CASE STUDY #8

CASE SERIES

firststep Dx BUCCAL PLUS

For individuals with autism and other disorders of childhood development

BENEFIT OF HIGH RESOLUTION CHROMOSOMAL MICROARRAY ANALYSIS (CMA)

Patient and Clinical Presentation

- 15-year-old girl with intellectual disability and multiple congenital anomalies
- Previous oligonucleotide microarray results (2009): deletion of 12p13.3-p13.1 that includes 71 genes

FirstStep^{Dx} Results

- Deletion of 12p13.31-p13.1 that is 6.2 Mb in size and includes 180 genes
- Deletion of 7p13 that is 73 kb in size and includes the *CCM2* gene
  - Consistent with autosomal dominant cerebral cavernous malformation (CCM) disorder
  - CCM is associated with risk for hemorrhagic stroke and seizures

Case Study Summary

- The higher resolution of FirstStep^{Dx} provided a more accurate deletion size:
  - gene content was more accurately established in order to understand the rare 12p13.31-p13.1 deletion
- Identified the deletion of *CCM2* that was not identified on the previous microarray
- The physician can now implement medical management changes and inform the family of associated health risks including:
  - monitoring and treatment for seizures
  - annual imaging (brain gradient echo or susceptibility – weighted imaging) for monitoring of hemorrhage
  - avoidance of medications that increase the risk for hemorrhage (heparin, NSAIDs, aspirin, *etc*)
  - Testing of at-risk family members is recommended for determination of hemorrhage and stroke risk

Patient and Clinical Presentation

- 6-year-old boy with intellectual disability, multiple congenital anomalies, and seizure disorder
- Previous karyotype results: deletion of 4pter-4p15.31, which is consistent with Wolf-Hirschhorn syndrome

FirstStep^{Dx} Results

- Terminal deletion of 4pter-4p15.31 that is 18 Mb in size and includes 270 genes
- Adjacent duplication of 4p15.31 that is 579 kb in size
- The co-occuring deletion and duplication signify a very rare mechanism that is nearly always new in the child; this alleviates concern for parent testing

Case Study Summary

- Previous karyotype and laboratory report were relatively uninformative and only stated that a phenotype of Wolf-Hirschhorn syndrome was expected
- Knowing the gene content can help inform future medical risks
- Karyotype analysis did not allow for identification of the adjacent duplication because of limited resolution
- After karyotype analysis, follow up parental testing was recommended to exclude a parental balanced translocation
  - However, because of the further information gained from CMA, parental testing is now known to not be necessary

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