Case Report

Oro-Facial-Digital Syndrome Type II

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Abstract

Oro-facial-digital syndrome type II (OFD-II) is characterized by frenulated tongue, midline cleft lip, high arched or cleft palate, micrognathia, syndactyly and polydactyly, bilateral reduplicated hallux, conductive hearing loss, choroidal coloboma and normal intelligence. There are nine forms of oro-facial-digital syndromes with different modes of inheritance. A young female with features of oro-facio-digital syndrome type-II is being reported.

Introduction

Oro-facial-digital syndromes are a heterogeneous group of developmental disorders in which at least nine different forms have been described. Oro-facial-digital syndrome type-II (OFD-II) is transmitted as an autosomal recessive condition and is characterized by malformation of face, oral cavity and digits.[1] Facial and oral features include cleft upper lip and cleft palate, frenulated tongue, Micrognathia. Digital features include syndactyly, pre- and post-axial polydactyly and duplication of the first toe. Other systemic features include conductive deafness and choroidal coloboma. Diagnosis is mainly clinical. We report a young female with Oro-Facial- Digital Syndrome type-II (OFD II)

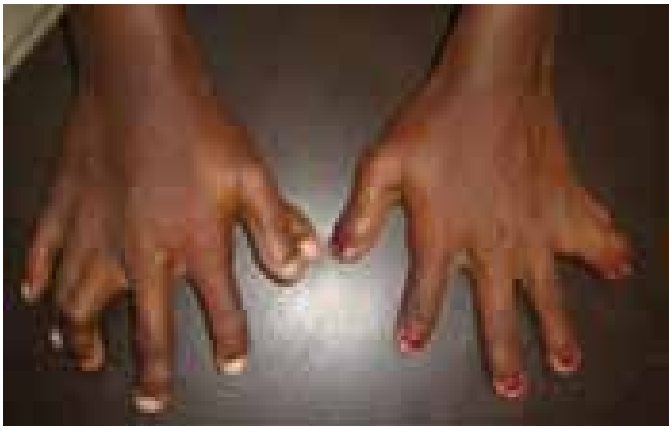

Fig. 1 : Bilateral manual hexadactyly, duplicated thumb on Right hand

Fig. 2 : Bilateral polysyndactyly of halluces

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Case History

29 year old female, presented with Swelling of both lower limbs, Breathlessness since 15 days. She is the third child of parents with first degree consanguineous marriage, was born at full term with no family history of genetic disease and mental retardation. She has three siblings and they are normal. During infancy she had difficulty in feeding due to cleft lip, cleft palateand high arched palate. Suckling of breast was futile. She was put on orogastric feeding via infant feeding tube with expressed breast milk for 2 months. Later on she was able to feed and swallow normally. No history of milestone development delay. There was no history of radiation exposure or any significant drug intake or any major illness during pregnancy period of her mother. Vital signs revealed pulse 90/min, regular, BP: 120/80mmHg Rt arm supine position. Clinical examination revealed mild pallor, pitting edema both lower limbs, bilateral manual hexadactyly, duplicated thumb on Right hand and bilateral polysyndactyly of halluces, (Figures 1 and 2), cleft of the upper lip, Micrognathia, Mal-aligned teeth, High-arched palate, Cleft-palate (Figure 3) Frenulated tongue (Figure 4). Cardiac, Respiratory, Abdominal, Neurological examination were unremarkable and intelligence was normal. The female external genitalia and secondary sexual characteristics were

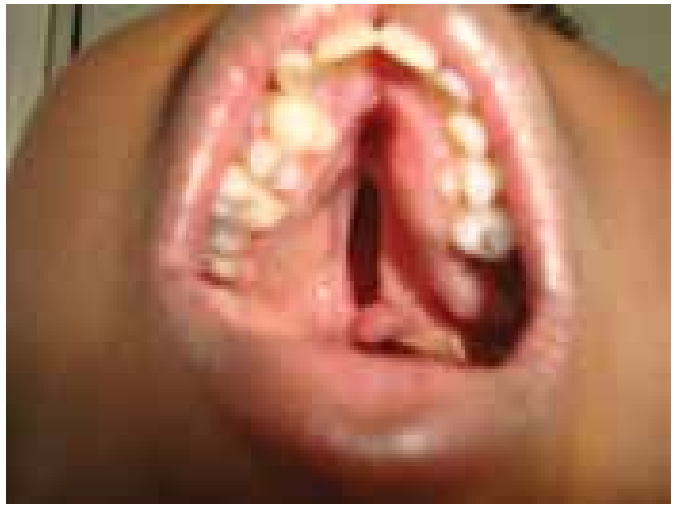

Fig. 3 : High-arched palate, Cleft-palate

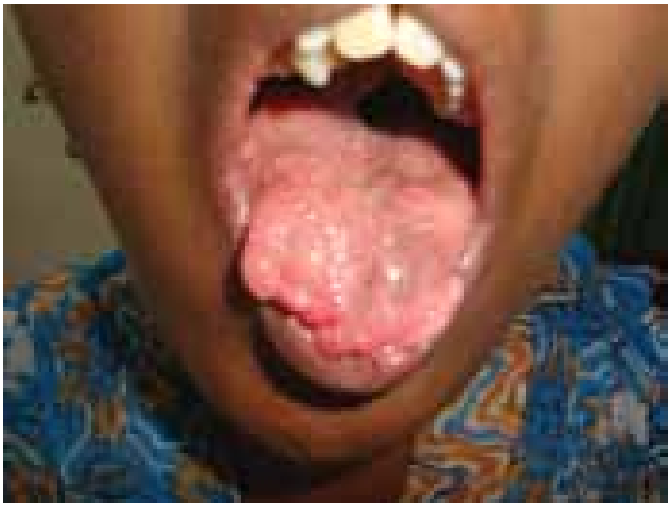

Fig. 4 : Frenulated tongue

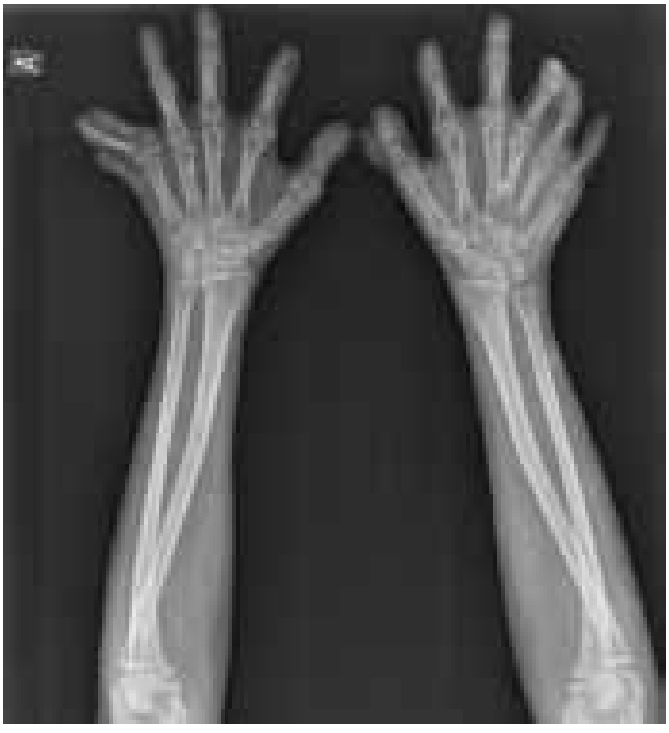

Fig. 5 : X-ray both hands with forearms AP view revealed 6 metacarpals in Right hand showing fusion proximally of third and fourth metacarpals. Left little finger shows accessory phalanges

normal. Fundus examination showed choroidal colobomas both eyes. Measurements : Height – 150 cm, Head circumference – 50 cm, Right upper limb - 63 cm, Left upper limb - 62 cm, Right lower limb - 85 cm ,Left lower limb - 86 cm, Arm span – 136 cm, Abdominal circumference – 66 cm ,Chest circumference- 71 cm.

On Investigations, Hb- 7.0 gm%, TLC - 7900 cells/mm^3, DLC - P_{57} L_{39} E_3 M_1, Platelets - 2, 25,000.Peripheral smear showed Microcytic hypochromic. LFT, RFT and S. Proteins were normal. Urine examination was normal. ECG and 2D echo were normal.

X-ray both hands with forearms AP view revealed 6 metacarpals in Right hand showing fusion proximally of third and fourth metacarpals. Left little finger shows accessory phalanges (Figure 5). X-ray both feet AP view revealed 7 metatarsals on Right side and 6 metatarsals on Left side. Large great toe on the Right is formed by two metatarsals with proximal phalanges articulating with second metatarsal and one with first metatarsal. Big great toe on the left side is formed by 2 metatarsals with an accessory proximal phalanx in between them. Two distal phalanges on the medial side are fused together (Figure 6). Normal thoracic cage and spine. Abdominal ultrasonography was normal. MRI Brain was normal. Audiometry showed bilateral mild conductive hearing loss. Patient was put on Iron supplements and symptomatically improved.

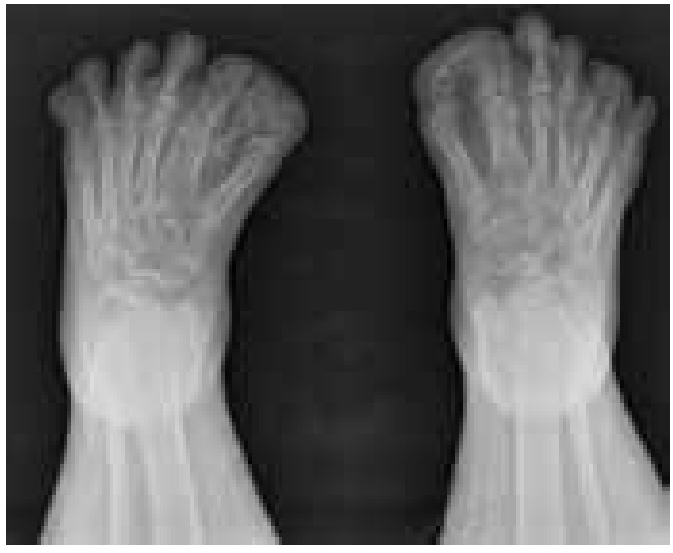

Fig. 6 : X-ray both feet AP views revealed 7 metatarsals on Right side and 6 metatarsals on Left side. Large great toe on the Right is formed by two metatarsals with proximal phalanges articulating with second metatarsal and one with first metatarsal. Big great toe on the left side is formed by 2 metatarsals with an accessory proximal phalanx in between them. Two distal phalanges on the medial side are fused together.

Discussion

Oro-facial-digital syndromes (OFDS) are a heterogeneous group of rare malformative diseases, characterized by abnormalities of the oral cavity, maxillo-facial region and digits. Such phenotypical pattern was first described by Mohr in 1941[1] and later defined as oro-digital-facial dysostoses by Papillon-Léage and Psaume in 1954[2] and finally named OFDS in 1967 by Rimoin and Engerton. There are at least 9 different forms of OFDS on the basis of inheritance transmission pattern and phenotypical spectrum of which the first two types are of common occurrence as compared with other varieties.[3,4] OFDS II is a rare autosomal recessive disease whose diagnosis is based only on clinical evidence. Frequency is rare 1 in 300,000 live births. The molecular genetic basis is still unknown.[5]

Because of the variable clinical expression, even intrafamilial, the attribution of the correct diagnosis among the several forms of OFDS is often difficult.[6] In addition, the molecular genesis is still unknown for all OFDS except for the OFD I which is related to the CXORF 5 gene (Xp22.2-22.3) coding for OFD1 protein.[7] Therefore, in order to achieve the correct diagnosis and offer adequate genetic counseling, it is necessary to search carefully for any possible abnormality associated with the oro-facial-digital spectrum of defects. In the present patient, the presence of conductive deafness, choroidal coloboma and the characteristic facial, oral and limb abnormalities allowed us to recognize the diagnosis of OFD II considering the differential diagnosis with OFDS I.[8] Patients' with OFD II have normal intelligence and

plastic surgery is indicated for cleft lip or palate, frenulated tongue and partial reduplication of the hallux. Early accurate diagnosis is important from a genetic counseling point of view, since it implies a one in four risk of recurrence in siblings.

We suggest that every newborn or infant with structural abnormalities of face, oral cavity and digits should be evaluated for oro-facial digital syndrome spectrum for future outcome and genetic counseling.

Characteristic features of different types of OFD are as follows:

OFD1: X-linked dominant, associated with hamartomas of the tongue, cleft palate, cerebellar agenesis with or without Dandy-Walker malformation, polycystic kidney disease.

OFD2: Autosomal recessive, primarily distinguished by polydactyly Cleft lip, Cleft palate, High arched palate, Micrognathia, Frenulated tongue, choroidal coloboma conductive hearing loss. Affected individuals do not have polycystic kidney disease.

OFD3: Autosomal recessive characterized by seesaw winking, polydactyly, myoclonic jerks and low-set ears.

OFD4: Autosomal recessive has tibial involvement, polydactyly, pectus excavatum and short stature.

OFD5: Autosomal recessive includes polydactyly and median cleft lip only.

OFD6: Autosomal recessive distinguished by polydactyly and cerebellar malformations.

OFD7: Autosomal dominant includes Excess mouth frenula, Cleft lip, Tongue split in two, polydactyly, somatic and psychomotor retardation, cleft lip/palate, Adult polycystic kidney disease.

OFD8: X-linked recessive includes polydactyly, tibial and radial defects.

OFD9: Autosomal recessive includes retinal abnormalities and non-median cleft lip.

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