Oral-Facial-Digital Syndrome Type I

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Oral-facial-digital syndrome (OFD) is a collective term, which includes thirteen distinctive, genetic disorders. These syndromes are a form of ectodermal dysplasia, which affects the development of the skin, nails, hair, eyes, face, fingers, toes and the oral cavity. In addition, cardiovascular, renal and central nervous malformations are commonly associated with these conditions. The affected individuals may present with speech and learning disabilities, impaired mental ability, and seizures which are directly related to the severity of central nervous system involvement.

The inheritance pattern and phenotypic expression mainly distinguish the rare 13-subtypes. OFD type I has the highest incidence compared with the other subtypes, and equally distributed among different races and ethnicities. We present a thirteen-year-old female who presented with OFD syndrome, type I. OFD syndrome is a form of ectodermal dysplasia affecting the development of the skin, nails, hair, eyes, face, fingers, toes and the oral cavity.

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Oral-facial-digital syndrome (OFD) is a form of ectodermal dysplasia affecting the development of the skin, nails, hair, eyes, face, fingers, toes and the oral cavity. The central nervous system, cardiovascular, renal, and cutaneous abnormalities have been linked to this disorder[1,2]. Also, impaired mental ability, speech, learning disabilities, and seizures are directly related to the severity of central nervous system involvement[2]. Some cases were reported with malformation of the stapes which led to conduction deafness[3].

Thirteen different subtypes of OFD were reported in the literature[4,5]. OFD type I has the highest incidence compared to other subtypes; it affects all races and ethnicities in equal numbers[1,4,6]. Approximately 75% of cases of OFD I are sporadic and approximately 25% are hereditary[7]. OFD I is transmitted as an X-linked dominant condition, with prenatal mortality in homozygous males[8]. Few male cases have been reported in the literature with the XXY genome[4,7,8].

The phonetic expressions vary in severity, as the naming indicates it is characterized by affecting the face, oral cavity, and the digits. The face of affected individuals may present with asymmetry, frontal bossing, hypertelorism, a broad and flat nasal bridge and different size nostrils. In addition, hypoplasia of the malar bones, cleft or pseudo-cleft lip, and vanishing milia on the face and ears. The hair is most commonly dry and brittle with zones of alopecia[4,5].

Abnormalities of the oral cavity occur in many types of the oral-facial-digital syndrome, which include cleft or highly arched palates, cleft or an unusual lobed shape tongue, growth of non-cancerous tumors on the tongue. Other characteristic features are the hyperplastic frenula that abnormally attach the lip to the gums; in addition to alveolar ridge notching and thickening. Furthermore, teeth present as enamel dysplasia, supernumerary teeth, missing teeth, impaction whether with or without retained deciduous teeth[4,5,14].

Gnathical variations which may present in these patients are an anterior open bite and maxillary or mandibular micrognathia[4]. Digital malformations affect hands more frequently than feet, and it includes syndactyly (fusion of digits), brachydactyly (shortened digits), clinodactyly (curved digits), and polydactyly (extra digits)[9].

The aim of this presentation is to report a case of oral-facial-digital syndrome, type I.

THE CASE

A thirteen-year-old female presented with oral-facial-digital syndrome for assessment of malocclusion. The patient was delivered by Cesarean section. At presentation, the patient had an average motor and sensory development. The parents were healthy and unrelated.

The patient's mental and motor development was within the normal range and did not illustrate any evidence of conduction deafness. Upon extra-oral examination, the patient presented with brachydactyly (shortened fingers) of the index, middle and ring fingers of both hands, and clinodactyly (curved fingers) of the bilateral fifth fingers, see figure 1 (A). Head and neck examination revealed mild facial asymmetry, frontal bossing, broad nasal base, uneven nostrils, hypertelorism, pseudo-clefting of the lips, vanishing milia on the face, dry skin and coarse hair, see figure 1 (B). Mildly low setting ears were seen from the lateral view, see figure 1(C-D).

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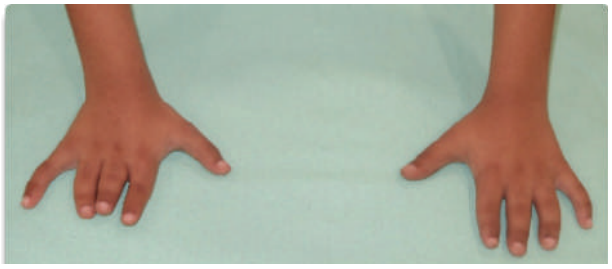

Figure 1 (A): Upper Limbs Extremity

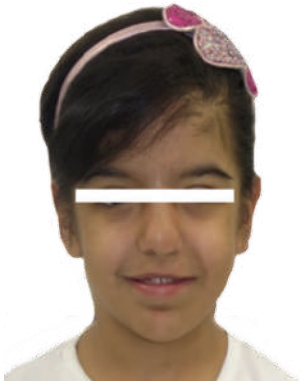

Figure 1 (B): Frontal View

Figure 1 (C): Lateral View

Figure 1 (D): 45° View

Figure 1 (A-D): (A) Extra-Oral Images (B-D) Facial Anomalies Associated with The Syndrome

Intraoral examination revealed multiple hyperplastic buccal frenula, which are corresponding to the alveolar notching between the laterals and canines, see figure 2 (D-E). The lower lingual fraenum was hyperplastic but offset to the right side, see figure 2 (E). The tongue has a lobulated margin and a hamartoma on the right lateral side, see figure 2 (G-H). Clinical dental examination revealed multiple carious teeth, retained primary teeth, supplemental maxillary right lateral incisor, and multiple missing teeth, see table 1. In addition, generalized enamel hypoplasia and an anterior open bite of 5mm, which was measured from upper left deciduous canine and upper left permanent canine.

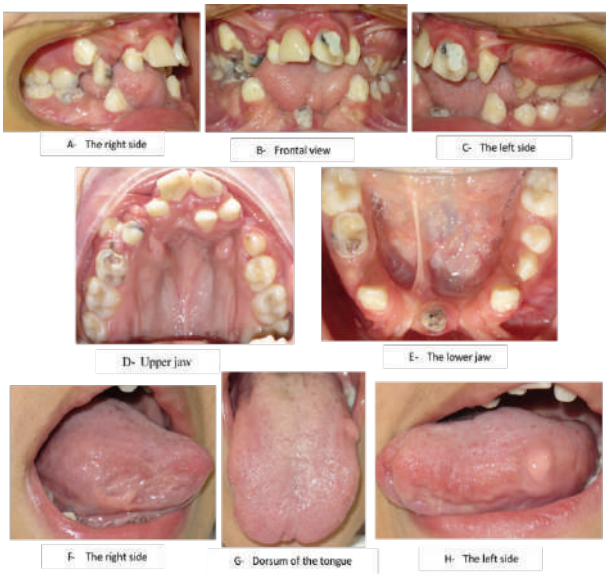

Figure 2: Intraoral Images, (A\B\C): Multiple Carious Teeth, Retained Deciduous Teeth, Missing Teeth (C\D) Supplementary Maxillary Right Lateral Incisor (B) An Anterior Open Bite of 5 Mm (From ULD-LL3) (D\E), Bilateral Alveolar, Notching Between Upper Laterals and Canines and Corresponding Hyperplastic Multiple Buccal Frenula and an Offset Lingual Fraenum (G) Lobulated Tongue Margin and (H) A Hamartoma on the Left Lateral Side

Table 1: Dental Findings According to the Clinical and Radio-Graphical Assessment

Root remnant	URD
Caries	URE,URC, ULC , ULE ,LRE , LR1,
Defective restoration	UL1
Hypodontia	UR8, UR5, LL2, LL1
Supernumerary tooth	Supplemental Maxillary Left Lateral Incisor
Impacted	LR2

Figure 3 is a dental-pantograph (DPT) scan from a cone beam computed tomography (CBCT), which revealed the impaction of the upper permanent canines and lower permanent right lateral incisor and confirmed that the upper right permanent third molar, second premolar and lower left lateral and central incisors are developmentally missing. A small (9mm) well corticated, oval-shaped radiolucency apical to the lower left third molar, which might represent the follicle of an undeveloped distomolar.

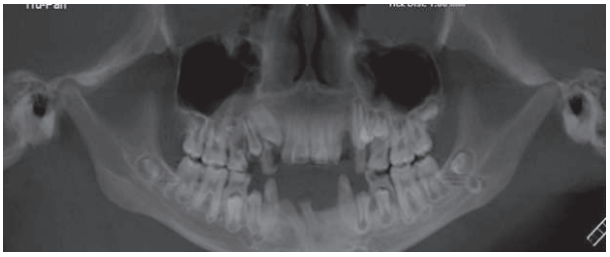

Figure 3: A DPT Scan from a CBCT

A clinical diagnosis of OFD-I was contemplated, based on the characteristic dysmorphic features of the mouth, face, and limbs. Definitive diagnosis for this subtype can be further confirmed by karyotyping for the mutated OFD-I gene or if the patient developed polycystic kidney disease in adulthood[4,10-12].

The dental treatment plan for this patient was as follows: prevention/control phase, which includes oral hygiene instructions, nutritional counseling, topical fluoride therapy, manual scaling and dental prophylaxis, temporization of all active caries and extraction of hopeless teeth; definitive phase includes permanent fillings and orthodontic treatment. The final phase is the maintenance.

DISCUSSION

Studies reported thirteen different subtypes of OFD[4,5]. The different types are classified by their patterns of signs and symptoms. It can be distinguished from each other through clinical examination radiographs, and observation of the phenotypic gene expression and patterns of inheritance[4].

OFD, type I, is also known as Papillon-League-Psuame syndrome which is named after two French dental practitioners who discovered it in 1954. In 1964, the name oral-facial-digital (OFD) syndrome was suggested as it presents a clear clinical description of the condition[3,12,13]. OFD-I has the highest incidence compared with the other subtypes, the incidence of this condition ranges from 1/50,000-250,000 live births[6,13]. Moreover, it is characteristically associated with malformation of the brain and polycystic kidney disease[8-12].

The CXORF5 gene was renamed OFD-I and has been associated with the oral-facial-digital syndrome. OFD-I gene provides instructions for making a protein whose function is not entirely understood. However, it appears to play an essential role in the early development of the brain, face, limbs, and kidneys. A mutation in the OFD-I gene prevents cells from making enough functional OFD-I protein, which disrupts the normal development of these structures and results in oral-facial-digital syndrome type I[4,10-12]. This gene is found on the short arm of the X chromosome; it is inherited as an X-linked dominant pattern. In females, a mutation in one of the two copies of the gene is sufficient to cause the disorder. In males, mutations result in a total loss of the OFD-I protein, and a lack of this protein is usually lethal very early in the development of homozygous males[9,11]. However, males have been reported in the literature with this disorder with the XXY Klinefelter's syndrome[4,7,8].

Many features of OFD-I overlap with the clinical manifestations of the remaining subtypes making the diagnosis difficult[13-15]. Patients with this syndrome show a wide range of presentation due to the different degrees of somatic mosaicism[4].

Oral cavity malformations are present in almost all patients (96.8%)[16]. Dental anomalies, in particular, are a well-documented feature of the OFD syndrome, and they may occur as an isolated phenomenon. Tongue anomalies are widespread, affecting up to 84.1% of patients; hamartomatous masses on the ventral surface of the tongue are seen in 70% of the cases[17]. On the other hand, digital abnormalities are considered less common. In 1962, it was estimated that 42% of affected subjects had no digital involvement. A similar proportion are mentally retarded. Central nervous system anomalies are present in 48.4%, and intellectual disability, learning disabilities or cognitive impairment in 28.9% of patients[15].

A definitive diagnosis for this subtype can be confirmed by karyotyping for the mutated OFD-I gene, or by the development of polycystic kidney disease in adulthood[4,10-12]. Management of patients with OFD syndrome depends upon the particular features present in the individual case. Cleft lip/palate and limb incongruities can be corrected through plastic and reconstructive surgery; early surgical intervention is indicated to relieve respiratory, feeding, or speech problems. On the other hand, surgical reconstructive and corrective procedures associated with multiple buccal frenula and digital deformities are considered to be less urgent and can be carried out selectively[15]. Our patient had no history of either respiratory or feeding abnormality. Therefore, no surgical correction was performed.

Intervention with speech-language pathologists is indicated to assess any speech and hearing problems. Neurological involvement would require proper neurological testing, counseling for diminished mental capacity and proper management of seizure if diagnosed. Psychological counseling is essential especially for pre-school children with facial disfigurements[13-15].

Patients should be screened for polycystic kidney disease, as, the incidence in patients older than 18 years rises to 63%. Kidney cysts associated with OFDS-I are usually bilateral; involving both the cortex and medulla[14].

CONCLUSION

OFD-I shows a wide variety in the phenotypic expression of abnormalities. Clinical diagnosis is established mainly from the oral, facial, digital abnormalities and patterns of inheritance. However, a definitive diagnosis is established either by genetic testing or diagnosing an associated polycystic kidney disease later in life. The management is best provided by a multidisciplinary team including medical, surgeon, pediatrician, pedodontic, orthodontic, audiologist, speech-language pathologist and psychologist.

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