Uniparental disomy of chromosome 12 which leads to a phenylketonuria case

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Introduction

Phenylketonuria (PKU) is one of the most prevalent amino acid metabolism disorders caused by deficiencies in the PAH gene located on chromosome 12(12q23.2). Affected persons are born from carrier parents with autosomal recessive pattern of inheritance.

Material and Method

A 9 -year -old boy who was identified to be affected through newborns screening for PKU referred to our laboratory. Sanger sequencing of PAH gene was performed by extracted DNA from peripheral blood sample.

Linked STRs and VNTR analysis were done in parallel. MLPA (multiplex ligation-dependent probe amplification) technique was utilized to detect probable deletion in PAH gene. Performance of DNA fingerprinting by evaluation of 16 different DNA markers for the child and his mother.

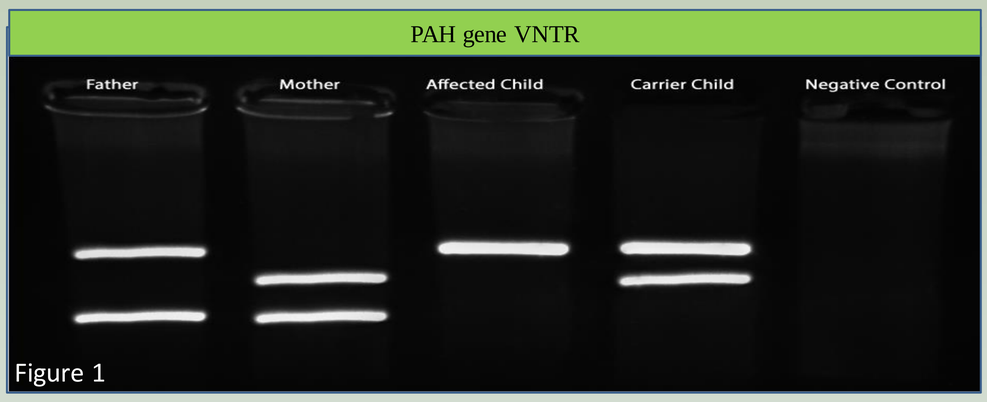

Figure 1

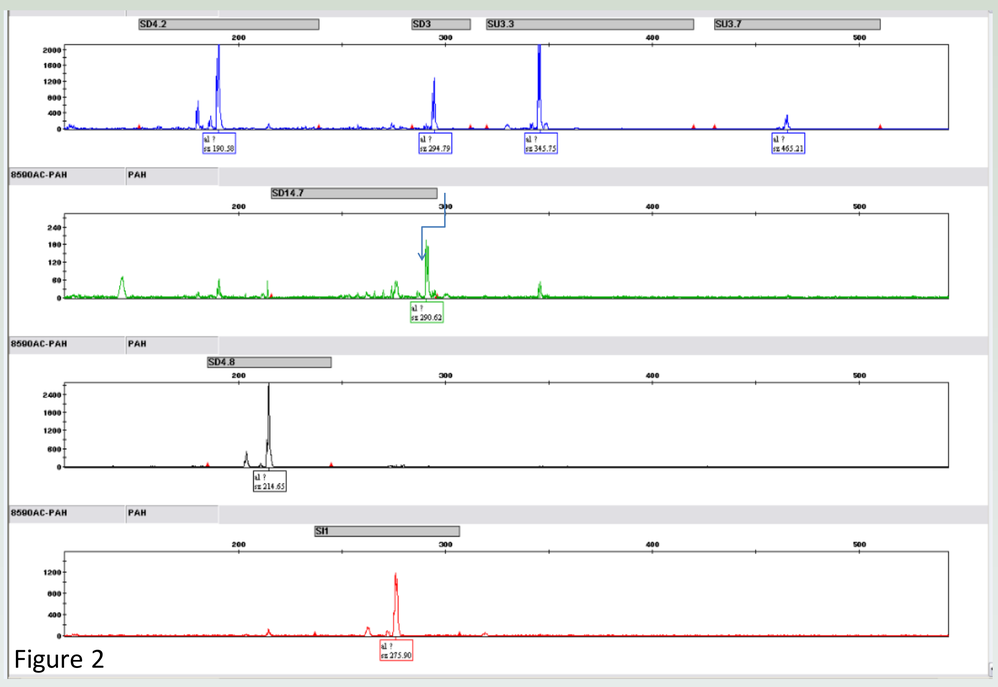

Figure 2

PAH gene Haplotype

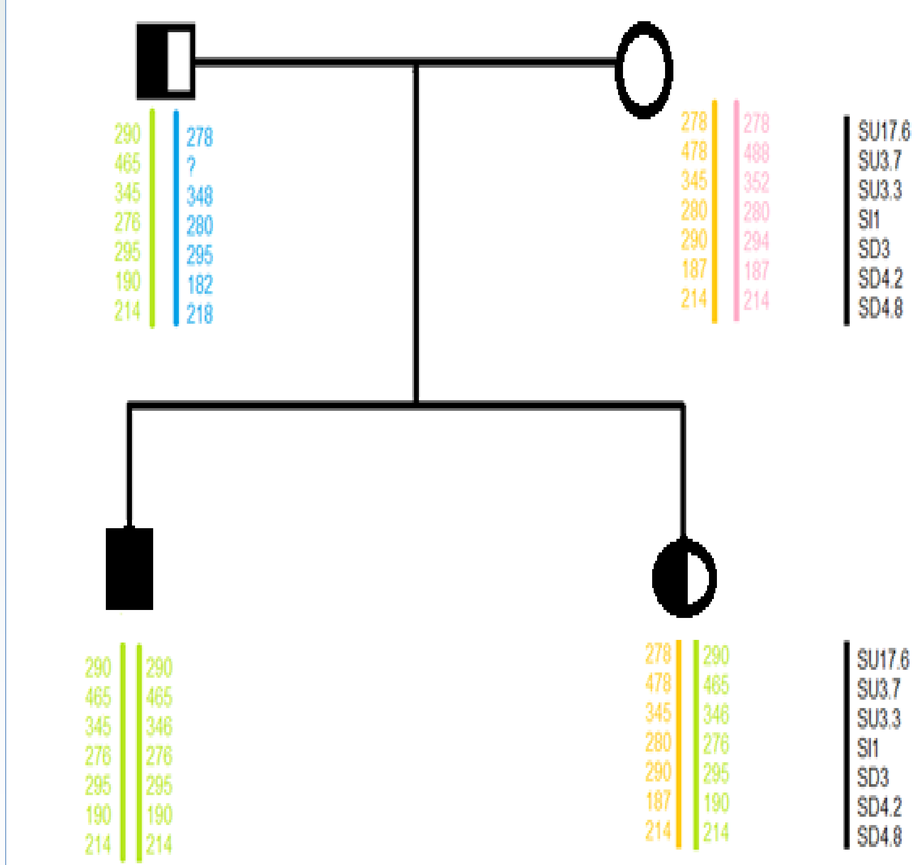

Figure 3

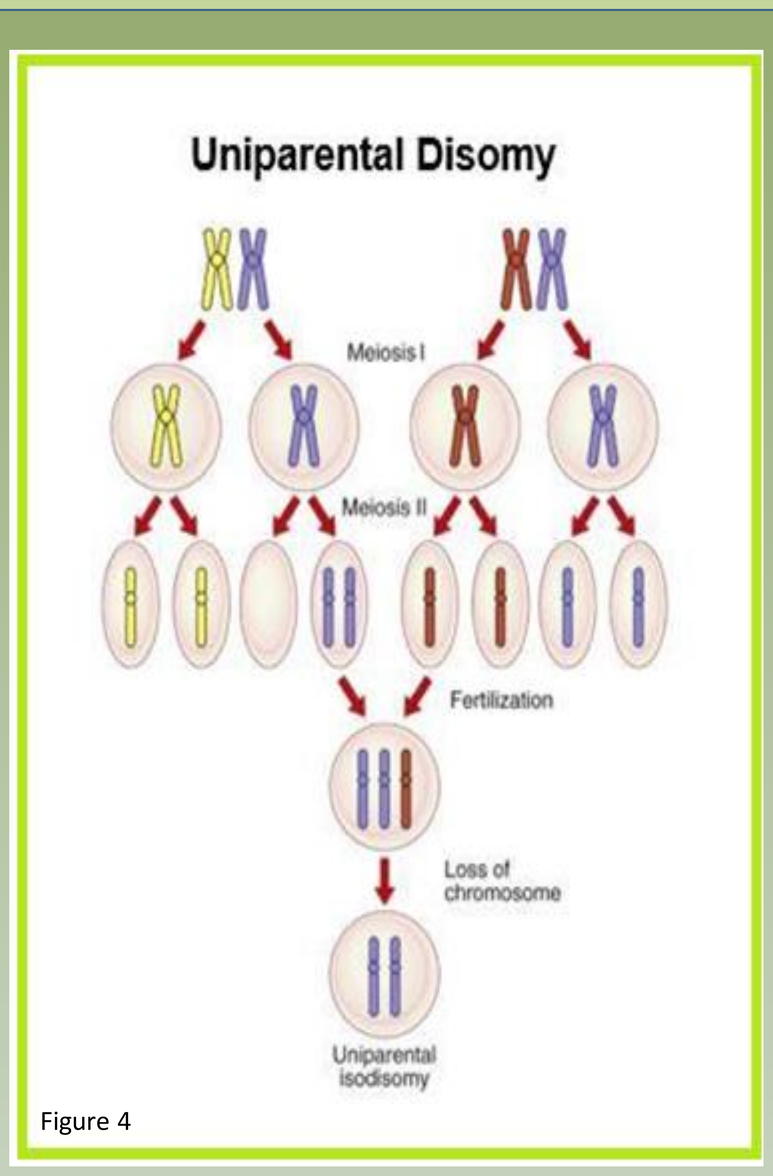

Figure 4

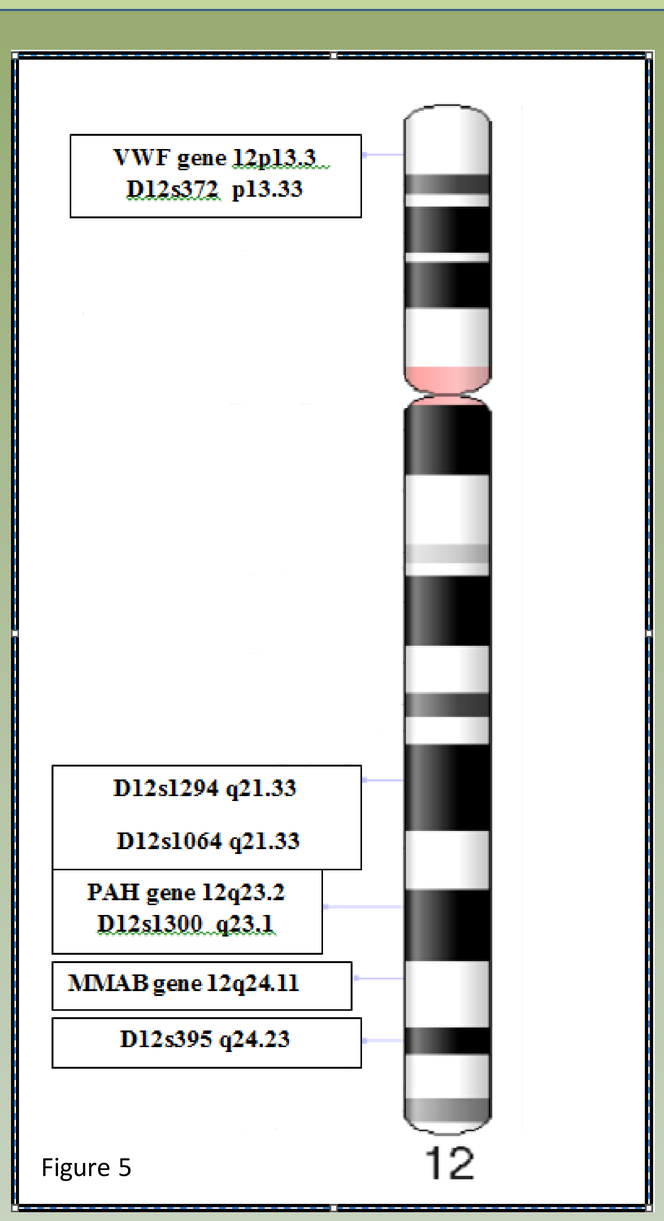

Figure 5

Result

PAH: c.782G>A mutation was detected in patient. His father was heterozygote for the same mutation while surprisingly his mother was normal (Fig 6). DNA fingerprinting confirmed maternity with over 99.9% certainty. MLPA results did not show any deletion for the affected child and also his mother. No common haplotype in STR analysis and same number of repeats in VNTR was found for the affected child and his mother (Fig 1-3). The probability of uniparental disomy (Fig 4) of chromosome 12 was verified observing homozygous haplotype in STR markers located on this chromosome (Fig 5).

Markers on chromosome 12	Father	Mother	Affected child	Carrier child
D12SI1VWF	196/203	196/203	196/196	196/203
D12SI2VWF	286/290	286/313	290/290	286/286
D12s372	345/345	341/341	345/345	341/345
D12s1294	239/243	251/268	243/243	243/268
D12s1064	374/389	374/389	389/389	374/389
D12PAHSU17.6	278/290	278/278	290/290	278/290
D12PAHSU3.7	?/465	478/488	465/465	465/478
D12PAHSU3.3	345/348	345/352	345/345	345/345
D12PAHSI1	276/280	280/280	276/276	276/280
D12PAHSD3	295/295	290/294	295/295	290/295
D12PAHSD4.2	182/190	187/187	190/190	187/190
D12PAHSD4.8	214/218	214/214	214/214	214/214
D12s1300	204/212	200/200	212/212	200/212
D12MMABSU20.45	301/305	305/305	301/301	301/305
D12MMABSU19.8	238/238	238/250	238/238	238/238
D12MMABSD0.1	204/204	224/220	204/204	204/224
D12MMABSD0.59	220/228	228/240	220/220	220/240
D12s395	287/287	303/303	287/287	287/303

Conclusion

Paternal uniparental isodisomy of chromosome 12 is a rare chromosomal anomaly. This study highlighted the importance of STRs and VNTRs analysis along with mutation detection to specify necessity of prenatal diagnosis.

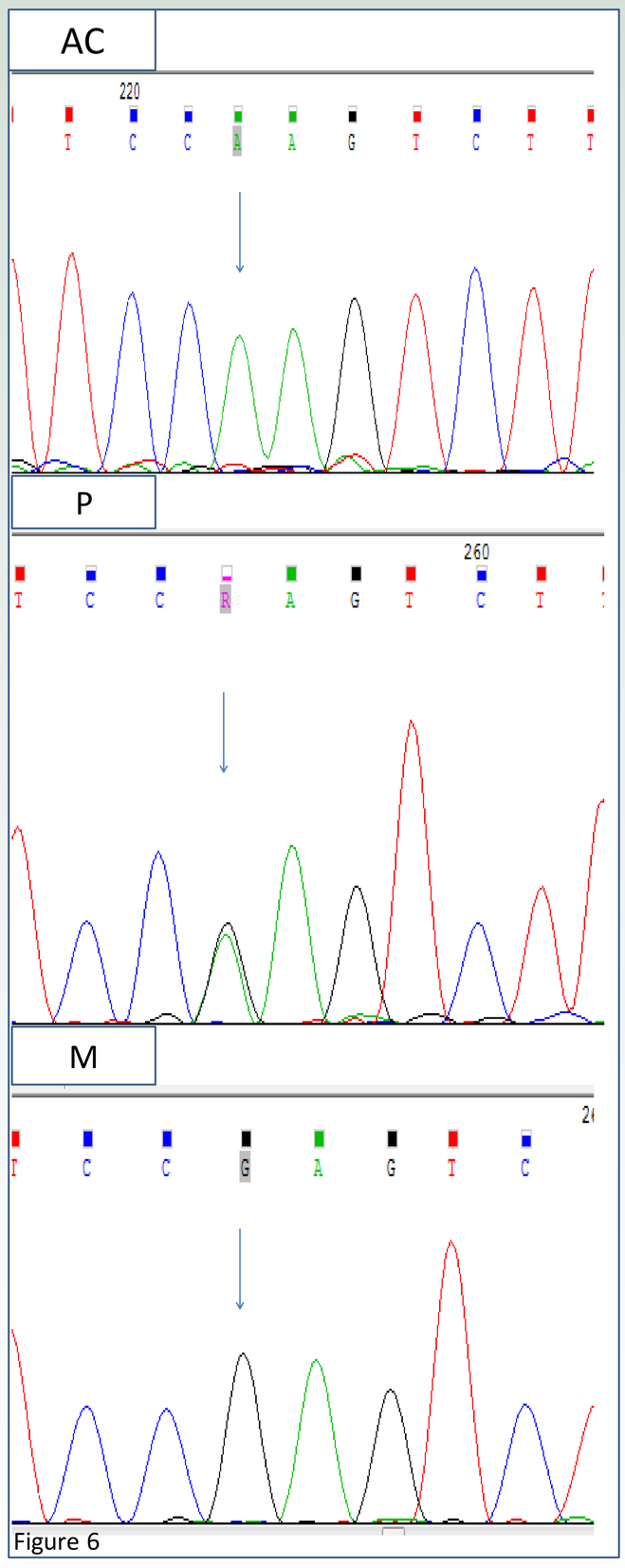

Figure 6