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Audiological Manifestations in Kabuki (Niikawa-Kuroki) Syndrome

ABSTRACT

Objective: To describe the audiological profile, clinical features and briefly summarize the speech and language development of a child with Kabuki syndrome (KS). KS is a rare malformation syndrome that usually presents with mental retardation and multiple congenital anomalies including ear diseases and hearing loss.

Methods:

Design: Case report
Setting: Tertiary Public University Hospital
Subject: One patient

Results: A five-year-old female diagnosed with KS at age three presented with moderate to severe conductive hearing loss in the right ear with a drop at the high frequencies and moderate to severe conductive sloping hearing loss in the left ear. She also had fluctuating tympanometric findings. She was fit with binaural hearing aids.

Conclusion: Ear diseases and hearing loss should immediately be considered in patients diagnosed with KS. A comprehensive audiological and otolaryngological evaluation should also be performed when presented with a KS case.

Keywords: *Kabuki syndrome, Niikawa-Kuroki syndrome, hearing loss, multiple anomalies*

KS is a rare disorder discovered by Japanese doctors Norio Niikawa and Yoshikazu Kuroki in 1981. The syndrome received its name due to the resemblance of the characteristic facial features of patients to the make-up used in the traditional Japanese Kabuki play.[1] Niikawa and Kuroki independently described the syndrome in a subset of ten Japanese children that were reported to have distinctive facial features, skeletal abnormalities, dermatoglyphic abnormalities, short stature and mental retardation.[2]

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Hearing loss is also a frequent finding in patients with KS, comprising 82% of the reported cases in the literature.[3] Most of the cases of hearing loss were due to otitis media. Other cases were attributed to inner ear deformities or severe ossicular malformation.[4]

We present the case of a five-year-old female diagnosed with KS at age three. She presented with bilateral moderate to severe hearing loss determined by puretone audiometry and auditory brainstem testing. Fluctuating tympanometric findings were reported in both ears. Knowledge of the audiological and speech manifestations as well as the physical deformities of patients with KS could be useful to the clinician in the diagnosis of hearing loss in future cases.

CASE REPORT

Our patient was born full term via caesarean section to a 26-year-old *gravida* 1 *para* 0 mother. At birth, the patient was cyanotic and had difficulty breathing. She was confined in the neonatal intensive care unit for 12 days where an atrial septal defect (that spontaneously closed later) was diagnosed. She was re-admitted for persistent diarrhea at 24 days of age and for pneumonia at one month of age. She failed her newborn hearing screening at one month of age, and though she was already suspected to have hearing difficulties, no intervention was made for hearing loss at that time. An auditory brainstem response test at 18 months of age revealed mild to moderate hearing loss in the left ear and moderate to severe hearing loss in the right ear.

At seven months of age, the patient was hospitalized for a urinary tract infection and enterocolitis, the latter condition resulting in six further admissions in twelve months. She also had benign febrile convulsions and premature thelarche.

At 12 months of age, puretone audiometry revealed moderate to severe conductive hearing loss in the right ear with a drop at the high frequencies and moderate to severe conductive sloping hearing loss in the left ear. A summary of unaided audiometry results can be found on *Figures 1A and 1B*. The patient was also fit binaurally with behind-the-ear digital hearing aids (PowerMAXX 411, AD and PowerMAXX211, AS; Phonak; Manila Hearing Aid Center). She reportedly wore both hearing aids for an average of eight hours per day.

At 12 months of age tympanometry revealed type B tympanograms bilaterally. Otorhinolaryngologic consultation was recommended but was not completed at this time. Three years later, tympanometry revealed a type A tympanogram on the right and a type C tympanogram on the left. A summary of tympanometric findings can be found on *Table 1*.

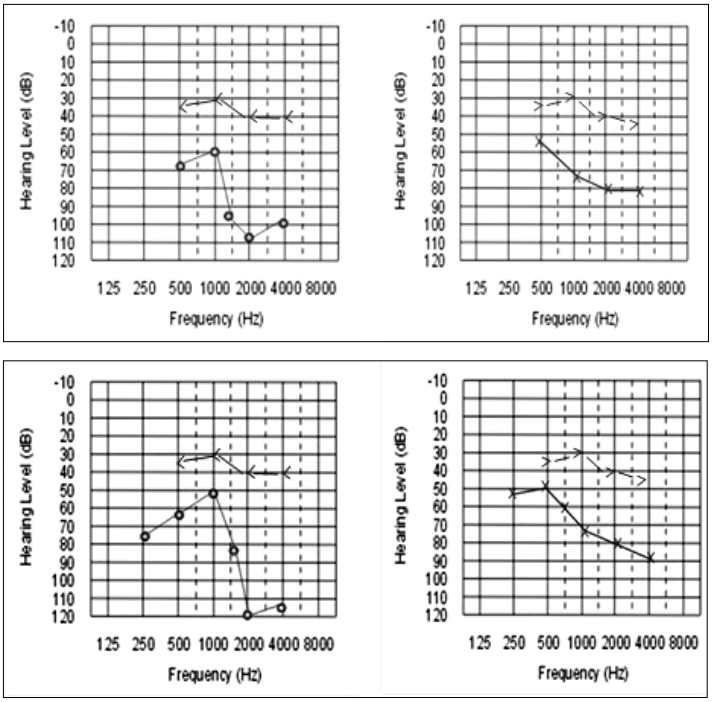

Figure 1 (A). Puretone Audiometry results obtained last December 6, 2006 showing moderate to severe conductive hearing loss in the right ear with a drop at the high frequencies and moderate to severe conductive sloping hearing loss in the left ear. (B) Puretone Audiometry results obtained last July 13, 2009 showing similar results to (A)

Table 1. Summary of tympanometric findings

	December 6, 2006		July 13, 2009	
	Right ear	Left ear	Right ear	Left ear
Type	B	B	A	C
ECV	0.66 ml	0.54	1.35 ml	1.20 ml
Compliance	0.16 ml	0.08	0.86 ml	0.33 ml
Pressure	-393daPa	-146 daPa	-12 daPa	-129 daPa

Table 2. Speech and language milestones

Skill	Age expected (years:months)	Age Acquired (years:months)
Receptive Language		
Localizing to sound	0 – 0:6	< 1:0
Localizing to voice/calling by name	0:5 – 0:9	2:0
Recognizing names of familiar people and object	0:6 – 1:0	3:0
Following simple commands	1:0 – 1:6	3:0
Answering simple questions	1:0 – 2:0	3:6
Expressive Language		
Cooing	0:2 – 0:3	Unrecalled
Babbling	0:4 – 0:6	Unrecalled
Imitated adult sounds	0:6 – 1:0	Unrecalled
1-word utterances	1:0	Unrecalled
2-word utterances	1:6 – 2:0	Unrecalled
Phrases/sentences	3:0	Still unable

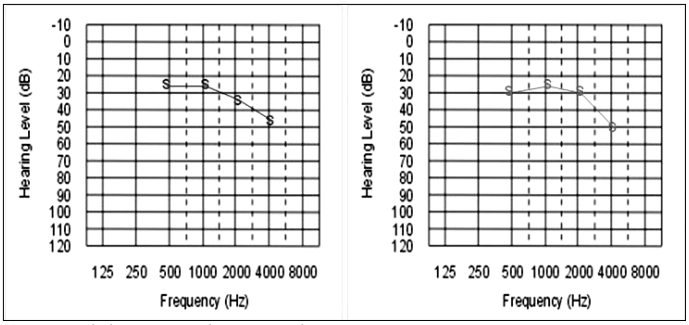

Figure 2. Aided puretone audiometry results

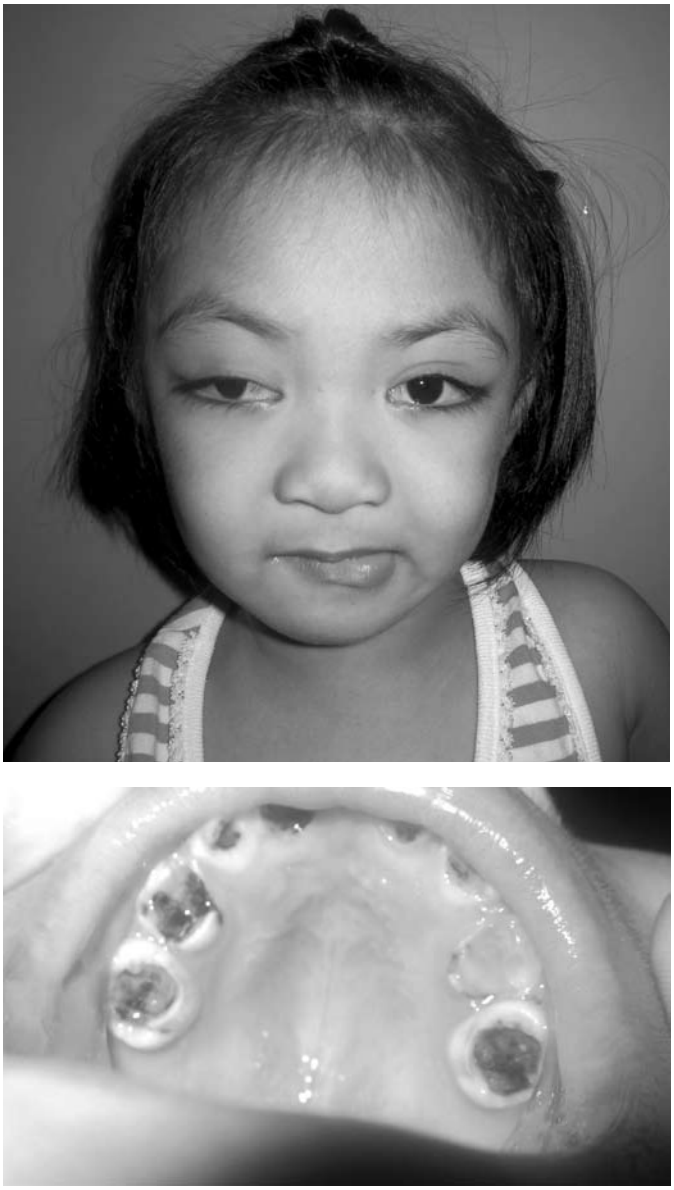

Figure 3 (A).). Facial features of Kabuki Syndrome i.e. arched eyebrows, large palpebral fissures, large protruding ears, depressed nasal tip, and (B) widely spaced teeth. Photos printed in full with permission.

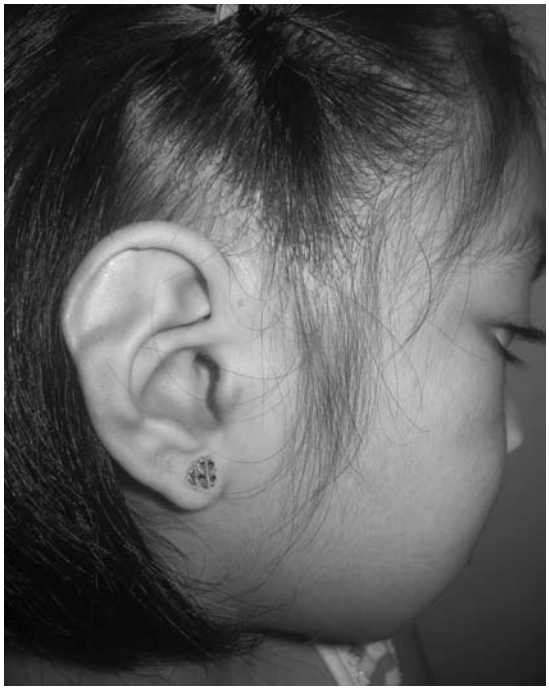

Figure 4. Pre-auricular pits on both the right and left ear of the patient.

At three years of age she was diagnosed with KS by a developmental and behavioral pediatrician. An assessment using the Denver Developmental Screening Test (Denver Developmental Materials, Inc.; Denver, Colorado, USA) resulted in a diagnosis of mental retardation.

At four years of age, three years post-amplification, the patient's speech and language was assessed by a speech pathologist. It was noted that there was a delay in receptive and expressive language *(Table 2*). A general observation of the patient's latest speech and language skills included localizing to environmental sounds, responding to her name, following simple commands, using 1-2 words to express her needs i.e. "*mama kain*" (mama, eat), "*akin yan*" (that's mine) and answering simple questions. She is currently undergoing speech and language habilitation.

Based on the latest aided puretone audiometry results *(Figure 2)*, her thresholds for both ears fall within the average speech spectrum from 250-4000 Hz. This suggests that she should have access to low, mid and high frequency speech sounds.

Before amplification, the patient was reported to solely use signs and gestures to communicate. Currently, she uses signs at school and at home and is now able to use speech as well. However, most of her speech was noted to be unintelligible to unfamiliar and familiar people under unknown contexts. According to her mother, she becomes frustrated and throws tantrums when she is not understood.

Currently, the patient manifests with arched eyebrows with the lateral one third dispersed or sparse, eversion of the lower lateral eyelid, depressed nasal tip, prominent ears *(Figure 3A)*, and widely spaced teeth *(Figure 3B)*—all of which are physical features typical of a patient with KS.[5] She was also found to have pre-auricular pits bilaterally *(Figure 4)*.

Otoscopy could not be performed because the patient was uncooperative but Computed Tomography (CT) findings of the temporal bone showed bilateral superior semicircular canal dehiscence *(Figure 5)*, patent cochlear aqueduct, AS *(Figure 6)* and enlarged vestibular aqueduct, AD *(Figure 7*).

DISCUSSION

Based on a review of 62 cases, Niikawa reported five cardinal manifestations of KS. These include; (1) abnormal facial features: long palpebral fissures, large protruding ears, arched eyebrows and a depressed nasal tip; (2) skeletal anomalies like scoliosis; (3) dermatoglyphic abnormalities, which have been cited in around 90% of the cases including increased digital ulnar loops and persistence of fetal fingertip pads; (4) mild to moderate mental retardation with average IQs of 50–62; and (5) postnatal growth deficiency.[5]

Although the etiology of KS is still unclear, recent studies suggest that it could be inherited as an autosomal dominant trait with variable expressivity.[6, 7] Although it is claimed to be genetic in nature, there are currently no genetic tests available for KS, nor are there any uniform diagnostic criteria for the syndrome. A diagnosis of KS is usually based on the physical manifestations of the disease.

Studies have shown that KS is not partial to a particular race or ethnic background.[8] The syndrome affects all races as well as males and females equally.[9] Because the phenotype takes time to develop, a diagnosis of KS is difficult to make in neonates.[10] According to the literature, a diagnosis is usually made by two years of age.[11]

In terms of findings related to otolaryngology and audiology, the most commonly reported problems are dysmorphic pinnae, otitis media, and hearing loss.[12] Prominent, cup-shaped ears are a usual finding in KS patients. Preauricular pits have also been reported in close to 20% of the cases and were present bilaterally in this case. One-third of the reported cases have also been found to have cleft palate. This, coupled with the fact that a majority of the patients have increased susceptibility to infections could also contribute to complications due to otitis media in a majority of cases.[1,13]

Cases of conductive, sensorineural and mixed hearing loss have all been reported. Conductive hearing loss is the most prevalent type in

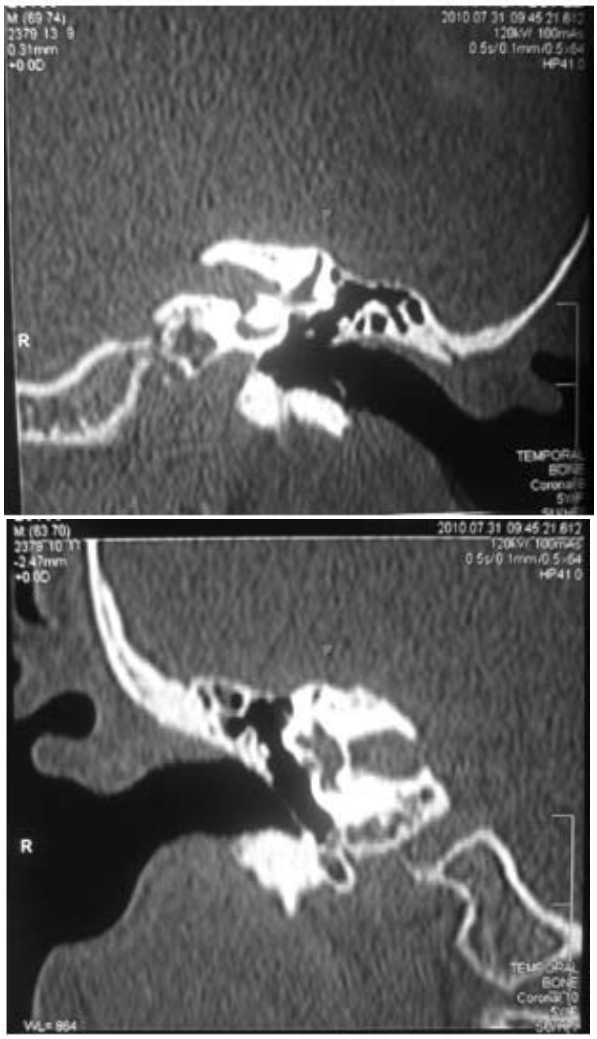

Figure 5. CT scan of the temporal bone showing bilateral superior semicircular canal dehiscence

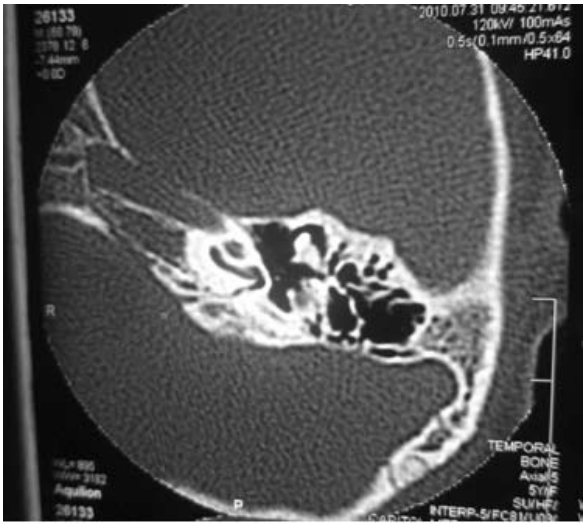

Figure 6. CT of the temporal bone showing patent cochlear aqueduct, AS

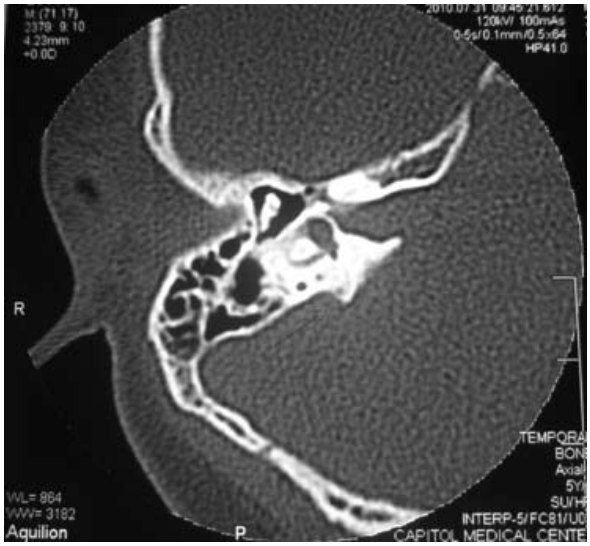

Figure 7. CT of the temporal bone showing enlarged vestibular aqueduct, AD

the literature. Sensorineural hearing loss is rare in patients with KS, and when present were mostly caused by anomalies of the inner ear such as bilateral absence of the cochlea with dilated dysplastic vestibules or unilateral enlarged vestibules. A study done at a multidisciplinary craniofacial clinic reported hearing loss in 82% of cases however, other studies have cited true prevalence to be somewhere between 20-30%.[1, 13, 14]

Aside from audiologic and otolaryngologic findings, studies have also reported vestibular findings in a small number of patients with KS. A study by Barozzi *et al*. found that in a group of patients with KS that underwent vestibular assessment, 8% were found to have abnormal results.[3]

The first report of a large vestibular aqueduct in a patient with KS was presented by Hempel *et al*. in 2005.[15] In this patient, the presence of bilateral superior semicircular canal dehiscence, enlarged vestibular aqueduct in the right and a patent cochlear aqueduct in the left may explain the presence of bilateral conductive hearing loss.

As KS presents with multiple anomalies, other organ systems are usually affected. Aside from the aforementioned findings, patients with KS may also present neurologically with hypotonia, dysarthria and dyspraxia.[9] Opthalmologic problems including ptosis, strabismus, and blue sclerae have also been reported in approximately one-third to one-half of cases.[16] Cardiovascular problems have also been reported in 40-50% of cases. Renal problems including malposition of the kidneys and renal hypoplasia have been reported in about 25% of cases. Cranial and vertebral abnormalities are commonly described along with other skeletal anomalies. In the literature, respiratory and gastrointestinal findings have been rare.

Studies have reported that the prognosis for survival into adulthood of patients with KS is good as long as congenital anomalies and other reported problems are properly managed.[3]

A rare case of KS has been presented and the clinical features, audiological manifestations, as well as a summary of the patient's speech and language development were discussed. Knowledge of these audiologic manifestations as well as the other findings in patients with KS may aid in the diagnosis of future cases.

It is recommended that when confronted with a diagnosed case of KS, the patient should undergo comprehensive audiological and otolaryngological evaluation. Patients should be examined for the following: hearing loss that is conductive, sensorineural, or mixed; otitis media, protruding ears, dysmorphic pinnae, preauricular pits, inner ear abnormalities, and cleft palate.

Vestibular assessment should also be considered in select patients with vestibular symptoms, sensorineural hearing loss, or inner ear abnormalities.[3] In patients that need vestibular assessment, caloric tests or Vestibular Evoked Myogenic Potentials testing can be done if the patient is cooperative.

Pure tone audiometry, immitance audiometry, auditory brainstem response testing and auditory steady state response testing should be included in the audiologic diagnostic test battery given to patients with KS. Patients should also undergo CT of the temporal bone to rule out inner ear abnormalities.

Management of the audiologic and otolaryngologic problems of patients with KS may include fitting hearing aids for the hearing loss, prescribing antibiotics for cases of otitis media, or surgery to repair dysmorphic pinnae.

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