CASE REPORT

Recognition of Kabuki Syndrome

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Port J Pediatr 2023;54(2):136-7
DOI: https://doi.org/10.25754/pjp.2023.24753

Keypoints

What is known:

- Kabuki syndrome is characterized by typical facial features, minor skeletal anomalies, mild-to-moderate intellectual disability, and postnatal growth deficiency.
- The facial features of Kabuki syndrome are well described. Other anatomical malformations may be associated in varying degree, some of which may be present at birth, while others arise later. Furthermore, not all features are present in all children.
- Kabuki syndrome has a broad clinical range of neurodevelopmental pathology, that presents as a degree of intellectual disability.

What is added:

- This case highlights the importance of a prompt cooperation between the different health professionals when a diagnosis is made, given the positive impact of multidisciplinary therapy in pediatric age, like reported in this case.
- It highlights also the importance of parents' genetic counseling, ensuring that they are equipped with the medical information necessary for their decision-making, adjustments and family reorganization, given the probability of transmission of the syndrome to offspring.

Introduction

Kabuki syndrome is a rare genetic syndrome characterized by intellectual disability, distinctive facial appearance, skeletal anomalies, and postnatal growth deficiency.[1-3] The prevalence of Kabuki syndrome is 1/32 000 people in Japan. Currently, only 16 patients are described in Portugal.[4] It can have several manifestations, some of which present at birth, while others arise later. Furthermore, not all features are present in all children. Aside from the cardinal diagnostic manifestations of Kabuki syndrome, other manifestations may include cardiopathy, neuromuscular dysfunction with neonatal hypotonia, seizures, genitourinary, orthodontic, ophthalmological, and endocrinologic abnormalities.

Kabuki syndrome can be diagnosed at any age based on clinical manifestations and a history of infantile hypotonia, developmental delay, and intellectual disability.[3] The majority of Kabuki syndrome cases are due to *KMT2D* gene variants with autosomal dominant inheritance.[5] However, a minority of them are due to the *KDM6A* gene variant, an X-linked dominant inheritance. These genes play a role in the regulation of other genes expressions.

We present the case of a 9-year-old Caucasian male, currently followed up by consultation, who was born at term by eutocic delivery. His birth weight and length were 2990 g (percentile 10) and 45 cm (percentile 3), respectively. Since birth, he presented with severe axial hypotonia and feeding difficulties. Over time, he failed to thrive and achieve psychomotor milestones, and developed dysmorphic facial features, leading to suspicion of congenital metabolic or genetic diseases as a differential diagnosis. Results of an initial metabolic work-up and an array comparative genomic hybridization CytoScan® 750K were normal. However, a genetic molecular test identified a hemizygous *KDM6A* gene mutation, which is associated with Kabuki syndrome.

He presented distinctive dysmorphic facial features (Figs. 1 and 2), including long palpebral fissures, broad eyebrows with a sparse lateral third, depressed nasal tip with a flat nose base, thin upper lip, and arched palate. On follow-up, he manifested severe intellectual disability, moderate motor impairment, convergent strabismus, brachydactyly (Fig. 3), and skeletal and orthodontic issues. Currently, he is totally dependent, benefiting from multidisciplinary interventions (therapies and special education) and medical follow-up. This study aimed to disclose a rare genetic disease and alert the medical community.

Keywords: Abnormalities, Multiple/diagnosis; Abnormalities, Multiple/genetics; Child; Craniofacial Abnormalities; Growth Disorders/diagnosis; Growth Disorders/genetics; Intellectual Disability/genetics

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Received: 12/06/2021 | Accepted: 05/11/2022 | Published online: 01/04/2023 | Published: 01/04/2023

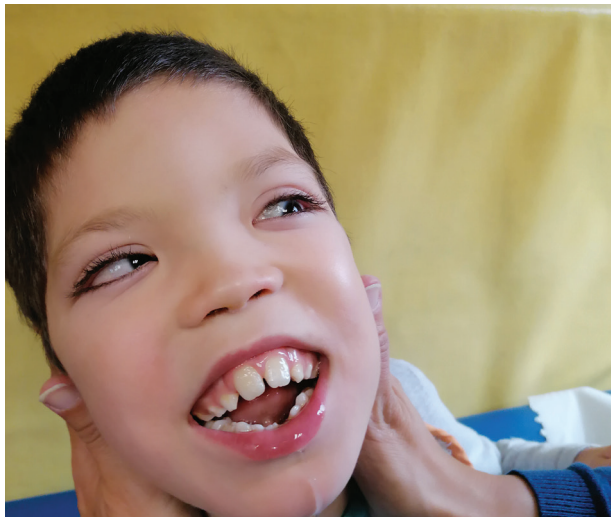

Figure 1. Distinctive features: palpebral fissures, a depressed nasal tip with flat nose base, thin upper lip, orthodontic problems, and convergent strabismus.

Figure 2. Distinctive features: broad eyebrows sparse in the lateral third, a depressed nasal tip with flat nose base and convergent strabismus.

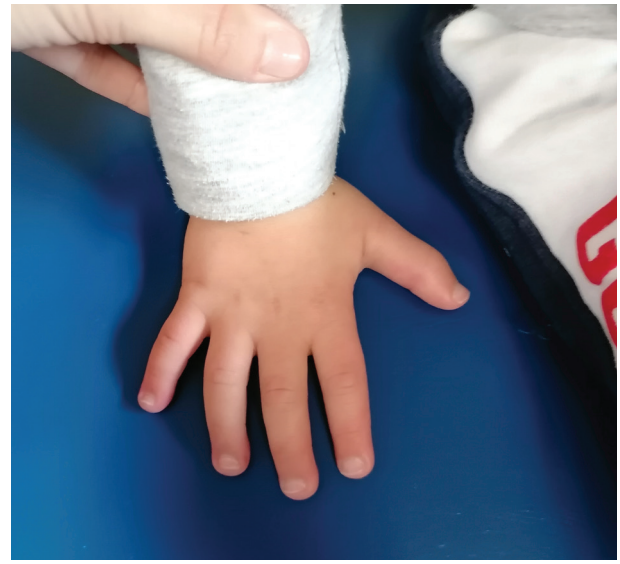

Figure 3. Brachydactyly.

Author Contribuitions

AGP, JS and NRS participated in the analysis or interpretation of data. RJP participated in the drafting of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this study.

Funding Sources

There were no external funding sources for the realization of this paper.

Provenance and peer review

Not commissioned; externally peer reviewed.

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

Consent for publication

Consent for publication was obtained.

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