Oculoskeletodental syndrome: a rare case report

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INTRODUCTION

Oculoskeletodental syndrome (OCSKD; OMIM#618440) is an ultra-rare monogenic disorder caused by *PIK3C2A* mutations (chr11p15.1). It is characterized by visual, skeletal, growth, and neurological impairments. Clinical findings include congenital cataracts, short stature, multiple skeletal abnormalities, coarse facies, developmental delay, among others. It was first documented in 2019, and only seven cases have been described in the literature so far. Here we describe the clinical presentation of the rare OCSKD in a Brazilian patient, caused by *PIK3C2A* frameshift deletions.

CASE REPORT

A male patient, one year old, was referred to the Genetics Outpatient Clinic of Hospital Universitário Júlio Müller (HUJM, Cuiabá-MT, Brazil) for evaluation. The patient is the first child of a healthy, non-consanguineous couple. Prenatal ultrasound revealed fetal hydrops, absence of the nasal bone, thickened nuchal fold, and shortened long bones. The patient was born preterm at 35 weeks of gestation via cesarean section due to premature dilation and contractions, with subsequent admission to the neonatal intensive care unit for 32 days due to respiratory distress. Multiple infectious episodes have been reported, mainly affecting the respiratory and gastrointestinal tracts. Upon physical examination, at 7 months old, bilateral epicanthal folds, ocular hypertelorism, a long philtrum, bitemporal narrowing, dysplastic and low-set ears, short neck, inverted nipples, gluteal fat atrophy, hepatomegaly, a sacral dimple with a pit, presence of fetal pads, and abnormal distribution of body fat were observed. Ophthalmological assessment revealed alternating convergent strabismus, low visual acuity, and an unspecified abnormality of the nasolacrimal ducts.

Due to the numerous dysmorphic characteristics and clinical findings, the primary hypothesis was a congenital disorder of glycosylation, and transferrin isoelectric focusing was requested but not performed. Karyotype is 46,XY with no evidence of major structural abnormalities. Whole exome sequencing identified two likely pathogenic variants at *PIK3C2A*: chr11: 17.113.740; NM_002645.4: c.4531_4534del: p. (Leu1511Argfs*3) and chr11:17.118.686; NM_002645.4: c.4243del: p. (Thr1415Hisfs*31), both in heterozygosity.

DISCUSSION

The clinical symptom constellation presented by the patient reported here is consistent with OCSKD, caused by *PIK3C2A* compound heterozygosity. Molecular testing was essential to reach diagnosis, given data scarcity on this condition due to both novelty and rarity. Additional manifestations, including dental abnormalities, developmental delay, and hearing impairment, may appear over time, thus requiring rigorous follow-up.

Table 1: Phenotype findings

	OCSKD*	Patient
Congenital cataract	+	-
Broad nasal bridge	+	+
Coarse facies	+	+
Teeth abnormalities	+	NA
Skeletal abnormalities	+	+
Hearing loss	+	NA
Hepatomegaly	+	+

"+" indicates presence of trait, "-" indicates absence of trait, N.A., not available. *Main abnormalities according to OMIM.

Pictures 1, 2 and 3: bilateral epicanthal folds, ocular hypertelorism, long philtrum, bitemporal narrowing, dysplastic and low-set ears, and short neck are shown.

Figure 1: Schematic representation of chromosome 11 showing *PIK3C2A* location (in red) according to DECIPHER.