

Case Reports

Otopalatodigital syndrome type 1: a rare skeletal disorder

Vasikarla Madhavi¹, Deepak Kumar Sharma¹, *Srinivas Murki¹, Tejo Pratap¹

Sri Lanka Journal of Child Health, 2016; 45(1): 44-45

DOI: <http://dx.doi.org/10.4038/slch.v45i1.8085>

(Key Words: Otopalatodigital syndrome type 1, cranio-oro-digital syndrome, facio-palato-osseous syndrome)

Introduction

Otopalatodigital syndrome type 1 (OPD1) is a disorder of skeletal system initially described by Taybi in 1962¹. OPD 1 is one of the otopalatodigital spectrum disorders². There are specific qualitative and quantitative features that make each syndrome unique³. In this case report, classical clinical features of OPD 1 syndrome in an index child helped in the prenatal diagnosis in a subsequent pregnancy.

Case report

A non-consanguineous couple was referred to our genetic clinic during the 3rd pregnancy as their previous child had dysmorphic features and they were worried about recurrence of similar malformations in the present pregnancy. Both parents were physically normal and the couple had only one live issue. On examination, the 18 month old boy had down slanting palpebral fissures, ocular hypertelorism and a broad and depressed nasal bridge (Figure 1). He also had cleft palate with small trunk, pectus excavatum, large sandal gap and short hallux. Audiometry showed bilateral sensorineural

hearing loss. Based on these clinical features, diagnosis of OPD Type 1 was considered. Parents were counselled about the inheritance pattern and Filamin A alpha (FLNA) mutation association and the importance of molecular diagnosis in the index child. However, they could not afford it. They were also counselled to have regular antenatal scans for early diagnosis of fetal malformations. Scan at 22 weeks revealed fetus with dysmorphic facies with hypertelorism, fetal ascites, claw hand deformity, curved long bones and ventriculomegaly. With these features, recurrence of otopalatodigital syndrome was suspected. Parents were told about the possible recurrence of similar problems and they decided to terminate the pregnancy. Autopsy of the fetus was done and the findings confirmed the prenatal diagnosis. Fetus had hypertelorism, depressed nasal bridge, and low set ears similar to sibling and bent long bones. The couple are now being regularly followed up in our genetic clinic.

Discussion

Otopalatodigital spectrum disorders have skeletal dysplasia as their primary characteristic and comprise five subtypes:^{4,5}

1. Otopalatodigital syndrome type 1 (OPD) type 1
2. Otopalatodigital syndrome type 2 (OPD) type 2
3. Frontometaphyseal dysplasia (FMD)
4. Melnick-Needles syndrome (MNS).
5. Terminal osseous dysplasia with pigmentary skin defects (TODPD).

OPD type 1, also known as cranio-oro-digital syndrome or facio-palato-osseous syndrome or FPO syndrome has an incidence of 1 in 100,000 population⁶. It has X linked dominant inheritance with complete expression in male but females are also noted to be affected with milder manifestation as females have one normal gene on the other X chromosome⁶. Type 1 is the mildest type of presentation in comparison with other syndromes of the family⁶. The affected infant has characteristic facial dysmorphism including wide-set and downward-slanting eyes, prominent brow ridges, small, flat nose and cleft palate. Skeletal abnormalities includes chest deformities like pectus excavatum, anomalies of the digits (square shaped finger tips, short broad distal phalanx of the thumb,



Figure 1: showing down slanting palpebral fissures, ocular hypertelorism, and depressed nasal bridge

*Permission given by parents to publish photograph

¹Department of Neonatology, DNB Neonatology, Fernandez Hospital, Hyderabad, India

*Correspondence: srinivasmurki2001@gmail.com

(Received on 21 August 2014; Accepted after revision on 19 September 2014)

The authors declare that there are no conflicts of interest

Personal funding was used for this project.

Open Access Article published under the Creative

Commons Attribution CC-BY  License.

over lengthening of the second toe and foreshortening of the great toe, syndactyly, short finger nails and dislocation of forearm bones)⁶. These patients also have conductive deafness with mild mental retardation and short stature^{2,3}. Diagnosis is by clinical examination for characteristic facial and skeletal abnormalities. Patient should be evaluated with complete skeletal examination for assessing the skeletal anomalies. Accurate risk assessment in families is dependent on assigning the correct diagnosis, which is best defined from the male phenotype. The disease has variable expressivity in female carriers which makes prediction of the severity of the disease in male offspring very difficult and unreliable⁷.

All typical cases of OPD1 are associated with mutations in the gene for the filamin protein (FLNA) which is located on Xq28 locus⁸. If a parent is homozygous for mutation of FLNA gene then the chance of transmitting the mutation in each pregnancy is 50%. When the mother has an FLNA mutation, males who inherit the mutation will be affected. Females who inherit the mutation have variable phenotypic presentations. Males with OPD1 transmit the disease-causing mutation to all of their daughters and none of their sons. Germ line mosaicism has been documented for OPD1 and therefore the risk of sib recurrence when the mother has tested negative for the causative FLNA mutation is higher than the background new mutation rate⁹. In the presence of a known FLNA mutation, prenatal diagnosis via chorionic villous sampling or amniocentesis is possible. Ultrasound scanning helps in detection of limb abnormalities, skeletal anomalies or dysmorphic facies which are associated with these syndromes³.

References

1. Taybi, H. Generalized skeletal dysplasia with multiple anomalies: a note on Pyle's disease. *Am J Roentgenol Radium Ther Nucl Med*. 1962; **88**: 450-7. PMID: 13919903
2. Dudding BA, Gorlin RJ, Langer LO. The oto-palato-digital syndrome: a new symptom-complex consisting of deafness, dwarfism, cleft palate, characteristic facies, and a generalized bone dysplasia. *American Journal of Diseases of Children* 1967; **113**: 214-21. <http://dx.doi.org/10.1001/archpedi.1967.02090170078006> PMID: 6019437
3. Langer LO Jr. The roentgenographic features of the oto-palato-digital (OPD) syndrome. *Am J Roentgenol Radium Ther Nucl Med*. 1967; **100**: 63-70. <http://dx.doi.org/10.2214/ajr.100.1.63>
4. Verloes A, Lesenfants S, Barr M et al. Fronto-otopalatodigital osteodysplasia: clinical evidence for a single entity encompassing Melnick-Needles syndrome, otopalatodigital syndrome types 1 and 2, and frontometaphyseal dysplasia. *American Journal of Medical Genetics* 2000; **90**: 407-22. [http://dx.doi.org/10.1002/\(SICI\)10968628\(20000228\)90:5<407::AIDAJMG11>3.0.CO;2-D](http://dx.doi.org/10.1002/(SICI)10968628(20000228)90:5<407::AIDAJMG11>3.0.CO;2-D)
5. Robertson SP. Otopalatodigital syndrome spectrum disorders: OPD types 1 and 2, frontometaphyseal dysplasia and Melnick-Needles syndrome. *European Journal of Human Genetics* 2006; **15**: 3-9. <http://dx.doi.org/10.1038/sj.ejhg.5201654> PMID: 16926860
6. Otopalatodigital syndrome type 1. Available from: <http://ghr.nlm.nih.gov/condition/otopalatodigital-syndrome-type-1>
7. Gorlin RJ, Poznanski AK, Hendon I: The oto-palato-digital (OPD) syndrome in females. *Oral Surg Oral Med Oral Pathol* 1973; **35**: 218-24. [http://dx.doi.org/10.1016/00304220\(73\)90288-0](http://dx.doi.org/10.1016/00304220(73)90288-0)
8. Parrini E, Mei D, Wright M et al. Mosaic mutations of the FLN1 gene cause a mild phenotype in patients with periventricular heterotopia. *Neurogenetics* 2004; **5**: 191-6. <http://dx.doi.org/10.1007/s10048-004-0187-y> PMID: 15459826
9. Robertson SP, Thompson S, Morgan T et al. Postzygotic mutation and germline mosaicism in otopalatodigital syndrome spectrum disorders. *European Journal of Human Genetics* 2006; **14**: 549-54. <http://dx.doi.org/10.1038/sj.ejhg.5201586> PMID: 16538226