MATERNAL UNIPARENTAL ISODISOMY AT CHROMOSOME 6 DISCOVERED IN PARENTAGE TESTING CASE

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An extremely rare inheritance pattern was demonstrated in what began as an apparently routine paternity test. Samples from the mother, child and alleged father were analyzed using PowerPlex® 16 and CS7, which comprise the initial testing battery used at LabCorp. This testing revealed genetic inconsistencies between the child and the alleged father at loci F13A01 and D5S818. Additional testing using PowerPlex® ESX failed to reveal any additional inconsistencies; however, HLA-A and B were also typed, revealing a third inconsistency. The child was homozygous for the maternal type at HLA-A and B, F13A01 and D5S818. HLA-A and B and F13A01 are positioned on chromosome 6. Testing of PowerPlex® Fusion and PowerPlex® LC5, which contains a third chromosome 6 locus, D6S1043, yielded a fourth inconsistency, this at D6S1043. The child was again homozygous for the maternal type at this locus. (PowerPlex® is a registered trademark of the Promega Corporation, Madison, WI, USA.) Based on the finding of three chromosome 6 inconsistencies with the child expressing homozygous maternal types, we advised the client to pursue genetic testing to confirm maternal uniparental isodisomy in this child.

Clinical genetics evaluation revealed the 10-month-old female had a history of premature birth (32 weeks gestation) and failure to thrive with weight and length less than the 3rd percentile. Her physical exam was otherwise unremarkable and developmental milestones were normal when corrected for prematurity. Due to concern for uniparental disomy of chromosome 6, chromosomal microarray testing was performed using the Agilent 4x180k aCGH+SNP array. This revealed two extended contiguous regions of homozygosity spanning the entire short and long arms of chromosome 6, which is a sign of isodisomy UPD.

Based on this confirmed diagnosis, the three chromosome 6 genetic inconsistencies were attributed to this condition and not considered in the interpretation of the results. The paternity case was reported as non-exclusionary with the D5S818 inconsistency calculated as a mutation following the method of Brenner (www.DNA-View.com) and incorporated into the combined likelihood ratio.