CASE REPORT

Peter's anomaly in a child with Kabuki make-up syndrome: a case report and review of the literature

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Abstract

This case report describes a unique case of Peter's anomaly in a child with Kabuki make-up syndrome. Kabuki make-up syndrome can be identified on the basis of the following eye findings: lateral lower lid ectropion; high arched eyebrows; and sparse hair in the lateral third of the eyebrow. These physical findings are highly characteristic, but subtle. We present a boy with signs of Kabuki make-up syndrome and Peter's anomaly. Clinicians should be aware of the features of Kabuki make-up syndrome and the possible association with Peter's anomaly. Kabuki make-up syndrome is commonly overlooked as a diagnosis, but its recognition may considerably aid families in planning social and developmental support. We discuss the relationship of Peter's anomaly to Kabuki make-up syndrome and other systemic, genetic diseases.

Key words: *Peter's anomaly, Kabuki make-up syndrome*

Introduction

Kabuki make-up syndrome (KMS) was first reported in Japan in 1981 by Niikawa *et al*[1] and Kuroki *et al.*[2] In 1988, their case series of 62 Japanese patients, aged 4 to 16 years, described five cardinal manifestations of KMS:

1. An unusual looking face (100% of patients), characterized by ectropion of the lower lateral eyelid; high, arched eyebrows, with sparse hair in the lateral third; a depressed nasal tip; and prominent ears.
2. Skeletal anomalies (92%), including excessively short fifth digits and a deformed spinal column, with or without sagittal cleft vertebrae.
3. Dermatoglyphic abnormalities (93%), including the presence of fingertip pads and deviations from normal fingertip patterns.
4. Mild to moderate mental retardation (92%).
5. Postnatal growth deficiency (83%).[3]

Kabuki make-up syndrome is so termed because afflicted children show facial features reminiscent of traditional Japanese Kabuki theater actors.

Most cases of KMS occur sporadically, although Hala *et al* have identified one family in which an affected father and a non-affected, non-consanguineous mother gave birth to children with KMS,[4] suggesting autosomal dominant inheritance. Genetic analysis has elucidated a paracentric inversion of the short arm of chromosome 4 in three children with KMS.[5] Males and females are equally affected, although at least three patients have been described to have a Y chromosome abnormality.[3] The overall incidence is estimated to be 1:32,000 newborns, but KMS is often unrecognized, and the actual incidence may be considerably higher.

Since the original reports, the syndrome has been identified in African-American,[6,7] Caucasian,[8] Sicilian,[9] Arab,[10] and Hispanic[11] children. A recent case series and review by Schrander-Stumpel *et al*[12] of both Japanese and non-Japanese patients found that short stature was more common

in the non-Japanese group, and that 66% to 80% of non-Japanese patients had serious neurological problems such as hypotonia and feeding problems, especially poor control of motor movements required to eat(mastication and swallowing). Several reports have noted the occurrence of KMS in conjunction with other diseases. These include early breast development in girls,[3] premature thelarche,[13,14] Turner's syndrome,[15] endocrine disorders,[16,17] congenital heart disease,[18] coarctation of the aorta,[19] blue sclera,[3] increased susceptibility to infection,[1,13] chronic idiopathic thrombocytopenic purpura,[20] and cleft palate.[21]

Although most reports of KMS have noted at least some of the ocular findings mentioned above, we report a child with KMS associated with unilateral Peter's anomaly and nasolacrimal duct obstruction. We are not aware of any previous report of this association.

Case report

A six-year-old Hispanic boy with a normal family history was evaluated for a left congenital corneal opacity (**Figure 1**). Systemic manifestations of KMS were present and consisted of large prominent ears, a depressed nasal tip, short stature, mental retardation, and dermatoglyphic abnormalities. He had bilateral shortened fifth fingers and fingertip pads (**Figure 1**).

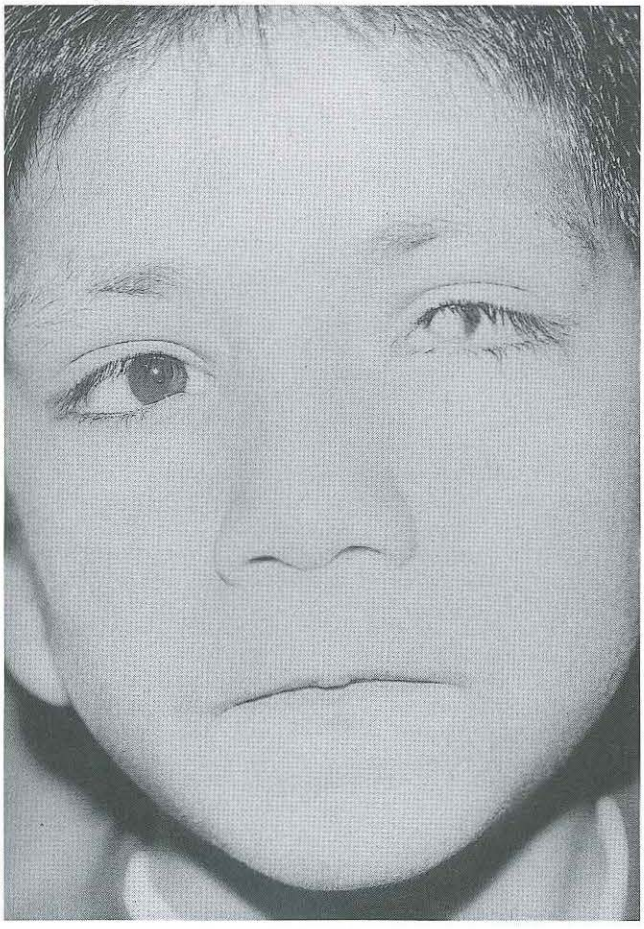

Figure 1. This child has facial features characteristic of Kabuki make-up syndrome. He has a lateral lower lid ectropion, sparse lateral third of the eyebrows, and large ears. Peter's anomaly is present in his left eye.

Eye examination demonstrated good visual responses in the right eye, but poor fixation in the left eye. Fine amplitude, fast frequency nystagmus was present in both eyes. The left eye showed epiphora. A large central corneal leukoma with a lenticulocorneal adhesion was present in the left eye. An electroretinogram showed normal photopic and scotopic responses in both eyes.

Discussion

Peter's anomaly occurs as a result of an error in the embryonic development of the eye, causing variable iridolenticulocorneal adhesions and corneal opacification. The primary microscopic characteristic is localized absence of Descemet's membrane,[22] but often includes defects in the corneal epithelium and posterior stroma as well. The clinical findings of lenticulocorneal adherence or corneal leukoma with iris adhesions allow the diagnosis to be made without histologic examination. Corneal opacification in Peter's anomaly is usually severe and may involve the entire cornea. Vision may be further decreased by concomitant lens malformation and opacification. Glaucoma, either congenital, infantile, or juvenile, often occurs in these patients as a result of angle malformation, and is frequently a major source of further visual compromise. The dense corneal opacities result in deprivation amblyopia if left untreated. Despite aggressive surgical and postoperative care, almost 50% of eyes lose all light perception, mainly due to glaucoma.[23]

Peter's anomaly may occur as an isolated condition,[24,25] in conjunction with other ocular malformations,[19,26-29] or as a component of a well-defined syndrome, such as fetal alcohol syndrome,[30] Warburg syndrome,[31] Pillay syndrome,[32] or Peter's-plus (Krause-Kivlin) syndrome.[33-35] Several systemic abnormalities have been reported in patients with defects in Descemet's membrane or lenticulocorneal contact, including craniofacial abnormalities,[36,37] ear anomalies,[38] congenital heart disease,[36,39,40] pulmonary hypoplasia,[41] syndactyly,[42] genitourinary disorders,[39,43] and central nervous system disorders, including mental retardation.[44]

When the anomaly is not accompanied by systemic congenital malformations, it may be inherited in an autosomal recessive[24,38] or autosomal dominant[25] manner. Although the exact cause of Peter's anomaly is unknown, Traboulsi and Maumenee propose that Peter's anomaly, at least in Peter's-plus syndrome, may be the result of a mutation or deletion of a homeotic gene that controls the differentiation of primordial cells and the development of different body segments.[45] Several different chromosomal abnormalities have been detected in patients with congenital malformations associated with Peter's anomaly, including *del* 18q,[46] 11q,[47] r21,[48] t(2;15q),[49] and 4p.[35] It is interesting that KMS has also been noted in a patient with a chromosome 4 abnormality.[5] Further study is, however, required to elucidate whether any true correlation can be made between the two loci.

In KMS, the ocular features are subtle, but distinctive. Our patient illustrates that a serious vision-threatening abnormality is also possible in KMS. Children with Peter's anomaly should be investigated for systemic abnormalities, including KMS.

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