Syndromic X Linked Mental Retardation

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Introduction :

Mental retardation is defined as incomplete or insufficient general development of mental capacities. Formal definitions of mental retardation that are currently recognized emphasize a descriptive diagnosis of persons with significant disability because of subaverage intellectual functioning and concurrent deficits or impairments in present adaptive functioning [i.e., how effective persons are in meeting the standards expected for their age by their cultural group] (1 , 2).

In addition, the manifestation of brain dysfunction must originate during the developmental period of life(1 , 2 , 3), this is descriptive definition , the quantitative definition is the IQ with the mean IQ for normal persons is 100 and anyone have IQ less than two standard deviation below the mean (IQ 70 or less) considered as mentally retarded (The

standard deviation (SD) of a test refers to the distribution of scores around the mean) , with the IQ we can also assess the severity of mental retardation as such : 70-55 mild , 55-40 moderate , 40-25 sever and less than 25 as profound mental retardation .

The prevalence of mental retardation is 6 to 20 per 1,000 (5,6,7,8) although we think that the prevalence is more in the developing country but we have no study yet assessing the true prevalence in Libya , in Saudia Arabia it is 8.9 / 1000 (9) in Pakistan it is 84.3 in 1998, in Bangladesh it is 20.3 in 1993(WHO records and 9).

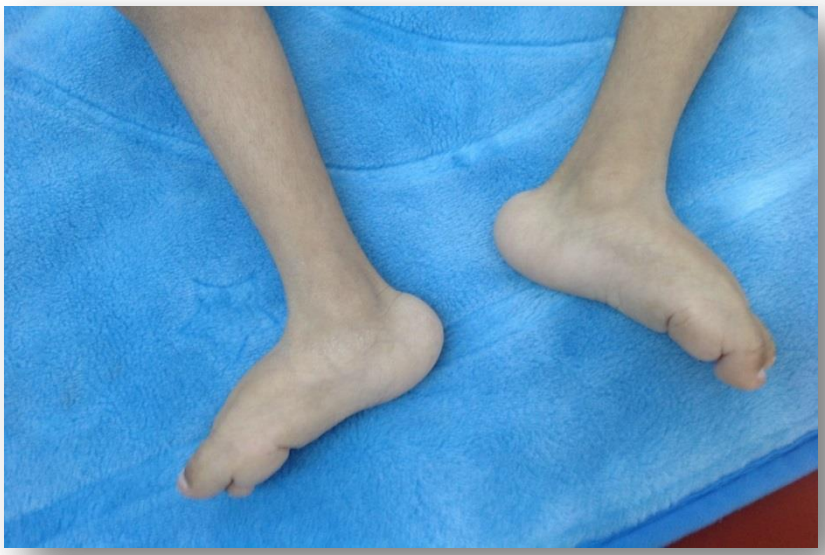
More than 1,000 defined syndromes involve multiple congenital abnormalities (4)

Case report :

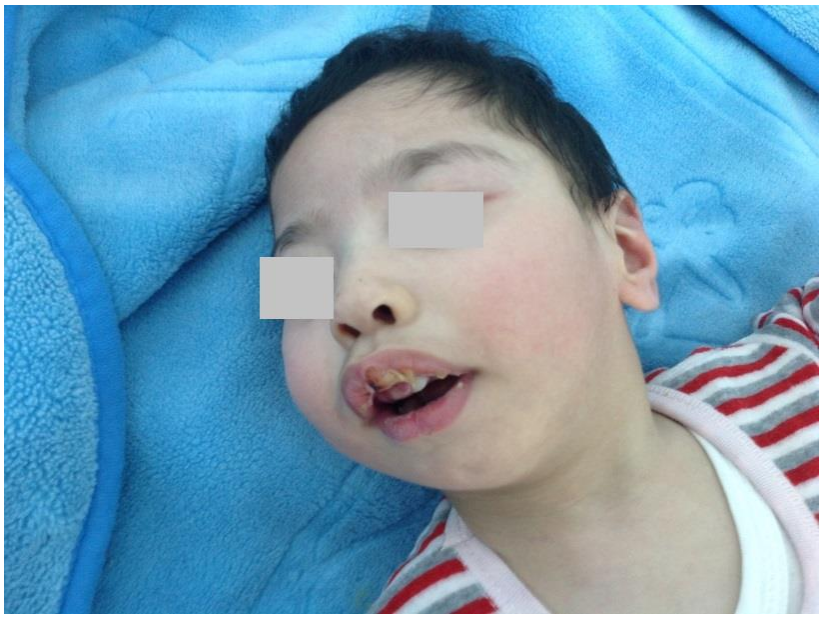
Yousef is 3 years old child delivered normally without any perinatal events to young couple , had poor sucking and swallowing since birth , referred to cardiologist for consultation and echocardiography was done and complex heart disease was found (sever subaortic membranous stenosis mild aortic regure PDA) , he has younger brother with hypoplasic kidney and older normal sister , the child when referred to me At the age 0f 2.5 years his length is 82 cm at (below 3rd centile) , OFC 41 cm (below 3rd centile)and he had :Microcephaly , Inverted V thick upper lip, Micrognathia , low set ears without any malformations , abnormally placed , long , curved thumbs , bilateral undescended testis , rocker botton feet with big toe long and curved , sever subaorticmembraneous stenosis , mild aortic regurge , patent ductus arteriosus and hort stature

Figre 1. abnormally placed , long , curved thumbs

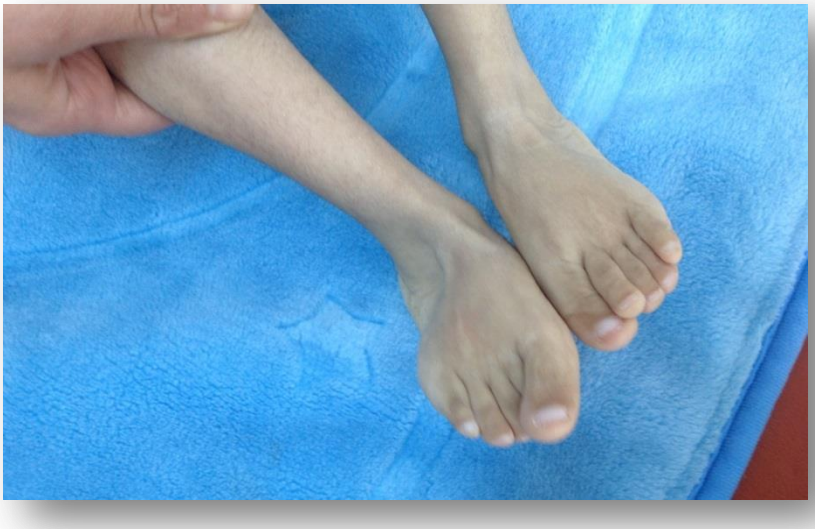
Figre 2. rocker botton feet



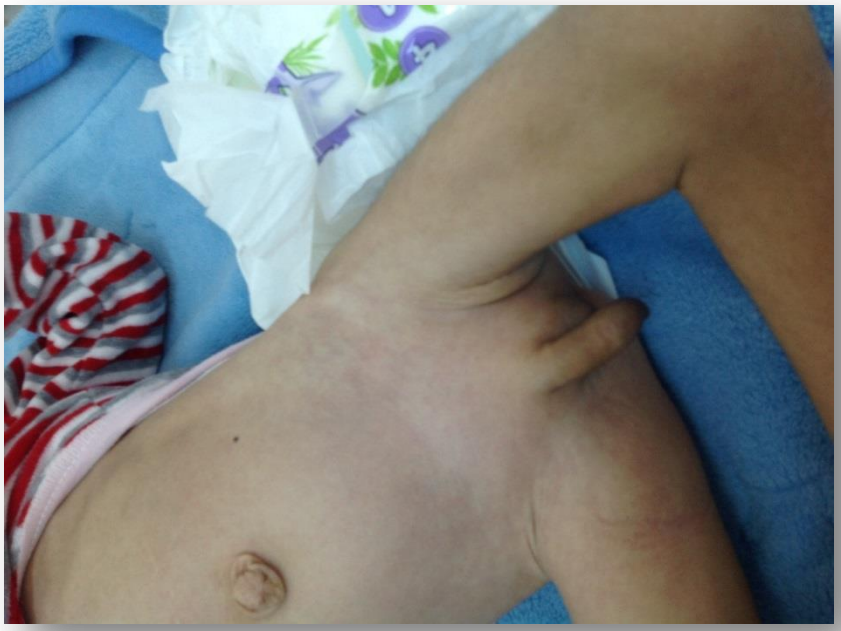
Figre 3. Inverted V thick upper lip, Micrognathia



Figre 4.



Figre 4. Bilateral undescended testis



Investigation done and it was normal , serum sodium , potassium , calcium , thyroid functions , rubella –toxoplasma-cytomegalovirus tests , aminoacid levels organic acids in urine all are normal .

MR : shows dilatation of subarachnoid space and slight dilatation of lateral ventricls as well as Harison sulci indicating brain atrophy no evidence of demyelinating disorder .

The technique used to test the defective genome are microarray-based compared genomic hybridization , Oligo microarray platform : Oligo microarray human genome 244K (Agilent Technologies).

The test shows Gain in the chromosome region Xq13.3 by a size of 185kb affecting the genes (UPRT , ZDHHC15) .

Discussion :

For the above imbalance , there is only one duplication (copy number variants CNVs) listed in the Database for Genomic Variants (http://projects.tcag.ca/variation update 02.11.2010) The imbalance affect UPRT and ZDHHC15 genes .

Mansouri and colleagues suggested that ZDHHC15 as strong candidate gene for non syndromic X Linked mental retardation (OMIM : MRX91; 300577) they reported a female case 29 years old with profound mental retardation , seizures , and a balanced translocation t(X;15)(Xq13.3;cen) .

The Database of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources (DEIPHER v.5.0) lists one male case of overlapping imbalance (Gain) of similar size who have feeding difficulty , mental retardation / developmental delay and short stature , the imbalance inherited from normal parents .

The ISCA (international Standards for cytogenomic Array Consortium) Database listed the overlapping imbalance of ZDHHC15 of same size in the categories of benign and uncertain significance .

Interestingly my patient shares the heart abnormality , mental retardation , short stature with the patients listed above . So far UPRT and ZDHHC15 are not associated with heart disease , however ZDHHC15 transcript in addition to the brain and other organs also expressed in the heart .

Conclusion:

So may be we are facing a case where these genes causing syndromic mental retadation.

The question is : is this case is a syndrome which collects all of the above mentioned cases reported in one syndrome or it is new syndrome not reported before ?

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