Case report

Ohdo-Madokoro-Sonodasyndrome:A case report

Abstract:

Ohdosyndrome is extremely rare,comprises a heterogeneous group of disorders characterized by intellectual disability (ID) and typical facial features, including blepharophimosis, ptosis, dental hypoplasia, hearing impairment and intellectual disability.

We report the case of a girl aged 5 years, was born to healthy and non-consanguineous parents,no other members of the family are known to be affected with a similar disorder. She had marked dysmorphic facial features, made of blepharophimosis, dental hypoplasia, hypertélorism, rétrognatism, microcephaly, trigonocéphaly, microphthalmia, nasolabial furrow, badly hemmed ear, pointed palace, associated with psychomotor and growth retardation of less than 2 DS.Exome sequencing showedthe presence of the variant NM_005120.3 (MED12):c.6352C>T(p.Gin2118Ter) in the heterozygous state and its absence in the parents, wich confirms the novo character of this variant , wich is compatible with the diagnosis of ohdo syndrome by heterozygous mutation of the MED 12.

Keywords: Ohdo-Madokoro-Sonoda syndrome, dysmorphic facial features, intellectual disability, heterozygous mutation of the MED 12.

Introduction:

Ohdo et al. [1986] delineated a syndrome of blepharophimosis, ptosis, dental hypoplasia, heart defect, and mental handicap, to which his name is currently attached. During the following years, other cases of ‘‘Ohdo syndrome’’ were reported, with large clinical variability beyond the presence of the palpebral anomaly. Most cases were sporadic.

Case Presentation:

A 5 year-oldgirl was born on 04/01/2018 to healthy and non-consanguineous parents, from a followed pregnancy. The delivery was done vaginally, the second of gravida 3 Para 3, Birth weight was 3300 g, her medical history is remarketed by an hospitalization on the 7th day of lifefor 13 days for neonatal respiratory distress,Although her 2 sisters were healthy,no other members of the family are known to be affected with a similar disorder.Developmental delay was noted,she began to sit at 24 months, to walk at 03 years and by the age of 4 she was able to speak a few words.

On physical examination, her height was 96, 5 cm (-2 SD), weight 15kg (Median), and head circumference 46 cm (-2 SD). She had marked dysmorphic facial features, made of blepharophimosis, dental hypoplasia, hypertélorism, rétrognatism, microcephaly,trigonocéphaly, microphthalmia, nasolabial furrow, badly hemmed ear, pointed palace,associated with psychomotor retardation and growth retardation of less than 2 DS , No heart murmur was noted.

Ophtalmological examination: squamous blepharitis, severe hypertelorism and epicanthus, a limbic dermolipoma in the left eye, and hypoplastic papillae with

tortous macula vessels having an appearance reminiscent of cherry red,chorioretenian atrophy.

Heart and abdominal ultrasonographyand a cranial CT scan were normal.

Karyotype and array-CGH did not show any pathogenic chromosomal imbalance.

Exome sequencing showedthe presence of the variant NM_005120.3(MED12):c.6352C>T(p.Gin2118Ter) in the heterozygous state and its absence in the parents, wich confirms the novo character of this variant, wich is compatible with the diagnosis of ohdo syndrome by heterozygous mutation of the MED 12.

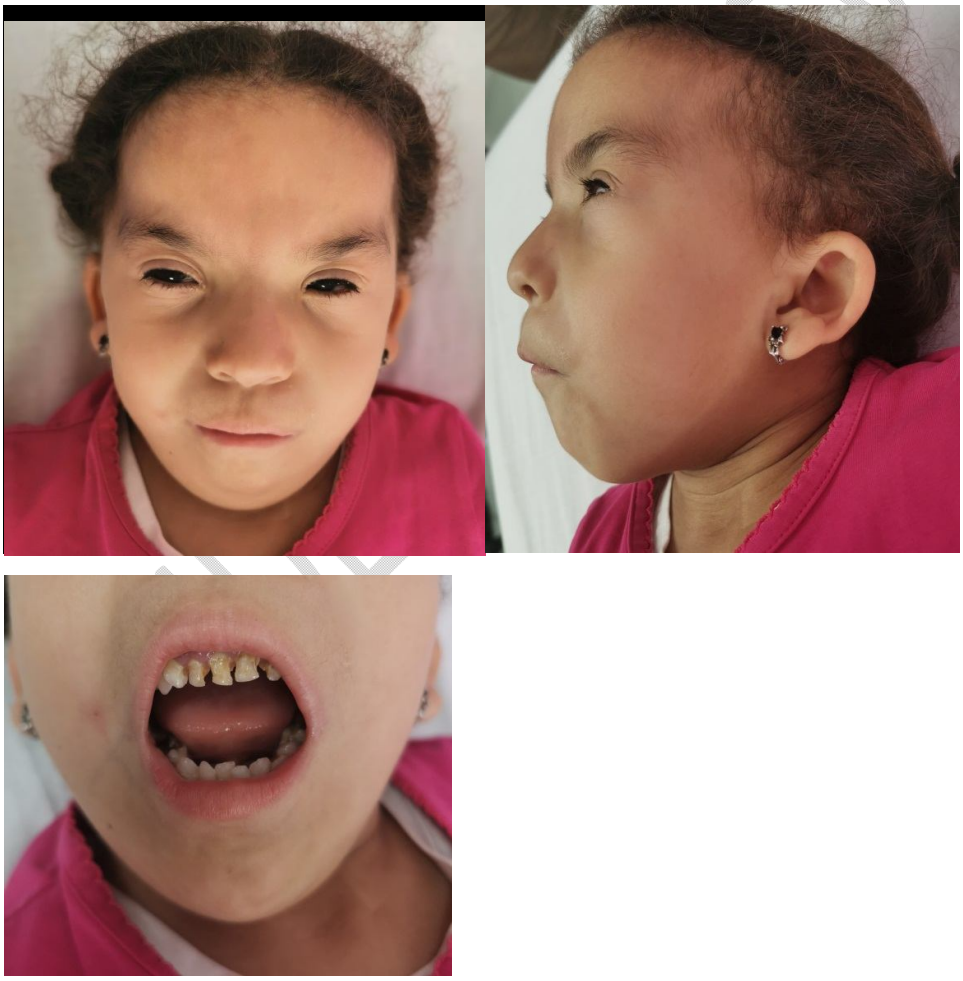

Image 1: Facial features of our patient include blepharophimosis, wide and flat nasal bridge, small and simple ears, and small teeth.

Discussion:

Previous reports by Ohdoet al, Say and Barber have documented the existence of a syndrome which includes dysmorphic facial features (most prominently blepharophimosis), mental retardation, and limb anomalies. **[2]**

Ohdosyndrome is extremely rare, characterized by intellectual disability (ID) and typical facial features, including blepharophimosis, ptosis, dental hypoplasia, hearing impairment and intellectual disability,male patients may show cryptorchidism and scrotal hypoplasia, to which his name is currently attached.

So far, less than 30 patients have been reported as Ohdo syndrome, including familial and sporadic cases,prevalence <1/1000 000.

The blepharophimosis-ID syndromes have been classified in five distinct subgroups. The first group can be distinguished from the others because it iscaused by deletions of the short arm of chromosome 3.The second group is designated as Ohdo type on the basis of the original report by Ohdo et al. **[3, 1]**These persons present with typical features of prognathism, short philtrum, and proteinuria, whereas hypotonia, abnormal growth, and limb defects are lacking. The Verloes type is a more severe condition with severe microcephaly, epilepsy, brain malformations, adducted thumbs, and abnormal genitals **[3].** The most clinically distinctive phenotype is the Say/Barber/Biesecker/Young/Simpson (SBBYS) type (MIM 603736), which is characterized by striking facial dysmorphisms that include a large to bulbous nasal tip; small and/or dysplastic, thick, simple, or overfolded pinnae; thick swollen cheeks; and retrognathia. In addition, hypotonia, hyperextensible joints, cryptorchidism, and a wide range of congenital malformations are present. **[3, 5]**This type was recently shown to be caused by mutations in lysine acetyltransferase 6B (KAT6B [MIM 605880]). [**6]**
Beseecher's case and that described by Say and Barber **[4]**offer little insight into the inheritance pattern of this disorder; the report of Ohdoet al **[1]**is puzzling in this

respect. They propose that the pedigree is compatible with multifactorial, autosomal recessive, and autosomal dominant modes of inheritance. It is reasonable to propose multifactorial or autosomal dominant inheritance (with variable penetrance), but it is unlikely that a rare autosomal recessive disorder would affect cousins in the absence of consanguinity or non-paternity. Mitochondrial or X linked inheritance is unlikely with transmission through the father in the report of Ohdo et al**[1]**. Although it is possible that a submicroscopic chromosomal abnormality could be present in the case of Say and Barber **[4]**the cases of Ohdoet al **[1]**would be incompatible with this aetiology. **[2]**

The family reported by Ohdo had an inheritance pattern that was suggestive of a cryptic rearrangement. **[3]**

Most reported cases are sporadic, except the original cases of ohdo who described two affected sisters and a first cousin, favoring autosomal recessive inheritance. Autosomal dominant, X-linked- and mithochondrial inheritance have also been suggested.

Mhanni et al (1998) reported vertical transmission of ohdo syndrome from mother to son, suggestive of autosomal dominant inheritance. The possibility of X–linked or mitochondrial inheritance cannot be ruled out by this case. Taken together with the previously reported cases, the authors suggested that autosomal dominant inheritance with incomplete penetrance is most likely. Genetic heterogeneity is also possible.

Moncla et al. [1995] first pointed to the overlap of Young–Simpson syndrome, Ohdo syndrome, and del (3) (pter) syndrome. Clayton-Smith et al. [1994] proposed to separate Ohdo syndrome (for the original family) and Ohdo-like syndrome, an entity that encompassed most of the patients described as Ohdo syndrome. Finally, Marques-de-faria et al. [2000] make the assumption that Ohdo syndrome and Young–Simpson syndrome may belong to the same clinical spectrum. **[3]**

White et al (2003) reported 2 cases of ohdosyndrome, one with mild and the other with severe features, illustrating the phenotypic variability of the condition. The authors noted that all cases with the severe phenotype have been sporadic. Subtelomeric FISH studies of all chromosome arms on their 2 cases showed no abnormality.

Conclusion :

Ohdo syndromeis a syndrome of multiple congenitalmalformations, very rare, its managements requires multidisciplinary collaboration and varies according to the degree of severity of the deficiency, the age of the child and the difficulties he has.

References:

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