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A Case Report

Oral-Facial-Digital Syndrome: A Case Report

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Abstract

Background: The oral-facial-digital (OFD) syndrome is a group of hereditary disorders, manifested by anomalies of the oral cavity, face and digits that may be associated with cerebral malformations and polycystic kidney disorder. The condition is associated with either X-linked or autosomal recessive inheritance. Herein, we report a case of OFD syndrome with various manifestations.

Case description: The case was a female baby with the features of the OFD syndrome. The family history was negative. The baby was the product of a non-consanguineous marriage. Diagnosis of OFD syndrome was confirmed by chromosomal microarray. The case had features of OFD type 1 in addition to central nervous system abnormalities. The chromosomal study of the parents was normal. Consultation with the related subspecialties were requested for management of the case.

Conclusion: OFD syndrome is a very rare conditions, which can be easily diagnosed. Cooperation of the related subspecialities is very important for better management of these cases.

Keywords: Anomalies; Oral-facial-digital syndrome; X-linked; neonates

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Introduction

The Oral-Facial-Digital Syndrome (OFDS) is a group of hereditary disorders, manifested by anomalies of the oral cavity, face and digits that may be associated with renal and cerebral anomalies. The syndrome is either X-linked or autosomal recessive. The X-linked gene of this syndrome is important in organogenesis and essential for fetal survival. Around 75% of cases are sporadic and almost lethal during the prenatal period in type 1 only with a prevalence estimates range from 1:50,000 to 1:250,000. The clinical manifestations of OFDS are wide. The lesions of the mouth include cleft palate and tongue, pseudo-clefting of the upper lip and dental anomalies. The lesions of the head include hypertelorism, frontal bossing, facial asymmetry, micrognathia and broadened nasal bridge. The digital abnormalities are brachydactyly, clinodactyly and syndactyly (1). The management of OFDS depends on the presence of abnormalities; for instance, surgery is the treatment of choice for cleft palate, lip and tongue nodules and syndactyly. Speech therapy and involvement in special education are recommended for treatment of mental retardation (2). In this report, we present a baby with various manifestations of OFDS.

Case presentation

Our case was a a 39–week-old female, delivered to a 28 years old Pakistani mother in the Women Wellness and Research Center (WWRC), Hamad Medical Corporation (HMC), Qatar. The mother was gravida 3 para 2. The two siblings (a boy and a girl) were normal. The mother had no history of medical problems. Serial ultrasounds had been performed from the 6th week of gestation. The 1st ultrasonographic abnormality was detected at 13th weeks of gestation in the form of cystic structure in fetal head, measuring 0.5 x 0.4 cm and 1.1 x 1.1 cm. The next ultrasound was done at the age of 23 weeks and revealed a suspected partial agenesis of the corpus callosum. At the age of 38th weeks, the ultrasound examination revealed the agenesis of the corpus callosum with large interhemispheric cysts and microcephaly in addition to marked paranasal edema. The baby was from a non-consanguineous marriage and was delivered by caesarean section with birthweight of 3.22 kg. She was delivered in good conditions with APGAR score of 9 and 10 at 1 and 5 minutes, respectively. Detailed examination revealed microcephaly with small anterior fontanelle, triangular forehead, paranasal swelling, low set ears, retrognathia, clinodactyly in the index fingers bilaterally, two cord vessels and cleft palate with the impression of OFD as the 1ry diagnosis. Apart from the previous abnormal features, other examinations including neurological features were normal. The case also had Glucose-6-Phosphate Dehydrogenase Deficiency. The baby was admitted to the neonatal intensive care unit (NICU) for further investigations, assessment and genetic workup. During the NICU admission, the girl was attended by an occupational therapist for oral feeding with orogastric tube and special nipple. Fluorescence in situ hybridization (FISH) was negative for chromosomes 13 and 21 abnormality. Chromosomal microarray analysis revealed a loss of ~382 kb within cytogenetic band Xp22.2. The deleted genomic segment contains OFD1 and TRAPPC2 genes. After confirmed diagnosis of OFDS, more workup was done to rule out associated abnormalities. For this purpose, transesophageal echocardiography was done and the result was normal. Genetic counseling was done and chromosomal analysis for the parents was normal, indicating a new mutation. Abdominal ultrasound was normal. Cranial ultrasound revealed the followings: multiple variable-sized interhemispheric cysts measuring 5.2 x 2.4 cm, 3.7 x 1.9 cm, 1.1 x 1.0 cm and, 1.6 x 1.2 cm (Figure 1A).

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There were wide separation of the lateral ventricles with straight parallel parasagittal orientation (Figure 1B). Moreover, frontal horns of lateral ventricles were separated from the midline and lateral convexity was noted (bat-wing appearance), while corpus callosum was absent (Figure 1C). Further evaluation by MRI scan showed absence of corpus callosum with large interhemispheric dorsal cyst, cortical dysplasia involving bilateral frontal lobes (Figure 1D), left frontal occipital small area of cortical/subcortical acute infarction with left occipital hemorrhages (Figure 1E) and suspected metopic craniosynostosis with trigonocephalic skull. Hip ultrasound was normal. There was no skeletal anomaly. After the optimization of child feed and training the family for orogastric tube feeding, the patient was discharged with follow up for further treatment.

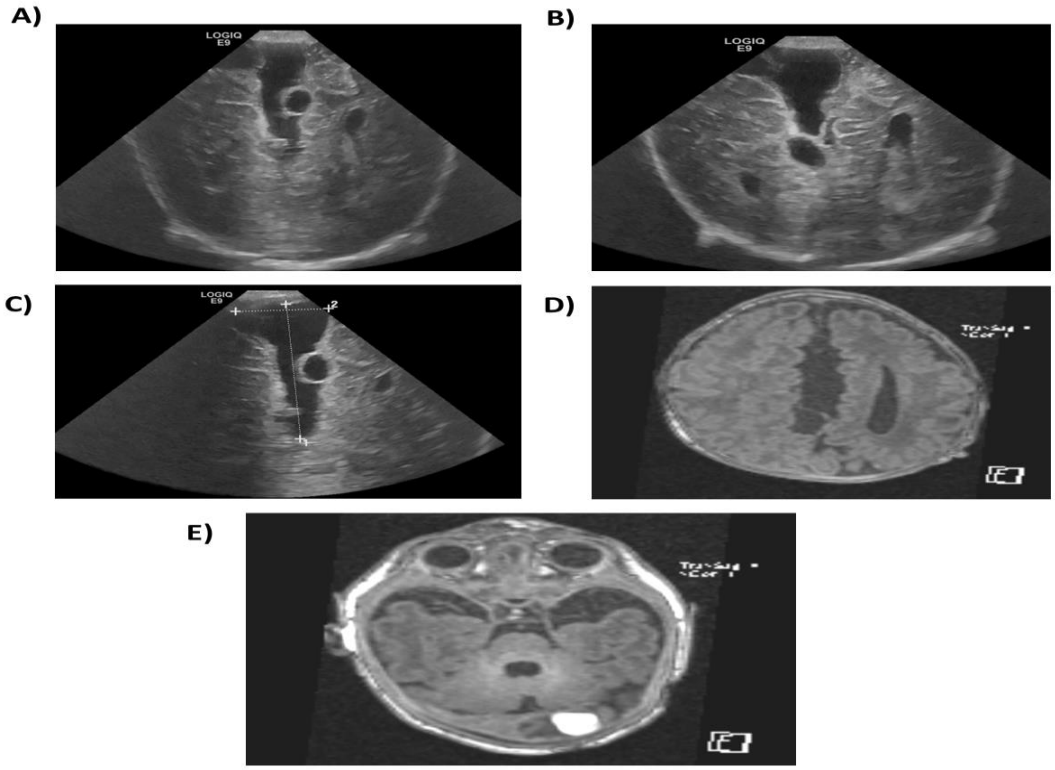

Figure 1. The ultrasound and MRI scan images of the case with Oral-Facial-Digital Syndrome. A) Presence of variable-sized inter-hemispheric cysts in ultrasonography. B) Wide separation of the lateral ventricles with straight parallel parasagittal orientation in ultrasonography. C) Detection of agenesis of corpus callosum in Ultrasonography. D) Absence of corpus callosum with large inter-hemispheric dorsal cyst and detection of cortical dysplasia involving bilateral frontal lobes in MRI scan. E) Left frontal occipital small area of cortical/subcortical acute infarction with left occipital hemorrhages in MRI scan

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DISCUSSION

OFDS is a group of disorders that affects the oral cavity, face and digits. Abnormalities of the oral cavity include a split tongue, a lobulated tongue, tongue nodules and hyperplastic frenula. Extra, missing or defective teeth may be also present in some cases. Cleft palate is a common feature of OFDS, while other facial features in the form of hypertelorism and wide nasal bridge may be also present. Abnormalities of the digits include syndactyly, polydactyly, clinodactyly and brachydactyly. Other features such as polycystic kidney disease, bone abnormalities, cerebral abnormalities, intellectual disability, vision loss and heart defects can also occur (1). Researchers have identified at least 13 potential forms of OFDS. However, the features overlap significantly, and some types are still not well-defined (2).

Variants of OFD:

Type I (Papillon-Léage-Psaume syndrome) is an X-linked dominant, lethal condition in males. Oral manifestations include hyperplastic frenula, lobulated tongue, cleft lip and cleft palate. Digital malformations are brachydactyly, clinodactyly and syndactyly. Abnormal features in the face include hypertelorism, frontal bossing, facial asymmetry, micrognathia and broadened nasal bridge. Agenesis of the corpus callosum, seizure and renal abnormalities may be also present (4). Type II (Mohr syndrome) is an autosomal recessive abnormality with oral manifestations in the form of midline cleft of the upper lip and a cleft tongue or palate. In addition to polydactyly, ocular hypertelorism, micrognathia and hydrocephalus as well as mental retardation can be present (5). Type III (Sugarman syndrome) is also anautosomal recessive condition, manifesting with oral anomalies including a lobulated tongue and a bifid uvula. Post-axial polydactyly of the hands and feet As well as significant mental retardation may also occur. Ceaseless "seesaw winking" of the eyes is suggested as distinguishing feature, but the small number of cases makes this hard to confirm (6). Type IV (Barrister-Burn syndrome) is autosomal recessive and characterized with a broad nasal root and tip, a hypoplastic mandible, many oral abnormalities and pre- and post-axial polydactyly. A distinctive clinical finding may be tibial dysplasia (7). Type V (Thurston syndrome) is autosomal recessive and manifests as midline cleft lip and post-axial polydactyly of the hand and feet (8). Type VI (Varadi syndrome) is also autosomal recessive and manifests as syndactyly and/or bifid toe, preaxial or mesoaxial polydactyly, lingual and sublingual hamartoma, hypothalamic hamartoma, cerebellar dysgenesis with molar tooth sign and optochiasmatic pilocytic astrocytoma in rare cases (9). Type VII (Whelan syndrome): X-linked, dominant.facial asymmetry, hydronephrosis. There is only one report of a mother and daughter with this case (10). Type VIII (Edwards syndrome) is X-linked recessive and not lethal prenatally in either sex. The manifestations include tongue lobulations, median cleft lip, pre- or post-axial polydactyly of the hands and feet, shortened tibiae and/or radii, forked metatarsals and developmental delay (11). Type IX (Gurrieri syndrome) is autosomal recessive manifesting as retinochoroidal coloboma, severe microcephaly, Dandy-Walker malformation, retrobulbar cysts and short stature (12). Type X (Figuera syndrome is autosomal recessive and characterized with fibular aplasia, limp shortening and pre-axial polydactyly (13). Type XI (Gabrielli syndrome) is autosomal recessive and manifest as postaxial polydactyly, ventriculomegaly, microcephaly, alar hypoplasia, duplicated vomer, cleft ethmoid and cleft vertebral bodies. (11). Type XII (Moran-Barroso syndrome) is autosomal recessive and characterized with myelomeningocele, stenosis of aqueduct of

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Sylvius and dysplasia of atrioventricular valves (14). Type XIII (Degner syndrome) is autosomal recessive distinguished by the presence of psychiatric symptoms, epilepsy and brain MRI findings of changes of the white matter (14).

As mentioned earlier, ODFS is either X-linked or autosomal recessive. The genes of type I and type VII are X-linked dominant and that of type VIII is X-linked recessive (3). The incidence of ODFS is 1 in 50,000 to 250,000 newborns. Type 1 is the predominant form, while other forms are very rare (2). The differential diagnosis includes different forms of OFDS and familial cystic renal disease. Meckel and Joubert syndromes should also be considered (15). Prenatal diagnosis and preimplantation genetic diagnosis are recommended for high-risk pregnancies and require identification of the disease-causing mutation in the family (16). Further evaluations following the initial diagnosis include the followings: 1. detailed examination of the face, hand and different body systems; 2. genetic consultation and genetic analysis of the parents; 3. audiologic evaluation; 4. developmental and behavior evluation. Treatments include cosmetic or reconstructive surgery for oral and hand abnormalities, special treatment and training for learning disabilities and other cognitive impairments, and speech therapy (7). The type 1 is lethal in males during the first or second trimester of pregnancy, while the prognosis in affected females is variable and depends on the associated malformations, treatment and the course of the disease (11).

CONCLUSION

OFDS is a very rare condition, which can be easily diagnosed. Cooperation of the related subspecialities is very important for better management of these cases.

DECLARATIONS

Funding

Not applicable.

Ethics approvals and consent to participate

Written informed consent was obtained from parents of the patient. All clinical investigations were conducted according to the principals of the Helsinki Declaration.

Conflict of interest

The author declares that there is no conflict of interest regarding publication of this article.

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