidemiological investigation of anotia and microtia in China during 1988—1992. Zhonghua Er Bi Yan Hou Ke Za Zhi 2000; 35: 62-65.
5. Harris J, Källén B, Robert E. The epidemiology of anotia and microtia. J Med Genet 1996; 33: 809-813.
6. Mastroiacovo P, Corchia C, Botto LD, et al. Epidemiology and genetics of microtia-anotia: a registry based study on over one million births. J Med Genet 1995; 32: 453-457.
7. Castilla EE, Orioli IM. Prevalence rates of microtia in South America. Int J Epidemiol 1986; 15: 364-368.
8. Tasse C, Böhringer S, Fischer S, et al. Oculo-auriculo-vertebral spectrum (OAVS): clinical evaluation and severity scoring of 53 patients and proposal for a new classification. Eur J Med Genet 2005; 48: 397-411.
9. Wang R, Martínez-Frías ML, Graham JM Jr. Infants of diabetic mothers are at increased risk for the oculo-auriculo-vertebral sequence: a case-based and case-control approach. J Pediatr 2002; 141: 611-617.
10. Hartsfield JK. Review of the etiologic heterogeneity of the oculo-auriculo-vertebral spectrum (hemifacial microsomia). Orthod Craniofac Res 2007; 10: 121-128.
11. Engiz O, Balci S, Unsal M, et al. 31 cases with oculoauriculovertebral dysplasia (Goldenhar syndrome): clinical, neuroradiologic, audiologic and cytogenetic findings. Genet Couns 2007; 18: 277-288.
12. Wieczorek D, Ludwig M, Boehringer S, et al. Reproduction abnormalities and twin pregnancies in parents of sporadic patients with oculo-auriculo-vertebral spectrum/Goldenhar syndrome. Hum Genet 2007; 121: 369-376.
13. Balci S, Engiz O, Alikasifoglu M, et al. Association of assisted reproductive technology with twinning and congenital anomalies. Indian J Pediatr 2008; 75: 638-640.
14. Kelberman D, Tyson J, Chandler DC, et al. Hemifacial microsomia: progress in understanding the genetic basis of a complex malformation syndrome. Hum Genet 2001; 109: 638-645.
15. Balci S. Familial microtia with meatal atresia in father and son. Turk J Pediatr 1974; 16: 140-143.
16. Balci S, Boduroglu K, Kaya S. Familial microtia in four generations with variable expressivity and incomplete penetrance in association with type I syndactyly. Turk J Pediatr 2001; 43: 366-368.
17. Keogh IJ, Troulis MJ, Monroy AA, et al. Isolated microtia as a marker for unsuspected hemifacial microsomia. Arch Otolaryngol Head Neck Surg 2007; 133: 997-1001.
18. Llano-Rivas I, González-del Angel A, del Castillo V, et al. Microtia: a clinical and genetic study at the National Institute of Pediatrics in Mexico City. Arch Med Res 1999; 30: 120-124.
19. Miller TD, Metry D. Multiple accessory tragi as a clue to the diagnosis of the oculo-auriculo-vertebral (Goldenhar) syndrome. J Am Acad Dermatol 2004; 50: S11-13.
20. Eavey RD. Microtia and significant auricular malformation. Ninety-two pediatric patients. Arch Otolaryngol Head Neck Surg 1995; 121: 57-62.
21. García-Reyes JC, Caro MA, Vega P, et al. Epidemiology and risk factors for microtia in Colombia. Acta Otorrinolaringol Esp 2009; 60: 115-119.
22. Okajima H, Takeichi Y, Umeda K, et al. Clinical analysis of 592 patients with microtia. Acta Otolaryngol Suppl 1996; 525: 18-24.
23. Sánchez O, Méndez JR, Gómez E, et al. Clinico-epidemiologic study of microtia. Invest Clin 1997; 38: 203-217.
24. Kountakis SE, Helidonis E, Jahrsdoerfer RA. Microtia grade as an indicator of middle ear development in aural atresia. Arch Otolaryngol Head Neck Surg 1995; 121: 885-886.