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REVIEW ARTICLE

ENT MANIFESTATIONS OF KABUKI SYNDROME: REPORT OF THREE CASES.

Nasrine Siham MEHTARI[1,2], Mohammed SAHRAOUI[1] and Isma BRAHAMI[1]

[1]ENT Department, Faculty of Medicine of Tlemcen,
[2]Toxicomed Laboratory, Abou Bekr Belkaid-Tlemcen University

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Corresponding Author:
Nasrine Siham MEHTARI

ABSTRACT

The Kabuki syndrome is a rare genetic disorder, mainly associating an intellectual deficit, a polymalformative syndrome and specific morphological variations of the face allowing the diagnosis. It is also a rare cause of syndromic deafness. The aim of our work is to draw the practitioner's attention to the ENT manifestations of this syndrome as well as the clinical and therapeutic particularities of the hearing loss associated with it. We report the case of 3 children seen in consultation. Each child has an ENT and general clinical examination, impedancemetry, ABR and ASSR exploration. Due to its characteristic facial dysmorphism, ENT clinical manifestations are almost constant in Kabuki syndrome. Deafness is one of the handicaps frequently encountered in these patients and must be systematically screened. The early and adequate management of ENT manifestations contributes to reducing the significant morbidity presented by these patients. Kabuki syndrome should be kept in mind when evaluating an individual with syndromic hearing loss.

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INTRODUCTION

The Kabuki syndrome (KS) is a rare genetic disorder, mainly associating an intellectual deficit, a polymalformative syndrome and specific morphological variations of the face allowing the diagnosis. It is also a rare cause of syndromic deafness (1). The aim of our work is to draw the practitioner's attention to the ENT manifestations of this syndrome as well as the clinical and therapeutic particularities of the hearing loss associated with it.

Patients and methods: We report the case of 3 children seen in consultation. Each child has an ENT and general clinical examination, impedancemetry, ABR and ASSR exploration.

First observation: B S, 4 years old, is brought in for consultation because her parents suspect that she has deafness. The girl has a history of pre and postnatal growth retardation, anemia, chronic diarrhea and celiac disease. Clinically, she has arched and sparse eyebrows in their outer third, elongated palpebral fissures with an eversion of the outer part of the lower eyelids, a depressed nasal tip, a thin upper lip as well as a bilobed aspect of the lower lip, bluish sclera and low set ears (Figure 1). The otoscopy shows Serous Otitis Media. Inspection of the hands found brachydactyly and persistence of fetal pulp pads. The child also has scoliosis. The cardiological examinations came back without abnormality. Impedancemetry shows a flat tympanogram with no stapedial reflex on both sides. The ABR and ASSR reveal bilateral moderate conductive hearing loss (figure 2).

His treatment consisted of an adenoidectomy with tympanostomy tube insertion ympanic ventilator on both sides. After a month we noticed a normalization of PEA and ASSR

Second observation: B A is a little boy, he is 10 years old with a history of a first degree parental consanguinity, moderate mental retardation with fine motor difficulties. The clinical examination found a microcranium, arched eyebrows, elongated palpebral fissures, a depressed nasal tip and a thin upper lip as well as micro-retrognathism. The ears are prominent and turbinate, the palate is ogival, the dentition is abnormal and spaced out and the sclera is bluish (figure 3). There are also musculoskeletal abnormalities including brachydactyly, brachymesophalangy and clinodactyly of the 5th finger (Figure 4). An attenuation of the fold of the distal interphalangeal of the 4th finger of the hand is also noted. This child presents also a persistence of fetal pulp pads (figure 5). Otoscopy and impedancemetry are normal. In ABR and ASSR there is a bilateral moderate sensorineural hearing loss (Figure 6). A CT scan of the rocks showed a hypoplastic appearance of the crus and head of the stapes and the long apophysis of the incus on the right. We indicated prosthetic auditory rehabilitation in air conduction by conventional prostheses associated with speech therapy.

Third observation: It's about a boy of 10 yaers old who presented for hearing exploration in the context of a syndromic case. We note the notion of recurrent pneumonia, growth retardation with mild mental retardation. The facies is very suggestive with: dysplasia of the auricles, depressed nasal tip, short columella, thin upper lip, eversion of the outer part of the lower eyelid, arched eyebrows with ptosis of the upper eyelids (figure 7).

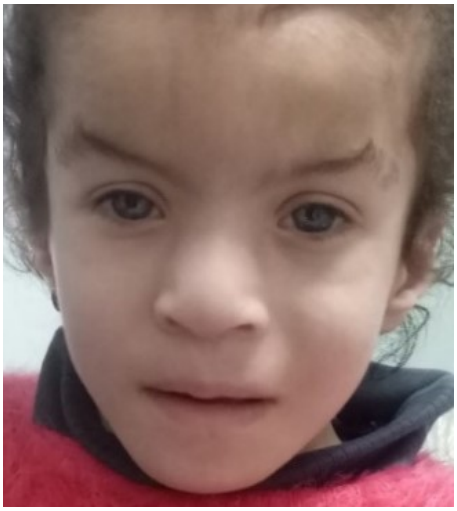

Figure 1. Characteristic facial dysmorphism of KS

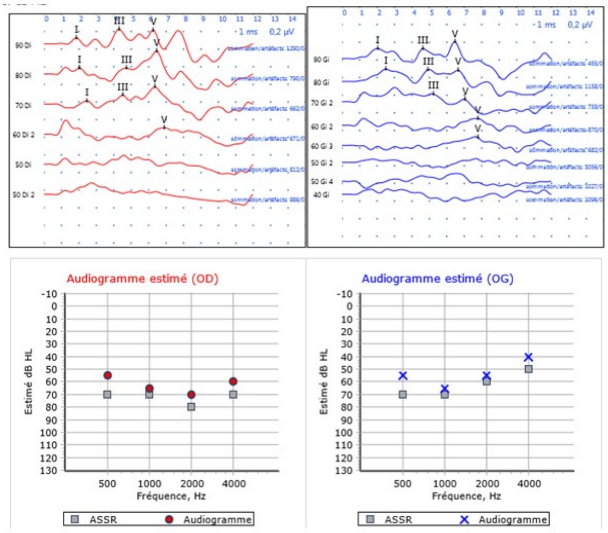

Figure 2. ABR and ASSR: Bilateral moderate conductive hearing loss

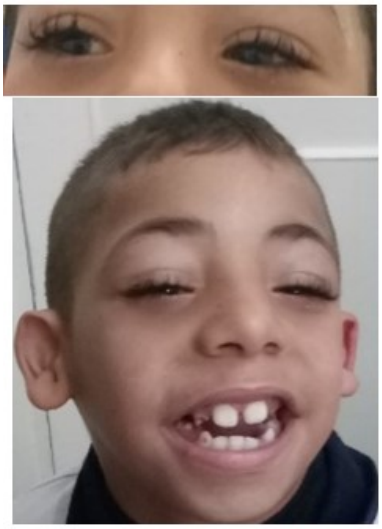

Figure 3. Bluishsclera and facial dysmorphism

There is persistence of the fetal pulp pads (figure 8), the nails are short and brittle with brachydactyly and clinodactyly of the 5th finger (figure 9). The otoscopy shows Serous Otitis Media with flat tympanogram and a stapedial reflex present on both sides in impedancemetry.

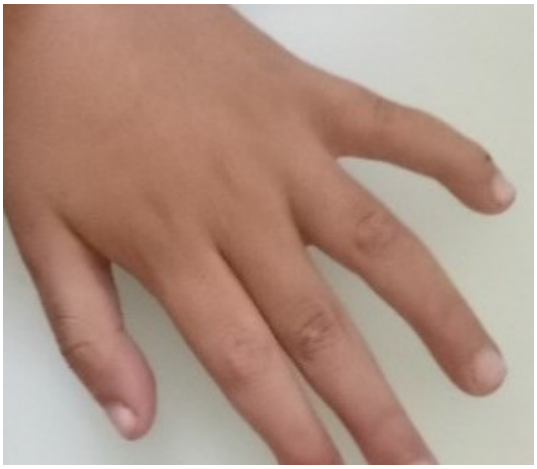

Figure 4. Brachydactyly, brachymesophalangy and clinodactyly of the 5th finger

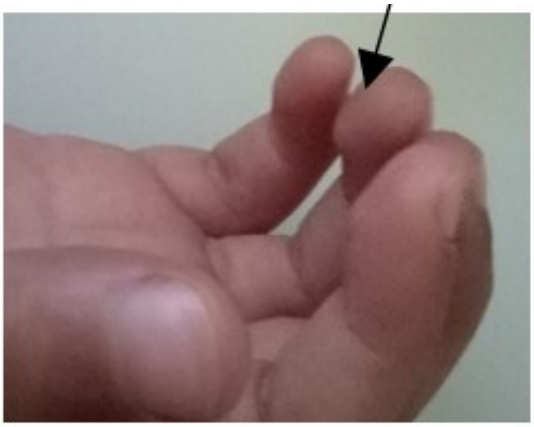

Figure 5. Persistence of fetal pulp pads

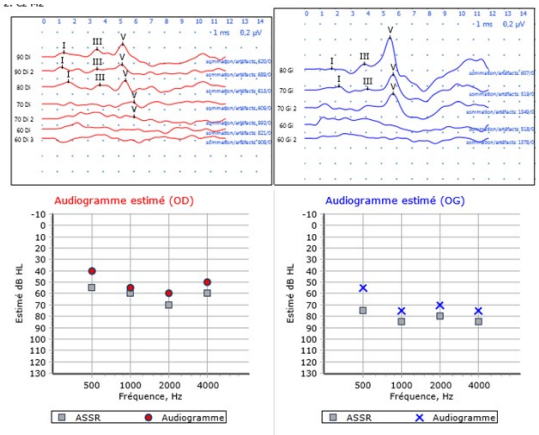

Figure 6. ABR and ASSR: bilateral moderate sensorineural hearing loss

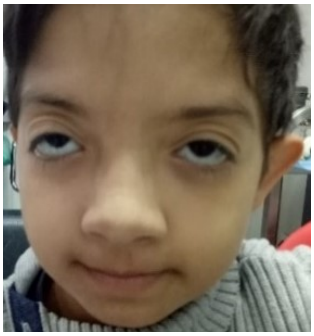

Figure 7. Facial dysmorphism of KS

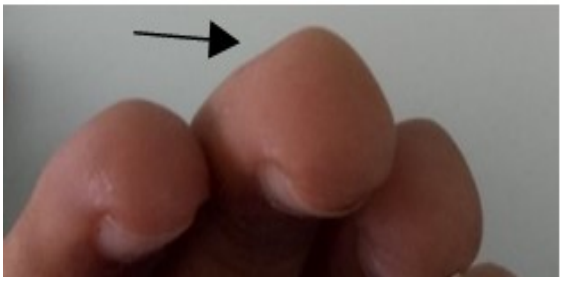

Figure 8. Persistence of fetal pulp pads

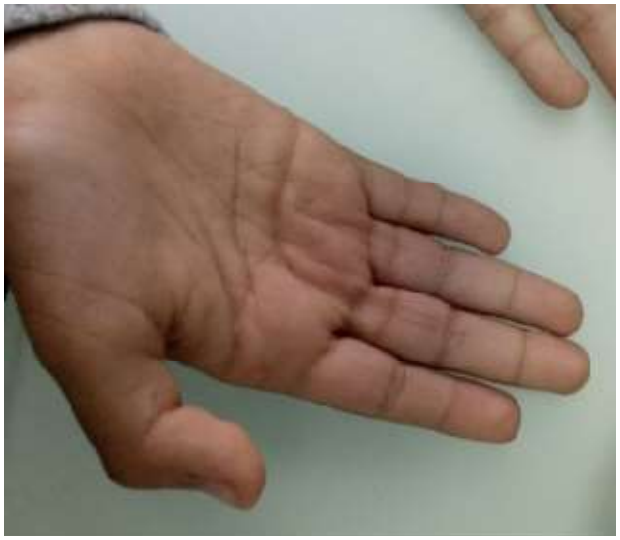

Figure 9. Brachydactyly of the 5thfinger

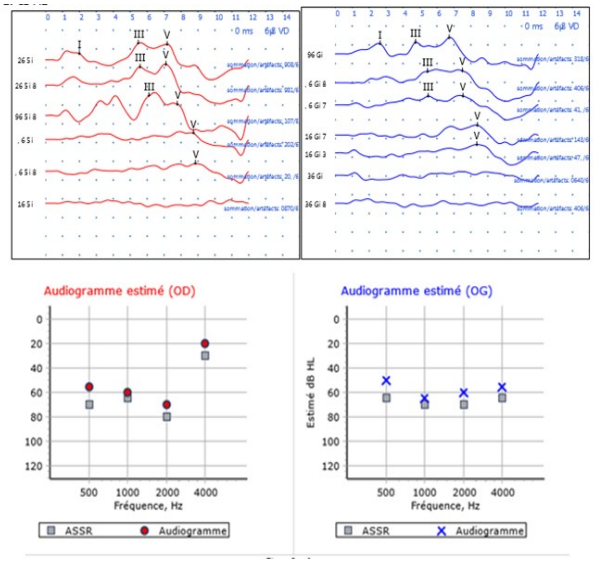

Figure 10. Bilateral moderate conductive hearing loss

A tonal audiometry is impossible to perform due to the mental retardation of the child. Objective auditory investigations, namely AEP coupled with ASSR, found moderate conductive hearing loss on both sides (Figure 10). This child had an adenoidectomy with placement of a tympanostomy tube.

DISCUSSION

Kabuki Syndrome or Niikawa Kuroki Syndrome is a rare genetic condition. Its prevalence is estimated at 1/32,000 (7). The name of this syndrome is related to the actors of kabuki, traditional Japanese theater. The first cases were described in Japan, but it has been observed in all ethnic groups. It nevertheless presents a strong clinical and biological heterogeneity with more rare but very diverse symptoms. KS is classically defined by 5 cardinal diagnostic criteria established by Niikawa Kuroki (9):

- Specific craniofacial morphological variations

They include elongated palpebral clefts with eversion of the outer part of the lower eyelid, arched eyebrows and often a 1/3 medium scatter, a short columella with a flattened nasal tip, and large, prominent, turbinate ears. All of these abnormalities are encountered in our patients. Other craniofacial abnormalities are found in the literature, which are also noted in them such as an ogival palate, abnormal dentition and ptosis

- A retardation of staturo-weight growth concerns 2/3 of people with KS and concerned the 3 reported cases.
- Mild to moderate intellectual deficit is present in 90% of cases. He interested all the children seen. Mental retardation is not related to microcrania, which may affect 29 to 56% of patients. The latter was observed in a single case.
- Musculoskeletal manifestations. Brachydactyly kind 5, brachymesophalangy, clinodactyly of the 5th finger and scoliosis are described in this syndrome and are found in these children 4th finger has recently been demonstrated, signifying low use of fingers (5). The latter is observed in the 2nd child reported. The specific presence of attenuation or congenital absence of the distal interphalangeal flexion creases of the 3rd or 4th finger has recently been demonstrated, signifying low use of the fingers (5). The latter is observed in the 2nd child reported.
- Anomalies of the dermatoglyphs are very variable and numerous. The persistence of fetal pulp pads are among the cardinal signs, and have made it possible to orient the diagnosis in these patients. In addition to these cardinal criteria, this syndrome has a very varied clinical aspect. Thus, ocular abnormalities have been described in 38 to 61% of patients with KS. Bluish sclera was similarly reported in the literature and affected two out of three children. Cardiac, immune, gastrointestinal and endocrine abnormalities are also associated with this syndrome.

The ENT manifestations of KS concern facial dysmorphism, the cardinal criterion, recurrent infections of the middle ear, chronic otitis media with an open eardrum, serous otitis and deafness. Moderately equivalent ear infections in approximately 70% of patients (3). They are favored by the tubal dysfunctions that accompany the velopalatine abnormalities and the state of immunodeficiency presented by these SK patients. Secretory otitis that accompanies craniofacial dysmorphisms in children with this syndrome is common. They are often associated with conductive hearing loss (3). In this way, 2 reported children out of 3 presented seromucous otitis associated with hearing impairment. Also, deafness is a characteristic symptom of KS, its prevalence varies in the literature from 20 to 65% of cases (1,2). The authors agree that conductive hearing loss is the most common. It is most often consecutive to these secretory otitis which disturb the acquisition of language (8. It can also be due to malformations of the middle ear, in particular that of the ossicles. Neurosensory impairment is more rarely associated with KS. It concerns all degrees unilaterally or bilaterally. This concerned only one of our cases. Thus, malformations of the inner ear such as Mondini dysplasia, vestibular dysplasia, aplasia of the cochlea and semicircular canals and widening of the vestibule aqueduct have been reported (4,6). The treatment of deafness seen in children with KS depends on its kind. It usually consists of the placement of a trans tympanic aerator for secretory otitis, the case of the two KS reported associated with this pathology. Auditory rehabilitation of sensorineural hearing loss is based on air conduction prosthetics. The expansion of indications for cochlear implantation to patients with other disabilities has allowed this type of rehabilitation in certain cases of KS with profound deafness, as reported by VESSEUR et al. in 2016 (10). In their studies, Barrozzi et al, report that 95% of KS

patients in their series had normal vestibular function (2). The diagnostic criteria for KS have not yet been established, but the diagnosis is based on the 5 cardinal signs mentioned above. Molecular analysis can confirm the diagnosis. KS is associated in 45 to 80% of cases with mutations of the MLL2 gene and deletions of the KDM6A gene have also been described (3).

CONCLUSION

Due to its characteristic facial dysmorphism, ENT clinical manifestations are almost constant in KS. Deafness is one of the handicaps frequently encountered in these patients and must be systematically screened. The early and adequate management of ENT manifestations contributes to reducing the significant morbidity presented by these patients. SK should be kept in mind when evaluating an individual with syndromic hearing loss.

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